Alpha Psychiatry

INVITED REVIEW
Alpha Psychiatry 2022;23(4):144-154
DOI: 10.5152/alphapsychiatry.2022.21783

Neuropsychiatric Consequences of COVID-19 Pandemic: A Synthetic Review from a Global Perspective

ABSTRACT

Some research suggests that distress, secondary to isolation and fear following COVID-19 infection, can negatively affect the long-term more than the COVID-19 infection itself. This narrative review aims to provide a global view on the neuropsychiatric consequences of COVID-19 that can be ascribed to several factors, ranging from the direct effect of infection, to the body's responses against the infection, or to the psychological sequelae of social isolation, unemployment, and fear for one's health and livelihood. Current findings show that the more severe the respiratory infection, the more likely are central nervous system (CNS) complications regarding the infection itself. The immune reactions to the infection may result in symptoms similar to chronic fatigue as well as neurocognitive deficits, which last long after the infection is gone. An increase in symptoms of depression, anxiety, and trauma-related stress may also follow upon economic fears and isolation from friends and family. The consequences of the pandemic are not limited to adults; children learning remotely and away from classmates and routine activities may develop adjustment disorders, acute stress disorder, and a variety of manifestations of grief. A summary of case reports suggests that COVID-19-related stress, economic recession, and political unrest increase the risk of suicidal behaviors and acts of violence. However, it is unknown whether manifestations of mental disorders result from social causes or whether CNS complications may be responsible.

Keywords: COVID-19, SARS-CoV-2, sleep, mental illness, psychiatry

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Introduction

Coronavirus infection (COVID-19) caused by the SARS-CoV-2 virus was first reported in China towards the end of 2019. The virus is transmitted by air and is highly infectious; hence, it quickly spread throughout the world.[1] As of January 8, 2022, there have been around 299 million cases of COVID-19 worldwide, with over 5.4 million deaths [https://covid19.who.int/]. Vast amounts of scientific reports have been published, e.g., 215 119 publications on PubMed as of January 8, 2022 on various aspects of the pandemic and its effects on life in every country on the globe.[2] It is impossible to cover all perspectives in one paper, especially because different communities were differently affected at different times, new strains of the virus continue to evolve, recommended therapies change, and currently, a variety of effective vaccines exist, although their availability and acceptance may differ.

The misinformation about the virus has spread more quickly than the sickness itself. Both healthcare providers and the public were subjected to contradictory claims about incubation periods, containment measures, and mitigation measures, such as hand washing, surface scrubbing, eye protection, social distancing, antigen and antibody testing, contact tracing, isolation periods, wearing masks, business closures, distance learning versus classroom teaching, the range of potential symptoms, the extent of asymptomatic spread, and the effectiveness of treatment.[3] There have been unsubstantiated claims regarding preventive measures and cures, post-infection immunity, and infectivity.[4] Over 100 different vaccines

have been or are being developed, tested, distributed, or are awaiting distribution. Some people are still not willing to take the vaccine.[5] Prioritization on who should get the vaccine first, and thereafter in which order, is difficult to determine practically and ethically. New strains of the virus evolve continuously, and the lethality of each strain is continuously in contention, which can be a source of anxiety in the vulnerable population.[4] The world was ill-prepared for this pandemic, and indeed, mistakes were made in handling the pandemic. According to the literature, this virus has had profound negative effects on daily life throughout the world. Even after the infection has run its course, the harm inflicted on people's livelihoods and mental health remains.[6]

Historically, during large pandemics, the risk posed to mental health has been greater than the risk to the physical health resulting from the infection itself.[7] Pandemics can precipitate new psychiatric symptoms in individuals with no prior history of psychiatric disorders and may worsen pre-existing mental illness in some. They may precipitate mental health problems in vulnerable caregivers, overworked health professionals, and those bereaved because of the epidemic. Fear of falling ill oneself or having a child or a parent succumb to the illness can be a major source of anxiety.[8] One psychological defense has been to blame specific persons or groups, institutions, or governments for spreading the virus, or for not doing enough to stop the virus or exaggerating the threat that it poses. Due to public health lockdowns, business closures are a common source of anger; mask-wearers attribute spread to non-mask wearers, and anti-Asian crime rates have soared in the USA, attributable to the virus having first emerged in China.[9] Some consider public health regulations to infringe on personal freedom. For others, protecting health and safety is an overriding priority, even when it destroys the economy and impairs the quality of life for most of the population. The much needed resilience and inventiveness are in scarce supply.

Neuropsychiatric morbidities have emerged from several sources. Some have been precipitated by fear, bereavement, social isolation, and financial loss,[10] and have taken various forms. They are expressed as panic attacks, depression, posttraumatic stress disorder, and somatic complaints. Prior psychiatric illness is often aggravated, and suicide rates have risen.[11] The social isolation of remote learning threatens children's mental health, while the elderly are afraid to step out of their homes.[12]

There are also biological reasons for neuropsychiatric symptoms; the SARS-CoV-2 virus infects the central nervous system (CNS), preferentially the hypothalamus, basal ganglia, and the prefrontal cortex. The virus produces structural brain changes such as the proliferation of oligodendrocytes and astrocytes. In addition, it alters neurotransmission by inducing inflammation, potentially resulting in delirium and cognitive decline.[13]

Aims of This Review

This narrative review addresses the mental health, neuropsychological, and neuropsychiatric sequelae of COVID-19. Using the currently available evidence, it attempts to answer 4 questions: (1) What are the neuropsychiatric manifestations of this virus? (2) Who is most at risk? (3) What preventive measures are needed? (4) What therapeutic measures are needed?

