Current Psychiatry Reports (2021) 23: 25
https://doi.org/10.1007/s11920-021-01237-9

PSYCHIATRY IN PRIMARY CARE (BN GAYNES, SECTION EDITOR)

Neuropsychiatric Complications of COVID-19

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Accepted: 23 February 2021 / Published online: 16 March 2021

Abstract

Purpose of Review To describe the presentation, etiologies, and suggested management of post-acute COVID-19 neuropsychiatric symptoms.

Recent Findings Over 30% of patients hospitalized with COVID-19 may exhibit cognitive impairment, depression, and anxiety that persist for months after discharge. These symptoms are even more common in patients who required intensive care for severe effects of the virus. In addition to the pandemic-related psychological stress, multiple biological mechanisms have been proposed to understand the neuropsychiatric symptoms observed with COVID-19. Given limited research regarding effective interventions, we recommend pharmacologic and behavioral strategies with established evidence in other medically-ill populations.

Summary Long-term, neuropsychiatric complications of COVID-19 are common and consequential. Because these are likely to co-occur with other medical problems, patients recovering from COVID-19 are best managed in clinics with highly coordinated care across disciplines and medical specialties. Future research is needed to inform appropriate interventions.

Keywords Neuropsychiatric · Neurocognitive · Mental health · COVID-19 · Post-COVID-19 · SARS-CoV-2

Introduction

The scope, magnitude, and speed of the COVID-19 pandemic have been staggering and continue to rapidly evolve. To date, more than 80 million people have been infected with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) worldwide and at least 1.7 million have died [1]. Consequently, the full impact of this global infectious disease catastrophe is not likely to be appreciated for years to come. Early in the pandemic, public and scientific attentions were focused on the acute morbidity and mortality associated with COVID-19. However, several months into the pandemic, reports emerged describing persistent physical and neuropsychiatric sequelae in the aftermath of SARS-CoV-2 infection.

Whereas residual or persistent neuropsychiatric symptoms are not uncommon in critically ill survivors following admission to an intensive care unit (ICU) [2••], post-COVID-19 follow-up studies reveal that mild and even asymptomatic infection may lead to cognitive impairment, delirium, extreme fatigue, and clinically relevant mood symptoms [3, 4]. These descriptions mirror historical reports of post-pandemic neuropsychiatric complications such as encephalitis lethargica [5, 6], as well as descriptions of sequalae from other respiratory illness pandemics [7].

Recent evidence suggests that psychiatric illness is both a risk factor for and consequence of COVID-19. In a large electronic health record (EHR)-based cohort study of over 60,000 COVID-19 cases, a documented psychiatric diagnosis in the prior year was associated with a 65% increased risk of COVID-19 when compared with a matched cohort of patients with physical health issues without psychiatric diagnoses [8••]. Furthermore, over the 3 months following COVID-19 diagnosis, 18% of patients were diagnosed with a psychiatric diagnosis, with nearly 6% representing a new diagnosis (e.g., dementia, anxiety, and insomnia). Similar increases in incident psychiatric diagnoses among US adults with COVID-19 were reported by Czeisler et al. [9•], who also noted that specific populations were disproportionally affected (e.g.,

This article is part of the Topical Collection on *Psychiatry in Primary Care*

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young adults, Hispanic and Black patients, essential workers, unpaid caregivers, and those with pre-existing psychiatric conditions).

This annotated review begins with an illustrative case and then summarizes the rapidly growing evidence base for persistent neuropsychiatric complications of COVID-19. Our aims are to describe post-acute COVID-19 neuropsychiatric complications, potential etiologies of these persistent central nervous system (CNS) symptoms, and provide recommendations for the evaluation and psychiatric management of recovering COVID-19 patients who present to primary care settings.

Case Example

A 62-year-old man with history of osteoarthritis, but otherwise no formal medical or psychiatric history, presented to the emergency department (ED) with a chief complaint of hip pain. In the ED, physical and mental status exam were relatively unremarkable. Specifically, the patient was afebrile, lung exam was normal, and his mental status was not grossly altered. Imaging and laboratory workup revealed an acute kidney injury (AKI, serum creatinine 1.7 mg/dL), which prompted hospital admission. COVID-19 testing was performed as part of his admission lab work and returned positive. Family noted that one of the patient's sons had recently been exposed to COVID-19 at work and later tested positive. They also reported that the patient had been "confused" in the days preceding his presentation. Within hours of admission to the COVID-19 unit, the patient's creatinine normalized, but he quickly became belligerent, refusing interventions, and demanding to be discharged. The inpatient consulting psychiatrist diagnosed the patient with acute delirium and, based on history obtained from his family, a pre-existing mild neurocognitive disorder. Risperidone 0.5 mg nightly was recommended for agitation, which gradually improved over his 5-day hospitalization. At time of discharge, the patient was connected with follow-up in a post-COVID clinic for ongoing management of his lingering neuropsychiatric symptoms, potentially precipitated by SARS-CoV-2 infection.

