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Rehabilitation of Neuropsychiatric Symptoms in Patients with Long-COVID: Position Statement

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Abstract

Long-COVID, a term used to describe ongoing symptoms following SARS-CoV-2 (COVID-19) infection, parallels the course of other post-viral syndromes. Neuropsychiatric symptoms of Long-COVID can be persistent and interfere with quality of life and functioning. Within the biopsychosocial framework of chronic illness, rehabilitation professionals can address the neuropsychiatric sequelae of Long-COVID. However, current practice models are not designed to address concurrent psychiatric and cognitive symptoms in adults living with Long-COVID. Thus, we present a biopsychosocial framework for Long-COVID and provide treatment

strategies based on evidence from current literature of post-viral chronic illness. These recommendations will guide rehabilitation professionals in 1) identifying common neuropsychiatric symptoms in Long-COVID that can be targeted for intervention and 2) addressing these symptoms via integrative interventions taking into account the biopsychosocial presentation of Long-COVID symptoms.

Keywords

Long-COVID, Neuropsychiatric, PASC, Post-Viral Syndrome, Fatigue, Pain, Cognitive Rehabilitation, Position Statement

Abbreviations

ICD-10 = International Classification of Diseases, Tenth Edition

PASC = Post-acute sequelae of SARS-CoV-2

CNS = Central Nervous System

PTSD = Post traumatic Stress Disorder

HIV = Human Immunodeficiency Virus

HSE = Herpes simplex encephalopathy

ME/CFS = Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome

CBT = Cognitive Behavioral Therapy

PRT = Pain Reprocessing Therapy

MRI = Magnetic Resonance Imaging

CR = Cognitive Remediation

ACT = Acceptance and Commitment Therapy

TBI = Traumatic Brain Injury

EFT = Ecosystem Focused Therapy

PT = Physical Therapy

OT = Occupational Therapy

SLP = Speech and Language Pathology

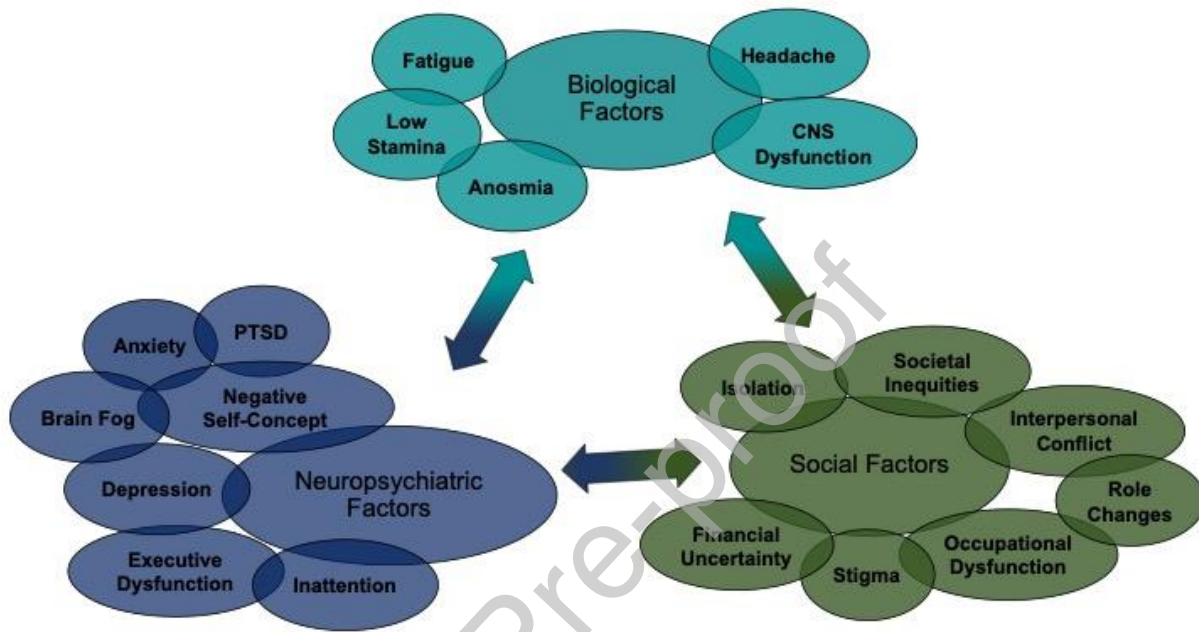
Background

The constellation of prolonged vascular, pulmonary, musculoskeletal, sensory, and/or neurological challenges following SARS-CoV-2 infection have been designated in the ICD-10 as “Post COVID-19 condition”, also commonly referred to as “post-acute sequelae of SARS-CoV-2 (PASC)” or “Long COVID”, among other terms.² Although Long-COVID describes a heterogenous range of presentations, the scope of this commentary will focus on