Review Method

Two authors, using PubMed/MEDLINE and Google Scholar, applied the following search terms to titles and abstracts: "Coronavirus" OR "COVID-19" OR "SARS-CoV-2" AND "stress" OR "bereavement" OR "fatigue" OR "anxiety" OR "psychiatry" OR "suicide" OR "mental health" OR "social isolation" OR "neuropsychiatry" OR "depression" OR "sleep" OR "minorities." Finally, all authors separately sifted through the extensive literature on these topics accumulated over the last 2 years and, by consensus, selected those papers that appeared best able to answer our questions. This review used the Synthesis Without Meta-analysis (SWiM) approach to ensure unambiguous reporting.[14]

MAIN POINTS

Preventive lessons for the next pandemic

- *Actively promote mental health throughout the world as soon as an epidemic emerges.*
- *Train mental health workers around the globe to ensure universal availability.*
- *Provide care and support to the most vulnerable.*
- *Pay attention to unique individual needs.*

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Received: December 4, 2021
Accepted: January 11, 2022

Cite this article as: Pandi-Perumal SR, Zaki NF, Qasim M, et al. Neuropsychiatric consequences of COVID-19 pandemic: A synthetic review from a global perspective. *Alpha Psychiatry*. 2022;23(4):144-154.

Reported Findings in the Literature

Neurological Impacts

Among other body organs, the COVID-19 infection also affects the brain. Around 36% of the patients from an early sample of 214 patients from Wuhan were found to exhibit neurological symptoms such as loss of taste and smell, headache, dizziness, muscular weakness and discomfort, cerebrovascular problems, and reduced awareness.[15] In the subgroup with severe respiratory disease (n = 88), 45% had neurological problems.[15] Encephalopathies were common among COVID-19 patients, and about one-fifth of patients in one study showed changes in consciousness that persisted for more than 24 hours.[16] One often sees encephalopathy after extubation, which could be a lingering effect of either mechanical ventilation or prolonged sedation. Encephalopathy normally recovers in a few days, although it can last for weeks or months and is frequently aggravated by subsequent bacterial infections. Pre-existing diagnoses such as dementia, subarachnoid hemorrhage, and epilepsy were found to increase the risk of neurocognitive effects. Treatment with sedation or mechanical ventilation and the subsequent occurrence of delirium considerably raise this risk, as do advanced age, immunocompromised state, and prior medical and psychiatric conditions.[17] Another cause of induced brain pathology is drug treatment. Dexamethasone, for instance, can produce short-term neuropsychiatric sequelae such as depression, hypomania, sleep disorders, cognitive deficits, psychosis, and delirium.[18] In addition, coagulopathy induced by the virus can lead to cerebrovascular accidents.[17] Altogether, a UK-wide surveillance study[19] reported that one-quarter of COVID-19 patients show some neurocognitive impairment.

CHRONIC FATIGUE SYMPTOMS

Of the millions who have been infected with SARS-CoV-2, a large percentage report ongoing dyspnea and exhaustion months after infection.[20] The terms "post-COVID syndrome" and "long-COVID" have been used to describe these pervasive phenomena.[21] Mental fatigue, poor concentration, myalgia, and headache are features of many viral infections, including COVID-19.[22] A study from China[23] reports that almost one-third of infected patients show myalgia and fatigue. Zhang et al[17] concluded from their study that three-quarters of patients report fatigue and that this is the most common of all the CNS-related symptoms. A meta-analysis[24] recently came to the conclusion that a significant percentage of patients experience fatigue and/or cognitive impairment after resolution of COVID-19 symptoms.

Anxiety and Depression

A meta-analysis[25] of 43 community-based studies on the prevalence of anxiety concluded that the prevalence of anxiety during the COVID-19 pandemic is 3 times higher compared to the pre-pandemic world. Similarly, a meta-analysis[26] of 29 studies reveals that anxiety and depressive symptoms among children and adolescents is twice that of pre-pandemic periods. COVID-19 survivors have shown a significant rate of emerging mental sequelae, with 55% of the group having a pathological score for at least one condition. Survivors are predicted to have a higher than usual prevalence of PTSD, severe depression, and anxiety, all of which are a high-burden non-communicable illnesses linked to years of incapacity.[27] A study of 1210 respondents in 194 cities in China reported that one-third suffered from moderate-to-severe anxiety, stress, and depression.[28] In this study, such symptoms were most pronounced in women and college students and were associated with the presence of coryza, myalgia, and dizziness.[28] According to a survey[29] conducted one month after the epidemic in Wuhan, the prevalence of post-traumatic stress disorder in a sample of 285 patients was 7%. Among students from a Chinese medical college, anxiety levels were highest among those whose family members had been infected.[30] Insufficient social support and a reduction in physical activity were linked to anxiety.[30] In the UK, lockdowns were associated with feelings of isolation from lack of connectedness with one's community.[31] Patients with pre-existing mood disorders reported increased distress and depression.[32] During the first lockdown in Italy, the prevalence of depressive symptoms and anxiety-related symptoms were reported as 25% and 23%, respectively.[33] Poor sleep and perceived stress were common in a sample of general population and healthcare workers in Saudi Arabia. The study further reported that distress was associated with recent changes in sleep habits, fear-related to coronavirus news, and lack of treatment for coronavirus.[34] A large study in Bahrain[35] also showed that the pandemic had a significant psychological impact on Bahrain's population, with almost one-third of the population experiencing some level of discomfort and anxiety symptoms.