Etiologies of Neuropsychiatric Symptoms

SARS-CoV-2 is a positive sensed, single-stranded, enveloped RNA virus with a crown-like morphology [10]. It is a human coronavirus (HCoV) in the beta genera of the *coronaviridae* family, along with severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1), Middle East respiratory syndrome related coronavirus (MERS-CoV), HCoV-OC43, and HCoV-KHU1 [10]. During cell entry, SARS-CoV-2 binds angiotensin converting-enzyme 2 (ACE2) on the target cell surface to facilitate fusion of viral and host membranes [11, 12]. ACE2 exists on cellular membranes in the lungs, gastrointestinal (GI) track, myocardium, renal tubules, and bladder [12]. Correspondingly, coronaviruses traditionally are considered pulmonary diseases, often with accompanying GI symptoms [11].

However, COVID-19 patients have demonstrated a high prevalence of neuropsychiatric symptoms [8••]. Of note, both SARS-CoV-1 and MERS-CoV have demonstrated the ability to infect the CNS, especially the brainstem [13]. Our knowledge of SARS-CoV-1 and MERS-CoV have contributed to four proposed mechanisms of CNS involvement by SARS-CoV-2.

First, neuropsychiatric symptoms of COVID-19 are most commonly due to a myriad of biological and environmental factors, including electrolyte abnormalities, liver inflammation, impaired renal function, impaired oxygenation [14], hyperinflammation [12], and isolation due to public health concerns, which lead to a multifactorial delirium. Older individuals are at greatest risk for delirium due to these multiple contributors, and may experience both acute and long-term neuropsychiatric effects following an episode of delirium. [15, 16].

Second, viral-induced immune reaction and autoimmunity (during or after acute infection) provide another route by which SARS-CoV-2 can impact CNS function. While the virus is rarely found in the cerebrospinal fluid (CSF), a viral-induced inflammatory response can lead to blood brain barrier (BBB) dysfunction, resulting in immune cell infiltration and CNS tissue damage [12]. Indeed, there have been reports of limbic encephalitis during SARS-CoV-2 infection [17], as well as brainstem involvement [18].

Third, SARS-CoV-2-induced coagulopathy has resulted in a wide variety of organ failure. Viral invasion of vascular endothelium leading to activated thrombotic and inflammatory cascades in the midst of a hypercoagulable state can lead to cerebrovascular events [12]. Stroke is the most common neurological finding on imaging of hospitalized patients for SARS-CoV-2 [19]. Stroke can even be a presenting symptom, though is more typically part of multi-organ involvement [20]. Furthermore, stroke itself is a risk factor for depression, and COVID-19 patients with strokes are at significantly increased risk for poor outcomes [21].

Finally, direct viral invasion of the CNS has been demonstrated, though this insult appears to be uncommon. A few reports have identified the virus in the CNS, but this is rare, even among patients who are severely symptomatic [22, 23]. Due to the well documented and prevalent loss of taste and smell in infected patients, direct CNS invasion by SARS-CoV-2 through olfactory axonal migration was proposed. However, subsequent work has shown that it is actually olfactory epithelial cells, which provide metabolic support for the olfactory sensory neurons, rather than the neurons themselves that are most likely involved [24, 25]. Therefore, direct SARS-CoV-2 invasion of the CNS more likely occurs at the blood brain barrier (BBB) via (1) transcellular migration (through

host endothelial cells); (2) paracellular migration (through tight junctions); and (3) an immune system "trojan horse" cell passing through the BBB [12].