neuropsychiatric symptoms. Long-COVID has a similar presentation and course as other post-viral syndromes.⁴ To date, a staggering number of individuals have been infected with COVID-19, and an estimated 13 – 33% are experiencing Long-COVID.^{1, 5} Moreover, Black, indigenous, Latinx, and other marginalized groups who have been disproportionately impacted by COVID-19, may be particularly vulnerable to chronic sequelae that are amplified by ongoing healthcare inequities.⁶ Long-COVID symptoms are diffuse and contribute to disability and a decline in quality of life for affected patients.⁷ Although there is an emerging literature to characterize the prolonged recovery process among individuals who experience severe infection and to provide recommendations for discrete facets of Long-COVID,⁸⁻¹¹ its interdependence of physical, psychological, and cognitive issues benefit from the contribution of methodology for a holistic approach to treatment.

In this communication, the neuropsychiatric sequelae of Long-COVID are contextualized within the framework of the biopsychosocial model (see Figure 1), to include the complex interplay of somatic, cognitive, and emotional symptoms.^{12, 13} Further, we examine the parallels between Long-COVID and other post-viral infections and chronic medical illnesses to provide a theoretical framework for multidisciplinary, evidence-based management of neuropsychiatric symptoms. We propose that central tenets for treatment of Long-COVID include assessment, identification of neuropsychiatric symptoms, and multi-disciplinary intervention that simultaneously targets both psychiatric and cognitive sequelae.

Fig 1 Biopsychosocial model of Long-COVID



Long-COVID Parallels to Other Post-Viral Syndromes

Human coronaviruses, including SARS-CoV-2, are known to be neurovirulent, neurotropic, and neuro-invasive and may target the brain through multiple pathways, thus contributing to neuropsychiatric sequelae.¹⁴ Primary neuronal infection and secondary immune overactivation, mitochondrial and microglial dysfunction,¹⁵ persistent inflammation and hypercoagulability, respiratory and cardiovascular insufficiency, are hypothesized mechanisms of acute and chronic neuropsychiatric symptoms of COVID-19.^{8, 15-17} Pathogenic apoptosis, disruption of neuronal integrity, secretion of neurotoxins, and excess release of glutamate may also contribute to neurological dysfunction.¹⁸ Chronicity of symptoms itself may promote the development of

“central sensitization”;¹⁹ a model of CNS plasticity in which adaptation to prolonged nociception maintains somatic symptoms like those described in myalgic encephalopathy, fibromyalgia, and other pain syndromes.¹⁹ Central sensitization is a useful construct for explaining persistent neuropsychiatric sequelae of Long-COVID, in which nociception reinforces the ongoing occurrence of other neuropsychiatric symptoms, thus creating maintenance of chronicity.²⁰

Post-infection factors which are relatively specific to COVID-19 may contribute to symptom maintenance as well. For example, grieving the loss of loved ones and colleagues who died of this virus, limited medical treatments and access to medical resources, uncertainty of long-term prognosis, stigma, discrimination, and ongoing healthcare disparities all exacerbate experienced distress and prolong neuropsychiatric symptoms.²¹ Further, COVID-19 illness is a traumatic experience for many, and patients hospitalized due to COVID may develop delirium putting them at risk for post-traumatic stress disorder (PTSD). However, COVID infection may contribute to PTSD regardless of severity and/or hospitalization status.^{22, 23} Thus, specific assessment and treatment may be required to address PTSD, per guidelines outlined and reviewed by Watkins et al. (2018).²⁴ Ongoing stressors specific to the pandemic (e.g., long-term social isolation, diminished activity, financial uncertainty, unstable housing) compound neuropsychiatric consequences in Long-COVID.^{21, 25} These individual and sociological stressors may potentiate maladaptive behaviors, such as treatment avoidance and unhealthy coping.^{21, 25}