Among frontline medical workers, symptoms of stress, anxiety, and depression were allegedly mediated via quality of sleep and availability of social support.[36-38] These were the same mediators reported by individuals self-isolating at home.[39,40] There is also evidence for another mediator, namely, coronaphobia or excessive fear of infection, as a source of anxiety.[41] Concerns about one's own health and the health of one's family cause worry and raise the risk of depression, anxiety, panic disorder, trauma-related illness, and obsessive-compulsive disorder.[42] On the other hand, denial of the seriousness of the pandemic, either due to conflicting media information or a personal belief system, may lead to overconfidence and dangerously reduced compliance with public health advisories.[43]

The overall pooled prevalence rate of anxiety symptoms is 46% in the general population, according to a recent systematic review and meta-analysis of 16 papers consisting of 25 779 participants in 8 countries.[37]

A systematic review of healthcare workers exposed to infected patients showed high levels of fear, psychological distress, anxiety, depression, posttraumatic stress disorder, and somatization, even among experienced and appropriately protected personnel.[44] In China, almost 50% of healthcare workers expressed anxiety and endorsed depression and related psychological problems.[45,46] Understandably, frontline workers were the most affected.[47] Shanafelt et al[48] listed the different foundations of anxiety in frontline professionals: exposure to infected patients, risk of conveying the virus to family members, restricted access to rapid testing when symptoms developed, and uncertainty, should they become ill, of the quality of care they would receive (see Figure 1).

It is suggested that viral infection may trigger bipolar disorders. The COVID-19 infection has been reported to trigger an initial manic episode where episodes of mania or hypomania can appear after a symptomatic COVID-19 infection, even in formerly healthy subjects.[49] In addition, a few case reports and case series have reported an association between COVID-19 and the appearance of mania and hypomania.[49-55] Risk factors for the development of mania and hypomania include psychosocial stress, increased inflammatory biomarkers, and

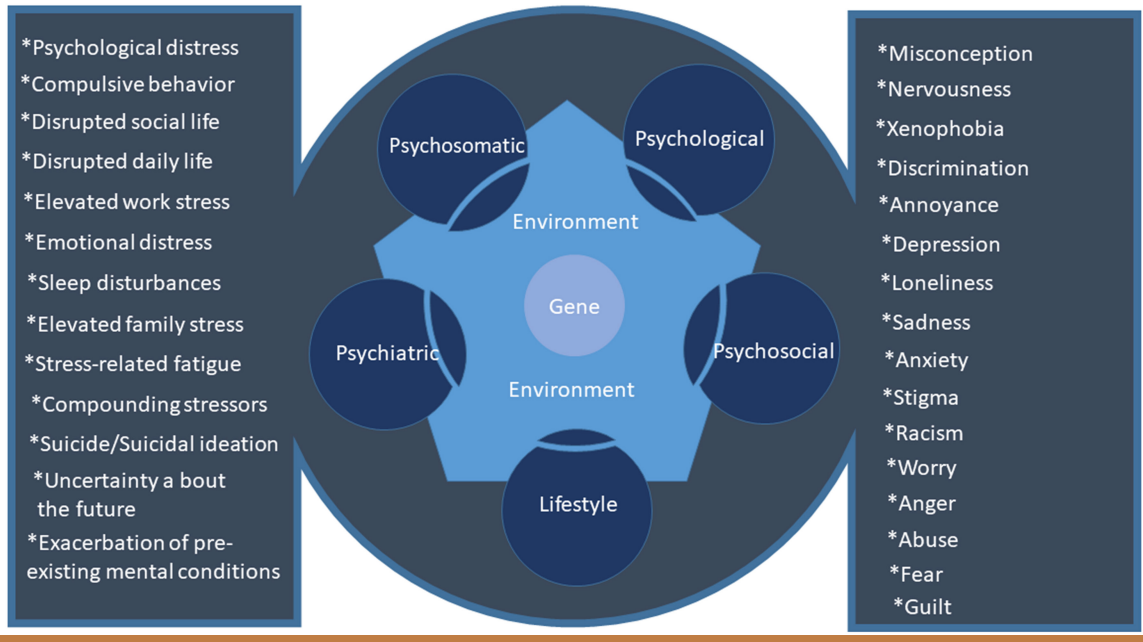

Figure 1. Psychological problems in response to the COVID-19 pandemic.

a history of bipolar affective disorder.[52] Nevertheless, the outcome of COVID-19-related treated mania and hypomania was found to be similar to that of naturally occurring mood disorder.[52]

Psychotic Disorders

There are reports of psychosis emerging during the pandemic.[56] A meta-analysis[57] of studies reporting psychiatric presentations of severe COVID-19 revealed that steroid-use related psychosis was observed in 0.7% of the patients. New-onset psychotic episodes, delusions, confusion, and hallucinations were observed in a single-center retrospective study.[58] Persons with pre-existing psychotic illness become more vulnerable to relapse either from stress and isolation from family and professional support or from difficulty maintaining their antipsychotic regimen. According to Yao et al.[59] individuals with serious mental disorders may unknowingly transmit the virus because of limited risk awareness and diminished regard for personal protection. For this reason, it has been suggested that this population be given priority for vaccination.[60]

Suicidal Risk

A meta-analysis[61] of 54 research studies revealed that during the pandemic, the rates of suicidal thoughts, suicide attempts, and self-harm were greater. Epidemics are associated with a heightened risk for suicide. Deaths by suicide increased both during the 2003 SARS epidemic in Hong Kong[62] as well as in Taiwan.[63] A cumulative synthesis of evidence in adolescents and young people during the first phase of the COVID-19-related lockdowns revealed that mental health issues such as stress, anxiety, and depression, and overwhelming academic distress, were associated with incidence of suicide.[12] Gunnel and colleagues suggested that epidemics increase the risk for suicide because of unemployment and the co-occurring financial crisis and domestic violence, and the rise in substance abuse due to isolation and quarantine[62] (Salahuddin et al 2021). The first published account of a COVID-19-related infanticide–suicide case identifies financial hardship and fear of infection as potential causes.[64,65] A review of case reports on COVID-19 suicides in Pakistan reveals that the economic downturn, fear of infection, stress, anxiety, isolation, and prejudice all play a role.[65] In India, the causal factors for the rise in suicide were found to be fear of infection, financial problems, loneliness, fear of being quarantined, and fear of social exclusion.[66] During the COVID-19 epidemic, many migrant laborers die not just due to suicide, but also due to road accidents or malnutrition.[67] Anxiety and insomnia have also been incriminated in the increased rate of suicide.[68]

Sleep Disturbances

The global pooled prevalence rate of various sleep difficulties among all groups was 35.7%, according to a recent systematic review and meta-analysis[36] of 44 publications comprising a total of 54 231 individuals from 13 countries. COVID-19 patients were found to be the most afflicted, with a combined incidence of 74.8%. Sleep disorders were found to affect 36.0% of health care professionals and 32.3% of the general population, respectively.