Neurocognitive Disorders

There are few data regarding the long-term cognitive consequences of COVID-19. One study of 279 patients hospitalized with COVID-19 found that 34% reported memory loss and 28% described impaired concentration approximately 3 months after discharge [26]. Similar findings have been observed following infection with other coronaviruses, in which 20% reported cognitive deficits months to years after initial infection [7]. In Taquet et al's large EHR study, new onset dementia following hospitalization for COVID-19 was 2–3 times more common than what was observed after hospitalization for other medical events [8••].

In more severe cases of COVID-19, long-term cognitive deficits are likely the sequelae of delirium experienced during the acute phases of illness. Particularly in older patients, as in our illustrative case, delirium is one of the most common symptoms in COVID-19 patients presenting to the ED, and can be the only or primary symptom of SARS-CoV-2 infection [15]. Delirium occurs in at least 30% of patients hospitalized with COVID-19 [27•, 28•] and is substantially more common in those requiring ICU admission [29••]. The implications of delirium on long-term outcomes in these patients can be gleaned from the existing ICU literature. For example, a seminal study in adults with respiratory failure or shock admitted to the medical or surgical ICU identified global cognitive impairment (of equivalent severity to mild Alzheimer's disease) in 24% at 1 year after discharge [2]. Of interest, delirium has also been described in COVID-19 patients who do not experience severe medical complications (also as represented in our case) [27•, 28•], and there have been reports of "brain fog" among patients experiencing milder symptoms who were never hospitalized and presumably did not experience delirium [3, 4].

The potentially prolonged and disabling neurocognitive effects of COVID-19 are of great relevance to providers practicing in primary care and outpatient specialist settings where these patients will be managed following hospitalization. Patients experiencing adverse cognitive effects of COVID-19 would benefit from longitudinal cognitive assessment with brief screening instruments (e.g., Montreal Cognitive Assessment [30]) and self-report measures (e.g., Patient-Reported Outcomes Measurement Information System Cognitive Function [31]). Comorbidities that affect cognition (e.g., depression, anxiety, fatigue, sleep disturbance) and reversible causes (e.g., nutritional deficiencies, endocrinopathies, metabolic derangements) should be screened for and corrected as indicated. Patients with more pronounced symptoms may benefit from formal neuropsychological evaluation, which may in turn clarify the potential utility of cognitive rehabilitation or pharmacotherapies. To that end, there are no evidenced-based medications for neurocognitive problems due to COVID-19 (or similar conditions), but stimulants or medications used for the treatment of neurodegenerative disorders (e.g., acetylcholinesterase inhibitors, memantine) may be appropriate depending on patient comorbidities. Suggested management of neuropsychiatric symptoms following SARS-CoV-2 infection is presented in Table 1.

Mood and Anxiety Disorders

During and following COVID-19 infection, patients are at increased risk for depression and anxiety [32•]. At approximately 1 month following infection, 31–38% of patients report depressive symptoms [33, 34], 22–42% report anxiety symptoms [33, 34], and 20% report obsessive-compulsive symptoms [33]. Rates vary depending on the population studied, methods used to evaluate symptoms, and how long after infection symptoms are assessed [32•]. Most studies are cross-sectional and the majority are from China [32•]. One prospective study of patients in New York City described symptom severity during hospitalization and 14–17 days later. During hospitalization, 36% of participants reported anxiety and 29% reported depression; 14–17 days later, the prevalence of

Table 1 Common principles for management of neuropsychiatric complications of COVID-19 in the primary care setting

•Consider SARS-CoV-2 infection, in addition to pandemic-related stress, as a possible causative factor for new or worsening neuropsychiatric symptoms
•Recognize that patients with pre-existing psychiatric illness are more likely to become infected with SARS-CoV-2, experience neuropsychiatric consequences of COVID-19, and suffer worse medical outcomes
•Symptoms should be monitored longitudinally, at regular intervals, using validated rating scales and questionnaires to screen for depression, anxiety, post-traumatic stress, substance use, suicidality, and cognitive concerns
•Evidence-based behavioral and pharmacological therapies used to address symptoms in other medically ill populations can be used in the setting of an active or resolving SARS-CoV-2 infection, but providers should be aware of potential drug-drug interactions, particularly in light of COVID-19's pro-inflammatory, pro-thrombotic, and arrhythmogenic effects
•Given the multiple organ systems affected by COVID-19, we recommend highly coordinated care alongside other specialists (e.g., cardiology, nephrology, infectious disease, pulmonology, neurology, rehabilitation medicine)
•Telehealth represents an opportunity to expand access to mental health care while mitigating the spread of the virus; however, providers should be mindful of the limited research regarding the efficacy of telepsychiatry for certain populations (e.g., psychotic disorders) and develop plans for necessary face-to-face care (e.g., administration of long-acting injectable medications, methadone treatment programs)

anxiety and depression had decreased (9% and 20%, respectively), but acute stress symptoms emerged in 25% [35•].