COVID-19 is one of many viral illnesses to instigate chronic symptoms. Post-viral neuropsychiatric symptomatology, including fatigue, is commonly reported following a diverse range of infections, including Epstein-Barr, herpes viruses, HIV, rubella, and West Nile infections.^{26, 27} Long-COVID has neuropsychiatric symptoms akin to the effects of other chronic medical conditions. Continuous fatigue, “brain fog”, mood dysfunction, diminished engagement

in daily tasks, and emotional distress are common among patients living with prolonged medical challenges, such as cancer and its treatment, trauma secondary to intensive care procedures, ME/CFS, or post-concussive syndrome²⁸⁻³¹ and are frequently under-recognized or invalidated by society at large.³¹⁻³⁵ Diagnostic and interventional approaches to Long-COVID can be gleaned from parallels with Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS), post-concussive syndrome, herpes simplex encephalopathy (HSE), rubella, West Nile, and human immunodeficiency virus (HIV).

Psychological Interventions in Chronic Medical Illness

Complex post-viral physical, psychological, and cognitive challenges require an integrated and multi-disciplinary treatment approach. The goals of neuropsychological intervention for Long-COVID, are similar to all chronic illness, and include reducing emotional distress, mitigating cognitive and physical dysfunction, and ultimately improving quality of life.

Interventions initiated early in recovery and which focus on ameliorating psychiatric symptoms, bolstering adherence to other treatments, and promoting psychological adjustment can reduce depression and disability, and improve the quality of life in patients with chronic illness.³⁶⁻³⁸ For example, among patients with fibromyalgia, Cognitive Behavioral Therapy (CBT) effectively treats symptoms of pain, fatigue, depression, sleep disturbance, and improves coping skills, enhancing quality of life.³⁹ In patients with chronic back pain, one randomized-controlled trial found that participants assigned to pain reprocessing therapy (RPT, a form of CBT) had significantly improved sleep, as well as reduced disability, pain, depression, and anger, in comparison with matched controls assigned to a placebo condition.⁴⁰ Further, RPT-related

symptom improvements were associated with decreased evoked pain-related activity on functional MRI.⁴⁰ Similarly, psychological interventions that provide psychoeducation and strategies for behavioral activation can improve mood and disability in adults with comorbid chronic obstructive pulmonary disease and depression^{36,37} when initiated early in the recovery process (i.e., inpatient rehabilitation settings). Post-stroke survivors diagnosed with major depressive disorder exhibited reduced depressive symptoms when treated with Ecosystem Focused Therapy (EFT). EFT engages caregivers in ameliorating post-stroke functional limitations and role changes and may improve physical and cognitive functioning in patients relative to controls.³⁸ Further, evidence-based treatments such as CBT and cognitive rehabilitation (CR) have been used in tandem to effectively to treat neuropsychiatric symptoms in a wide variety of medical populations with symptom chronicity including post-concussive syndrome,^{41,42} breast cancer treatment,^{43,44} and fibromyalgia.⁴⁵ CR and CBT have been effective in treating sequelae of other post-viral syndromes, as well as mild to moderate traumatic brain injury (TBI).^{41,46} Moreover, evidence-based practice standards from CR, as used for patients with TBI and stroke,⁴⁷ can be applied to treat similar cognitive symptoms in persons with Long-COVID.

Proposed Treatment for Individuals with Long-COVID within a Biopsychosocial Model

By applying evidence-based CBT/CR practices used in other chronic medical conditions, we may expect comparable efficacy in the Long-COVID population. The Stanford Hall Consensus Statement, derived from an interdisciplinary rehabilitation specialist meeting in response to the current global pandemic, Barker-Davies and colleagues concluded that, “For patients with

COVID-19, rehabilitation should be aimed at relieving symptoms of psychological distress and improving participation in rehabilitation, physical function and quality of life” (p.951).¹¹

The integration of Cognitive Rehabilitation /Cognitive Behavioral Therapy (CR/CBT) follows the biopsychosocial model by addressing symptom-chronicity maintenance, incorporating methods of behavioral activation, implementing emotional coping skills, and using cognitive remediation strategies that support goal-directed behavior. Although CR/CBT, can be thought of as a foundational aspect of treatment for emotional and cognitive symptoms of PASC, we propose an integrated treatment is that also incorporates techniques from other evidence based treatments, such as Acceptance and Commitment Therapy (ACT) and Mindfulness based approaches,^{48, 49} as outlined below in the proposed sequence of components. Goals of treatment within an integrated CR/CBT approach include increasing attentional control, developing compensatory strategies for self-management of cognitive dysfunction, diminishing impact of distress and negative self-perception, and reducing the influence of fatigue on behavioral engagement. CR/CBT aims to diminish avoidance and withdrawal that help maintain low mood and persistent disability. CR/CBT integrated with an interdisciplinary and multidisciplinary service delivery network of rehabilitation specialists, complements and supplements the expertise and co-occurring treatment modalities to promote optimal outcomes.