During the lockdown in Italy, the prevalence of sleep disturbances was 42%, with almost 20% reportedly showing significant insomnia.[33,69] According to multivariable meta-regression, both sexes had an increased prevalence of sleep issues during the lockdown period.[70] During the lockdown in the US, nearly half of the participants of one study reported suffering from insomnia.[68] According to the findings of one study including over 7000 participants, approximately one-fifth of the population suffered from poor sleep quality, with healthcare professionals having a higher frequency of insomnia than the general population.[71] Another study[72] reported that nearly one-third of healthcare workers suffered from poor sleep quality, again greatest among the frontline workers. Insomnia, depression, and anxiety were common in nurses and physicians working in medical care units.[16] Cellini et al[73] noted that sleep difficulties were associated with stress, anxiety, and depression symptoms. Lack of social support is a risk factor for sleeplessness,[41] which can be remedied by healthcare workers connecting patients with family members whenever possible.[74]

Sleep deprivation has been linked to a higher risk of contracting infectious diseases. Sleep difficulties have been referred to as "coronasomnia" or "COVID-somnia" during the current epidemic, a phrase used as a favored euphemism to improve communication.[75] Coronasomnia is caused by a combination of factors.[75] Variations in circadian timing caused by changes in light exposure during the lockdown, chronic stress (physical and emotional), the immediate and long-term effects of the immune response to the SARS-CoV-2 infection, and changes in sleep/wake cycles all contribute to short- and long-term sleep disorders. Even if individuals have recovered from the acute illness, sleep issues may occur later in the course of COVID-19. During lockdown conditions, this leads to alterations in sleep schedules and a deterioration in sleep quality and quantity. The lockdown disrupts people's normal routines in terms of physical exercise, eating habits, and technological device use. These factors appear to have influenced sleep habits, sleep quality, and sleep quantity.

Global societies have seen an increase in sleep disturbances (both in terms of quality and quantity) as well as typical sleep modifications. In the general population, studies have revealed a delay in bedtime and wake-time, as well as a reduction in overall sleep duration at night. Daytime napping also increased, maybe to compensate for the lack of nocturnal sleep (excessive daytime sleepiness). While lockdowns facilitate social isolation; the lack of social zeitgebers (time cues) during lockdown has been blamed for the delayed sleep and wake-up times. Other factors, such as chronotype (or circadian typology, which is a person's inclination to sleep at a given time during a 24-hour period) and age, were discovered to impact sleep pattern variation during lockdown. Changes in sleep patterns and schedules, however, were not uniform throughout the population (e.g., age, gender, race, and ethnicity), and certain traits appeared to increase the risk of the same.[76] Moving to later bedtime and rising hours, for example, was greatest in evening chronotypes and least in morning chronotypes; it was greater among younger persons than adults; and, finally, it was greater among women.[76] According to a self-administered cross-sectional study in Jordan, half of the participants (52%) reported sleeping for between 6 and 8 hours each day. At the same time, 43% of them need an hour to fall asleep. The majority of research participants reported either not waking up throughout the night (41%) or waking up once (41%). Approximately 88.9 % of individuals reported either waking up sooner or waking up slightly earlier than the targeted hour. Furthermore, the subjects reported an acceptable (47%) or slightly satisfactory (36%), sleep quality, and a satisfactory level of comfort when sleeping (48%).[77]

Healthcare workers are a group at particular risk from COVID-19. Figure 2 shows stresses on healthcare workers. So are ethnic minorities who live in crowded conditions and persons with pre-existing medical conditions, and those exposed to the virus by the nature of their employment. In general, the most economically and medically disadvantaged are most at risk. In addition, the elderly are at risk of exposure to the virus and the vulnerability brought on by age. Not surprisingly, these groups suffer from both high anxiety and disturbed sleep.[78] Sleep quality in an epidemic is important because it has been hypothesized that sleep debt impairs immune function and lowers resistance to infection.[79,80] Figure 3 shows healthcare professionals' psychological issues that result from the COVID-19 pandemic.

Child and Adolescent Mental Health

Although most children remain asymptomatic when infected by COVID-19, the pandemic exerts a significant psychosocial impact on children.[81] The distress experienced by parents is contagious and puts children's mental health at risk.[82,83] When schooling becomes remote, sleep and dietary habits change, and lack of social, recreational, and athletic activities imposes an important psychological burden on children.[84,85] Sprang and colleagues[83] found a higher frequency of adjustment disorder, acute stress disorder, and bereavement among solitary or confined children. An Italian study[86] found that social isolation, quarantine, and lockdown all had a harmful impact on children's mental health. A recent Saudi survey[87] reported that isolation during the COVID-19 pandemic quarantine increased psychological distress but not sleep quality (OR: 2.12 (95% CI: 1.10-4.08), $P = .03$).