While depressive and anxiety *symptoms* are more common than formal mood or anxiety *diagnoses* in COVID-19 survivors, a not insignificant proportion of patients meet diagnostic criteria for a psychiatric disorder. In the study by Taquet et al., a new or recurrent anxiety disorder was documented in 12.8% and depressive disorder in 9.9%. Severe COVID-19 disease was associated with higher rates of these diagnoses, but all patients with COVID-19 had higher rates of psychiatric diagnoses when compared to controls [8••]. Depressive and/or anxiety symptoms following COVID-19 are more likely in females [33, 36, 37] and those with infected family members [34, 36, 37], post-infection physical discomfort [34], severe infection [36], elevated inflammatory markers [33, 38], and prior psychiatric diagnoses [33].

Suicidal ideation is also elevated following COVID-19 diagnosis. In one study, 3.5% of respondents reported suicidality at 1 month following infection [33]. There have been numerous case reports of COVID-19 patients attempting to kill themselves during or prior to hospitalization [13, 39, 40]. Nonetheless, it remains prudent to withhold final judgment on the relationship between COVID-19 and suicide until definitive epidemiological studies can be completed [41].

There have been few interventional studies targeting anxiety and depression in COVID-19 patients. Progressive muscle relaxation training [42, 43] and an internet-based integrated intervention (including self-help with relaxation, mindfulness, self-compassion skills) [44] were both associated with lower depression and anxiety scale scores in patients admitted to Chinese hospitals. Due to the reported relationship between psychological resilience and lower anxiety and depression [45], psychotherapeutic approaches that enhance resilience would appear beneficial. To our knowledge, there are no well-defined pharmacologic guidelines for management of depression and anxiety following SARS-CoV-2 infection [46•]. However, the general approach to psychiatric symptom management in the medically ill can also be applied to this population. First, the goal is to avoid harm by considering the various organs that might have been compromised by the virus, and then either withhold medications, or adjust doses, accordingly. In many outpatients, hydroxyzine is a good first option for as needed anxiety management. If renal function is preserved, gabapentin, on a scheduled or as needed basis, can be efficacious for anxiety [46•]. Selective serotonin reuptake inhibitors (SSRIs) are generally well-tolerated options for depression and anxiety, though paroxetine is not recommended due to its short half-life, increased risk of drug-drug interactions, and withdrawal symptoms.

Post-Traumatic Stress Disorder

Post-traumatic stress disorder (PTSD) was one of the most common psychiatric disorders diagnosed among survivors of SARS and MERS, with a prevalence of nearly 40% at a 6-month post-discharge [47•]. Not surprisingly, the prevalence of PTSD among COVID-19 survivors is anticipated to be at least as high as with previous coronavirus outbreaks [7, 48, 49].

To date, the prevalence of PTSD among COVID-19 patients appears to range from 20 to 30%, while the prevalence of less strictly defined post-traumatic stress symptoms (PTSS) varies widely [50–53]. For example, in a study of more than 700 clinically stable, hospitalized COVID-19 patients in China, 96.2% reported significant PTSS associated with COVID-19 [51], where PTSS were observed in only 31% in a British cohort evaluated 4–8 weeks after discharge from a large university hospital [50]. By comparison, in a study of 64 Korean COVID-19 patients interviewed approximately 2.5 months following hospital discharge, 20.3% met criteria for PTSD [52]. And similarly, in a cohort of 185 Italian patients who had been hospitalized with COVID-19, 22.2% met criteria for PTSD at a 2-week post-discharge follow-up visit [53].

The most common risk factors identified to date for PTSD/PTSS following SARS-CoV-2 infection are younger age [50, 53], female gender [53], need for ICU-level care [50], and having a past psychiatric history [53]. Interestingly, in a study comparing patients with COVID-19 who were discharged from the ED to those who required inpatient hospitalization, being hospitalized was found to protect against PTSD [53]. Among patients admitted to the ICU, obesity increased risk for PTSD, but this association was not observed among patients admitted to general medical wards [50].