Long-COVID Intervention to Address Neuropsychiatric Difficulties

Guided by the expertise of those who have been at the fore of research on the neuropsychiatric effects of Long-COVID,^{21, 50} the goal here is to develop a flexible intervention protocol that can be utilized in a variety of modalities and platforms to increase accessibility of treatment.

Currently, members on the COVID-19 Taskforce of ACRM, drawing from their clinical experience with integrated CR/CBT techniques across varied institutions, are collaborating on an ordinal sequence of rehabilitative treatments for individuals with Long-COVID.

In caring for patients with Long-COVID, concurrently addressing both neuropsychiatric symptoms and barriers to treatment engagement is paramount. Three basic tenets are essential: first, psychoeducation regarding the biopsychosocial model can help patients understand the interaction and maintenance of their symptoms, thereby providing a framework for intervention. Neuropsychological treatment adherence can be emphasized in terms of longer-term physical and cognitive gains, thus diminishing disability. Second, psychoeducation on the hierarchy of cognitive domains, specifically the impact of fatigue on arousal, alertness, and autonomic regulation of the sleep wake cycle, can help patients understand the interaction between their fatigue and cognitive dysfunction. Third, functionality, rather than causality, needs to be emphasized throughout treatment. Such functional orientation bolsters patients' adjustment and promotes their adherence to other treatments. Elements of ACT are utilized throughout treatment. For example, tenets that can be applied to Long-COVID include: acknowledging and validating the ambiguous nature of Long-COVID, tolerating the unknowns of causality and long-term prognosis, accepting functional challenges, making daily commitments to a gradual process of recovery, engaging with tasks of daily living despite ongoing symptoms, coping with stigma, and maintaining symptom management.

Development of standardized intervention modules, conceptualized as an evidence-based, flexible toolbox for use in a variety of settings, would serve as a catalyst for clinical research on treatment efficacy in Long-COVID and promote translational research to optimize intervention

effectiveness. The exposure and response-prevention aspects of this treatment may also target symptoms related to trauma.

The following sequence with treatment components of CR/CBT is proposed:

1. Emotion regulation strategies are essential to introduce in the beginning of treatment in order to reduce anxiety and negative self-talk that may interfere with engagement in treatment protocol. Emotional strategies will be used throughout treatment to modify maladaptive self-messaging about cognitive dysfunction, increase tolerance of emotional distress, and diminish task- and treatment-avoidance.
2. Attentional control strategies, memory encoding/retrieval skills, and meta-cognitive strategies, including goal management training and problem-solving are all foundational to the treatment. These skills are consistent with mindfulness practice that emphasizes filtering out distraction whilst being fully present in order to fully utilize cognitive resources.
3. Behavioral activation strategies support cognitive functioning in the context of fatigue, increasing engagement and self-efficacy through techniques like pacing, introduction of aerobic exercise, and activity-scheduling. As these cognitive and behavioral strategies are internalized and used during everyday activities, increased efficiency of mental resources will contribute to diminished fatigue.

Moreover, neuropsychological intervention can foster patients' momentum in other rehabilitation therapies and reintroduction of role functions (e.g., work/school) that may not have been resumed since their acute COVID infection. For example, activity-pacing can help patients arrange their expenditures of energy to optimize physical engagement in PT, attentional control

can help patients master sequencing of everyday functional activities in OT, and meta-cognitive strategies can help patients attenuate the downstream impact of cognitive dysfunction on language to maximize their progress in SLP.

In summary, Long-COVID occurs in a significant proportion of the population, many of whom will experience debilitating functional decline. Although the techniques described here are a synthesis of evidence-based approaches that have shown efficacy in similar patient populations, it is important to note that the research literature on neurorehabilitation specific to Long-COVID is nascent and still rapidly evolving; as such, the reader is cautioned against interpreting this writing as an assertion that the clinical utility of CR/CBT exceeds other treatment modalities. Nonetheless, integrating and expanding existent evidence-based interventions will be vital for improving outcomes of people affected by Long-COVID

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