Possible Mechanisms for Neuropsychiatric Symptoms

Neurobiological Mechanisms: Both infections and psychological stressors such as loneliness and grief activate immune inflammatory pathways and induce nitro-oxidative stress, which can damage the brain and negatively impact CNS functions.[63] The level of proinflammatory cytokines rises under these circumstances, and oxidative stress toxicity is increased, while simultaneously, there is a drop in antioxidant protection, all of which lead to depression, chronic fatigue, psychosomatic symptoms, anxiety syndromes including posttraumatic stress, suicidal ideation and behaviors, even psychosis, and, as described above, neurocognitive deficits.[88-91]

Socio-political Effects: As previously stated, those who are impoverished or have suffered bad health in the past, as well as migrants and ethnic or racial minorities, suffer disproportionately during an epidemic. They have limited access to healthcare and are more likely to work in jobs with high virus exposure or in jobs in which they are the first to be laid off during economic downturns. Because of cramped living conditions, many people are unable to isolate themselves. Migrants, particularly those without documentation who are afraid of being reported to the authorities, frequently postpone seeking care when they become symptomatic.[92]

Figure 4 shows the many concerns of migrant workers, which include anxiety, fear of getting or spreading infection, harassment, and physical safety problems. Those in precarious financial circumstances are afraid of losing their daily wages; they fear hunger, loss of shelter, and the possibility that basic survival necessities will not be met. These are persons without health insurance who fear for the future of themselves and their families. Internally displaced people or refugees in crowded camps are at increased risk of COVID-19,[93,94] and suffer most from movement restrictions, travel bans, lockdowns, and quarantines. Stigmatized community members, namely migrants, refugees, physically and mentally disabled people, homeless people, and racial minorities, are most affected.[95]

The number of incidents manifesting xenophobia has increased. People of Chinese heritage, for example, have faced increased prejudice and isolated acts of violence solely because the virus originated in China.[96] Travelers from outside one's own country are viewed with suspicion, and political subgroups blame each other for rising case rates and vaccine hesitancy.

Domestic Effects: The imposition of social distancing isolates individuals from their support networks. Staying home from work results in sustained contact among family members, which may, in some situations, and abetted by substance abuse and economic stress, lead to anger, aggression, and abuse of women, children, and

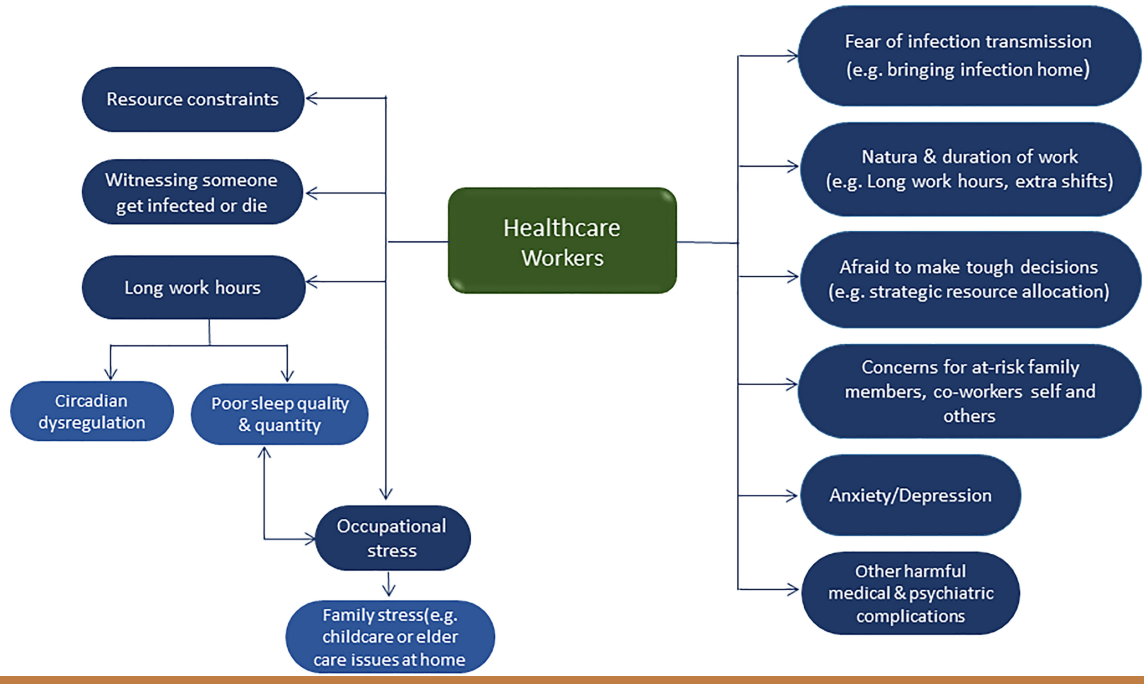

Figure 2. Stresses on healthcare workers.