Of interest, many risk factors for COVID-19 are also risk factors for PTSD. Specifically, high rates of obesity, diabetes, metabolic syndrome, cardiovascular disease, and autoimmune disease are observed in patients with PTSD [54–56]. COVID-19 patients also have disproportionately high rates of medical comorbidities, including obesity, diabetes, chronic pulmonary and cardiac disease, as well as immune dysfunction [57–59]. Delirium and ICU-level care, both common complications of COVID-19 [16, 26, 60], are also risk factors for PTSD/PTSS, with approximately 20% of critical care survivors experiencing PTSS at 12-months after discharge [61].

To our knowledge, pharmacologic treatment specific to PTSD/PTSS related to COVID-19 has not been studied. However, as discussed in our recommendations for management of anxiety and depression, basic principles of treatment for PTSD in the medically ill can be applied, considering potential drug-drug interactions and possible organ dysfunction when selecting medications and doses. While evidence supports use of the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine and SSRIs for PTSD in medically ill patients, potential risks should be carefully considered on a case-to-case basis [62]. Again, paroxetine is not recommended in medically ill patients due to its short half-life, anticholinergic side effect profile, and higher risk for drug-drug interactions. Several studies have shown a reduction in nightmare

frequency and intensity, as well as improvement in other PTSD symptoms, in patients prescribed the alpha-1 receptor blocker, prazosin [63]. There is some evidence that psychoeducational services provided online to COVID-19 survivors with PTSS have been helpful, though restricted Internet access and poor health status in many affected patients make in-person psychological interventions preferred when possible [51, 53]. Exposure-based cognitive behavioral therapy (CBT) has the highest level of evidence in those with PTSD, while supportive counseling, resilience training and psychological first aid have some evidence in treating PTSD [64]. Of note, psychological debriefing is *not* beneficial for PTSD, may cause harm, and should be avoided [64].

Psychotic Disorders

Beginning with the Spanish Influenza pandemic in 1918, higher rates of psychosis have been observed during many pandemics or epidemics [65]. Early in the COVID-19 pandemic, an observational study from China reported a 25% increased incidence of psychotic disorders [66]. This relationship has been largely attributed to the substantial psychosocial stress of the pandemic, but, as described previously, more direct mechanisms have also been suspected. Of interest, 0.9–4% of people exposed to viral infections develop psychosis [67], which is much higher than the incidence in the general population of 15.2 in 100,000 persons [68]. The ongoing CoroNerve surveillance study identified new-onset psychosis in 10 of the first 153 patients with acute COVID-19-related neuropsychiatric complications [28•]. There have been several cases from multiple countries detailing first-episode psychotic symptoms in COVID-19 patients [69–72]. There are insufficient data to clarify a typical presentation of COVID-19 psychosis, but notable disorganization and confusional features have been described [71, 72]. Compared to patients who develop psychosis precipitated by pandemic-related stress, these patients may be less likely to endorse paranoia or delusional content about COVID-19 [69]. They may also be less likely to have a family history of psychosis and more likely to present at an atypical age with subacute onset and relatively fast recovery following treatment with low-dose antipsychotics [71].

COVID-19 treatment may also precipitate psychosis. Specifically, chloroquine and hydroxychloroquine, which were previous mainstays of COVID-19 care, can cause hallucinations and other psychotic symptoms [73]. This risk is exacerbated in patients receiving combination therapy with lopinavir/ritonavir due to inhibition of CYP3A4 [73]. The administration of high-dose corticosteroids, which remains one of few effective treatments for severe COVID-19 infection, can cause psychotic symptoms, which has also been described specifically in the setting of treatment of viral illnesses [74, 75].

It is important to consider COVID-19 as a cause of new-onset psychotic symptoms [69]. Patients with COVID-19-related psychosis may exhibit elevations in CRP, ferritin, LDH, and D-Dimer, as well as either elevated or depressed WBC or platelets levels [71, 76, 77]. Low-dose antipsychotic medications may be helpful [67, 69, 71, 72], and patients hospitalized for severe COVID-19 may present to primary care settings on antipsychotics that were started during the acute period [71]. It is important to be mindful that antipsychotics increase risk of QT prolongation and Torsades de Pointes, particularly when used in conjunction with other QT prolonging medications (e.g., azithromycin). Additionally, COVID-19 infection itself is proarrhythmogenic [78]. Similarly, cerebrovascular complications are exceedingly common in severe COVID-19 [28•, 79], and exposure to antipsychotics may compound this risk [80]. While telehealth is an invaluable way of delivering care for patients during the pandemic, patients with psychotic disorders have lower utilization of mobile phones and technology compared to the general population [81] and there is a dearth of research regarding telepsychiatry interventions for patients with psychotic disorders [82].