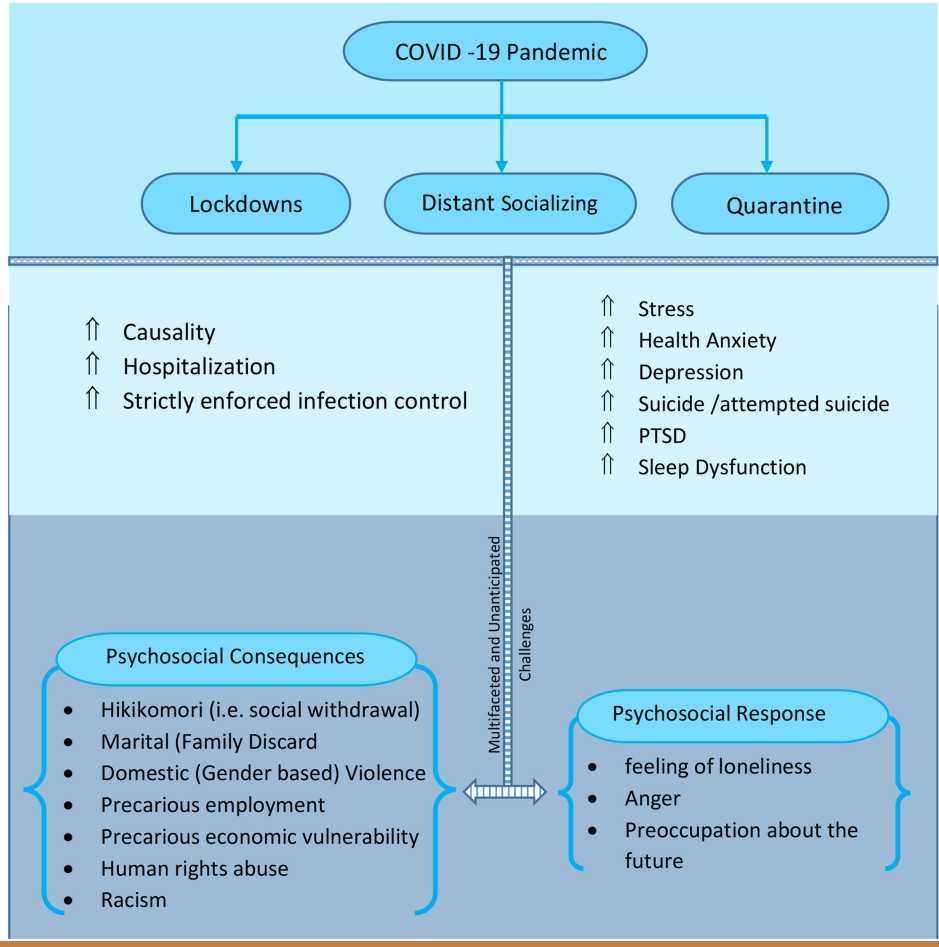

Figure 3. Healthcare professionals' psychological issues that result from the COVID-19 pandemic.

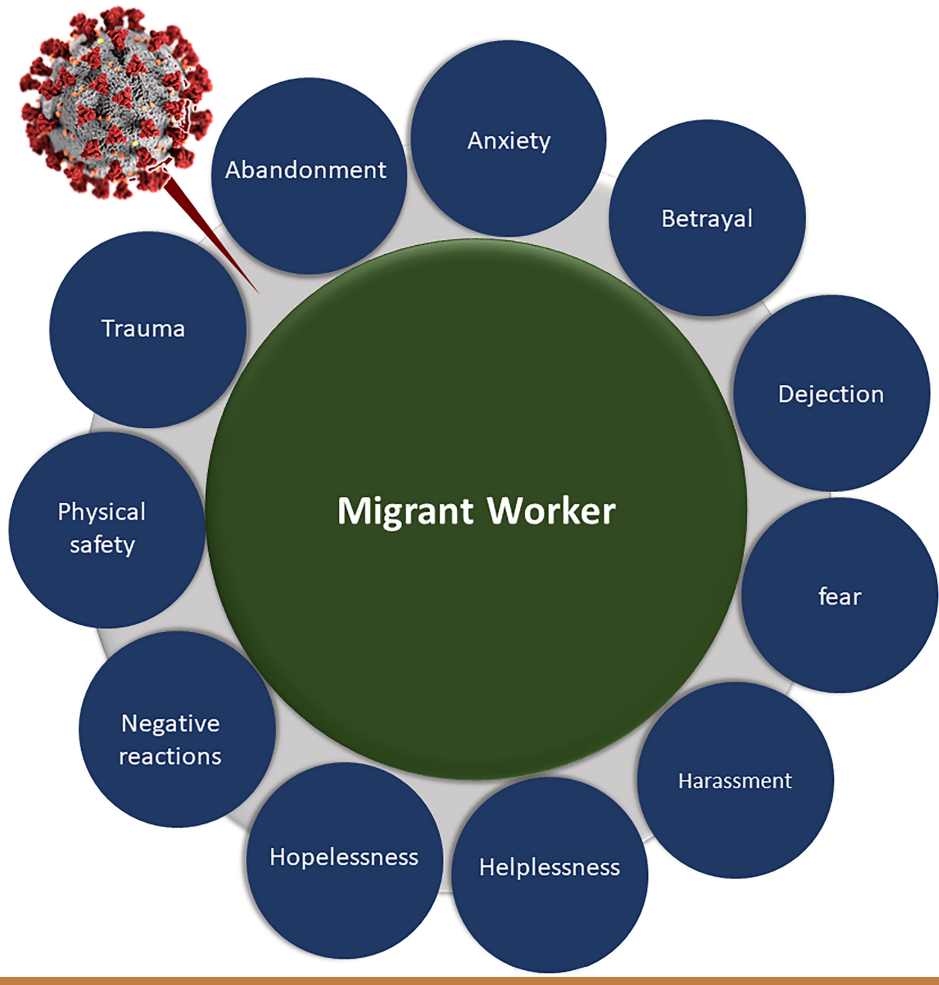

Figure 4. Forcibly displaced migrant workers and refugees encounter a variety of challenges.

the elderly.[60] The economic consequences of lockdowns have been the acute shortages of not only food but also essential drugs and pharmaceuticals.[97] Stock markets have fluctuated, causing fear for future economic security. There have been layoffs and evictions when residents could not pay their rent. Phenomena such as these cause incalculable distress to large numbers of people.[98] Though necessary to stop the viral spread, social isolation measures limit social support, exacerbating personal vulnerabilities.[99,100]

COVID-19 leads to immune activation, characterized by increased proinflammatory cytokines and chemokines, and accompanied by increased oxidative stress and depletion of antioxidant defenses.[101] Inflammatory and immune products enter the brain and lead to compromised brain function, which can last for many months after the infection clears. Figure 5 shows the mental repercussions of COVID-19 infection are depicted in this schematic illustration.

Recommendations to Reduce Risk

Vulnerable groups need special monitoring and attention. This includes pregnant women and persons in prisons, crowded shelters, refugee camps, orphanages, closed residential quarters, busy workplaces, nursing homes, and retirement homes. Indigenous communities living far from communication centers are also at risk.

Critical strategies indicated in the research on response to mass trauma include ensuring safety, remaining calm, improving community self-efficacy, boosting community connectivity, and instilling hope.[102] What makes the current scenario so problematic is that the reach of the epidemic shifts over time and varies according to geography and political decisions. This is illustrated by the uneven distribution of vaccines across the globe. Overall, we recommend the strategies noted in Table 1.

Concerning children, the National Health Commission of the People's Republic of China (NHC) has issued child-specific mental health guidelines. The NHC recommends that quarantined children receive access to information about the infection via audiovisual means, that family discussion is promoted, and that timely referral is made to mental healthcare when the symptoms outlined above emerge.[103,104] The World Health Organization (WHO) has also issued guidance on how to address the mental health of youngsters.[104] This involves encouraging creative activities such as playing or sketching, as well as keeping families together. When a child needs to be separated from a primary caregiver, it is advised that substitute care be carefully chosen and supervised, with regular parental contact offered through phone or video. The WHO encourages adhering to familiar patterns as much as possible, as well as providing parents with information and support. An example of important advice to

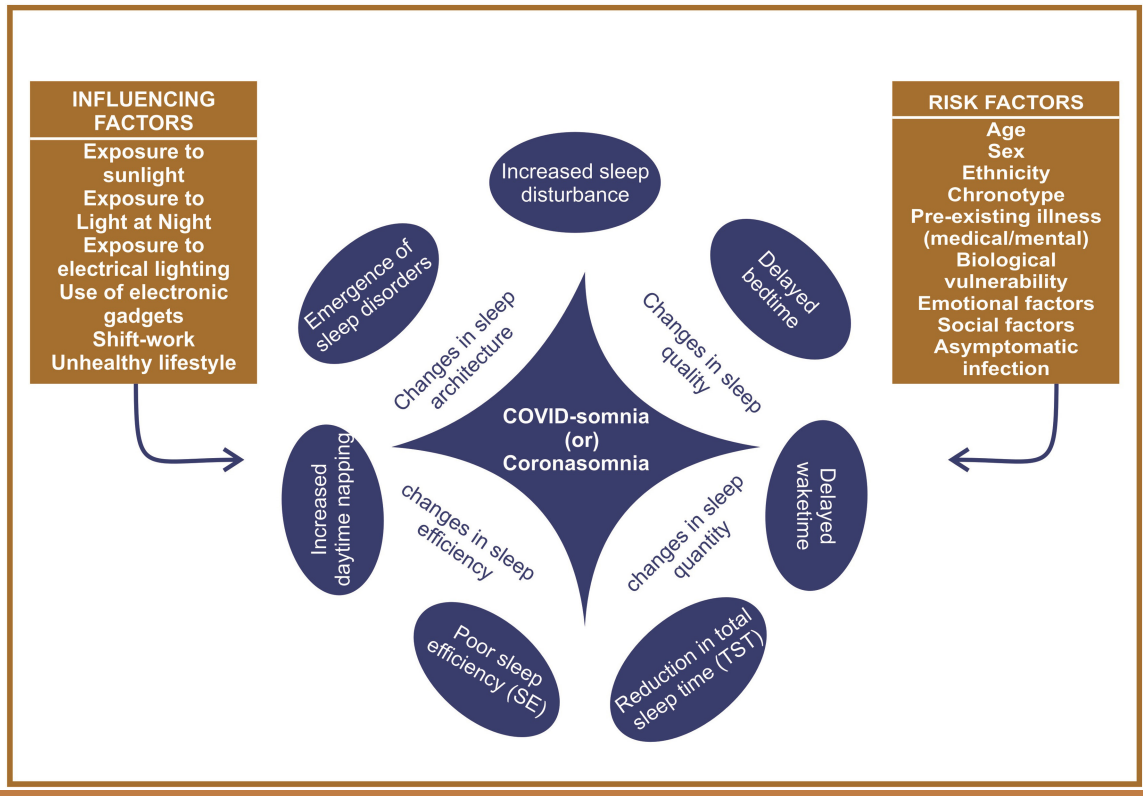

Figure 5. The mental repercussions of COVID-19 infection are depicted in this schematic illustration. Emotional responses vary.

parents is to meet disobedience in a child with compassion rather than punishment.

Conclusions

We have scoured the COVID-19 literature in an attempt to answer 4 questions: (1) What are the neuropsychiatric manifestations of this virus? (2) Who is most at risk? (3) What preventive measures are needed? (4) What therapeutic measures are needed? We have provided answers to 3 of the questions but have not been able to find literature that addresses the third question, related to the preventive measures. The question of prevention is always the hardest to address. It is always relatively easy to look back and see where the gaps have been. The most difficult is to look ahead and predict where the gaps will be. The COVID-19 pandemic caught the world unprepared; neuropsychiatric consequences followed. For the next pandemic, we borrow from the United Nations (2020) Policy Brief on COVID-19 and the Need for Action on Mental Health, and recommend the following preventive measures: (A) apply a national "whole-of-society response" and promote mental health as soon as an epidemic emerges; (B) ensure the availability of trained psychosocial and mental health support workers around the globe; and (C) support recovery-oriented strategies including social support, cohesiveness, care for the most vulnerable, and attention to individual needs.

Table 1. Strategies for Prevention of Neuropsychiatric Complications Due To the COVID-19 Pandemic.

Strategies
1. A public health response that is resilience-focused.
2. Allocating government funds for preventive as well as curative and rehabilitative mental health services.
3. Paying attention to the most vulnerable.
4. Close monitoring of potential substance abuse.
5. Establishing accessible psychological and social support to prevent, monitor, and treat neuropsychiatric problems.
6. Developing national and global infrastructure to sustain mental health disaster-readiness or preparedness, rather than response and recovery.
7. Promoting prevention, treatment, and care of mental health as a collective responsibility of government, faith groups, educational facilities, public health organizations, and charitable institutions.