Substance Use Disorders

When COVID-19 was declared a global pandemic, the USA was already in the midst of another public health crisis—the opioid epidemic. By June of 2020, the CDC reported that approximately one out of every 10 Americans had either started using illicit substances or increased the quantity and/or frequency of substance use because of the COVID-19 pandemic [9]. Not surprisingly, it is anticipated there will be more drug overdose deaths in 2020 than in any year prior.

Screening for substance use disorders (SUDs) will be an important part of follow-up care for COVID-19 survivors. Patients with SUDs are more susceptible to contracting COVID-19 due to the social and public restrictions implemented during the pandemic as compared to those without SUDs [83–89]. Across all patients with COVID-19, those with comorbid SUDs are more likely to require hospitalization (40.1% vs 30.1%) or die (9.6% vs 6.6%) [89••]. These adverse outcomes are disproportionately higher in African American patients [89••].

Both COVID-19 and illicit substances, especially opioids, can profoundly impair pulmonary function [90–92]. Patients with SUDs are more likely to have risk factors for severe COVID-19 disease (e.g., obesity, type-2 diabetes, cancer, cardiovascular diseases, and chronic liver, kidney, and lung disease) compared to those without SUDs [89••, 90, 91]. Additional biological mechanisms for worse outcomes in this vulnerable subset of COVID-19 patients include suppressed immune function due to complex opioid immune modulation, and drug interactions between the medications used to treat opioid use disorder and COVID-19 [92].

COVID-19 survivors need to be screened for SUDs and, when present, providers should encourage harm-reduction strategies if abstinence is not possible. Strategies to minimize harm include having a surplus of clean syringes and other supplies, not sharing syringes, pipes or other paraphernalia, having naloxone readily available, and having a back-up plan for how to get medical attention if emergency services are needed given possible increased response time due to the overwhelming volume on health care facilities [83, 87]. Medication-assisted treatment (MAT) with buprenorphine or methadone is first-line treatment for patients with opioid use disorder and measures should be taken to ensure patients have access to MAT [93, 94•]. Increased MAT waivers and alleviation of prescribing restrictions have facilitated access during the pandemic [86].

Post-COVID Clinical Infrastructure

Interdisciplinary post-COVID-19 clinics are currently being established in multiple medical centers [27•, 95]. At the University of North Carolina at Chapel Hill, a "COVID Recovery Clinic" was recently created. Since COVID-19 affects multiple organ systems and will require follow-up care across multiple specialties, this clinic aims to provide care in a systematic and carefully coordinated fashion. The purpose of the clinic is to support adult COVID-19 survivors who experience ongoing medical complications, residual symptoms, and/or loss of functional independence. The clinic integrates providers with complementary expertise to improve patient care and provide educational outreach to healthcare professionals and the community. The lead specialty for the clinic is Physical Medicine and Rehabilitation. The core clinic group is comprised of clinicians from internal medicine, psychiatry, neuropsychology, physical therapy, occupational health, and speech therapy. There is also a collaborative group that includes cardiology, nephrology, infectious disease, pulmonary, geriatrics, neurology, nutrition, and other specialists. Patients are screened over the telephone with a battery of validated instruments and, as indicated, evaluated in-person in clinic for further assessment and management. In addition to the goal of providing exceptional clinical care for patients affected by sequelae of COVID-19, the clinic has been designed to facilitate unique teaching and research opportunities.

Conclusion

Scientific understanding of the impact of COVID-19 continues to evolve rapidly. There are emerging data concerning for a wide range of neuropsychiatric sequelae following SARS-CoV-2 infection. Due to the complexity of COVID-19 and its treatment, affected patients may require longitudinal follow-up most appropriately delivered by multi-disciplinary teams. To accelerate medical knowledge regarding the long-term effects of COVID-19, it would be extremely fruitful for these post-COVID clinics to pool data into shared databases. Clinical trials are also urgently needed to clarify optimal treatment strategies for neuropsychiatric and other potentially long-term impacts of COVID-19.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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