Peer-review: *Externally peer-reviewed.*

Author Contributions: *Concept – S.R.P., N.F.W.Z.; Design - A.S.B., H.J.; Supervision - S.R.P., H.J., M.V.S.; Resource - C.R.S., R.K., A.M.; Materials - S.R.P., A.S.B., M.D.M., H.J.; Data Collection and/or Processing - N.F.W.Z., M.Q., N.E.M., M.D.M., A.S.B.; Analysis and/or Interpretation - M.N., T.P., A.M., H.J., R.G., I.T.; Literature Search - N.F.W.Z., M.D.M., A.S.B., R.G.; Writing - S.R.P., N.F.W.Z., M.Q., M.D.M., R.G., R.K.; Critical Reviews - M.B., S.H.K., D.J.S., S.M.S., D.S.C., M.V.S.*

Acknowledgment: *Dr Michael Berk is supported by a NHMRC Senior Principal Research Fellowship (1156072).*

Conflict of Interest: *The authors have read the journal's policy and have the following potential conflicts:*

Seithikurippu R. Pandi-Perumal, MSc., is a stockholder and the President and Chief Executive Officer of Somnogen Canada Inc., Toronto, Canada. He declares that he

has no competing interests that might be perceived to influence the content of this article. This does not alter the authors' adherence to all the journal policies.

Dr Michael Berk has received Grant/Research Support from the NIH, Cooperative Research Centre, Simons Autism Foundation, Cancer Council of Victoria, Stanley Medical Research Foundation, Medical Benefits Fund, National Health and Medical Research Council, Medical Research Futures Fund, Beyond Blue, Rotary Health, A2 milk company, Meat and Livestock Board, Woolworths, Avant and the Harry Windsor Foundation, has been a speaker for Abbot, Astra Zeneca, Janssen and Janssen, Lundbeck and Merck and served as a consultant to Allergan, Astra Zeneca, Bioadvantex, Bionomics, Collaborative Medicinal Development, Eisai, Janssen and Janssen, Lundbeck Merck, Pfizer and Servier – all unrelated to this work.

Ravi Gupta, MD, PhD, is a Member of the Advisory Board of Eisai Inc and Blackbeard Technology Private Limited, India. He declares that he has no competing interests that might be perceived to influence the content of this article. This does not alter the authors' adherence to all the journal policies.

Dan Stein, MD, PhD, received research grants and/or consultancy honoraria from Lundbeck and Sun. He declares that he has no competing interests that might be perceived to influence the content of this article. This does not alter the authors' adherence to all the journal policies.

Stephen M. Stahl, MD, PhD, Dsc (Hon.) is a consultant of the following companies: Acadia, Alkermes, Allergan, Arbor Pharmaceuticals, Axovant, Axsome, Celgene, Concert, ClearView, EMD Serono, Eisai Pharmaceuticals, Ferring, Impel NeuroPharma, Intra-Cellular Therapies, Ironshore Pharmaceuticals, Janssen, Lilly, Lundbeck, Merck, Otsuka, Pfizer, Sage Therapeutics, Servier, Shire, Sunovion, Takeda, Taliaz, Teva, Tonix, Tris Pharma, and Viforpharma. He is a board member of Genomind and on the speakers' bureau of Acadia, Lundbeck, Otsuka, Perrigo, Servier, Sunovion, Takeda, and Vertex. He received research and/or grant support from Acadia, Avanir, Braeburn Pharmaceuticals, Eli Lilly, Intra-Cellular Therapies, Ironshore, ISSWSH, Neurocrine, Otsuka, Shire, Sunovion, and TMS NeuroHealth Centers. He declares that he has no competing interests that might be perceived to influence the content of this article. This does not alter the authors' adherence to all the journal policies.

Dr. Charney reports, in addition, that he has a patent • US Patent No. 10 478 405 – Method for Treating Post-Traumatic Stress Disorder (issued November 19, 2019) issued; a patent • US Patent No. 10123737 – Systems and Methods for Treating a Psychiatric Disorder (issued November 13, 2018) licensed to Click Therapeutics, Inc.; a patent • US Patent No. 9592207 – Intranasal Administration of Ketamine to Treat Depression (issued March 14, 2017) licensed to Janssen Pharmaceuticals, Inc.; a patent • US Patent No. 9539220 – Methods for Treating Suicidal Ideation (issued January 10, 2017) licensed to Janssen Pharmaceuticals, Inc.; a patent • US Patent No. 8785500 – Intranasal Administration of Ketamine to Treat Depression (issued July 22, 2014) licensed to Janssen Pharmaceuticals, Inc., a patent • US Serial No. 16/189059 – and related foreign patent applications – Systems and Methods for Treating a Psychiatric Disorder, licensed to Click Therapeutics, Inc.; a patent • US Serial No. 17/041770 and related foreign patent applications – System and Methods for Processing Connectivity Values Between Sub-Processing Regions licensed to Click Therapeutics, Inc.; a patent • US CON Patent Appl No. 16/674381 and related foreign patent applications – Method for Treating Post Traumatic Stress Disorder (PTSD) pending; a patent • US Serial No. 14/889746 and a related European patent application – Treatment of Mood and Anxiety Disorders pending; and a patent • US Serial No. 16/844090 and US Serial No. 15/930140 – Intranasal Administration of Ketamine to Treat Depression. (Continuation patent applications in the same patent family as issued US Patents 8785500 and US 9539220 and US 9592207) licensed to Janssen Pharmaceuticals, Inc.

All remaining authors declare that they have no proprietary, financial, professional, or any other personal interest of any nature or kind in any product or services and/or company that could be construed or considered a potential conflict of interest that might have influenced the views expressed in this manuscript.

Financial Disclosure: *The authors declared that this study has received no financial support.*

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