

Tutorial

Potential for Cognitive Communication Impairment in COVID-19 Survivors: A Call to Action for Speech-Language Pathologists

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Purpose: Severe acute respiratory syndrome coronavirus 2 is the virus resulting in COVID-19 infections in nearly 4.3 million Americans with COVID-19 in the United States as of July 29, 2020, with nearly 150,000 deaths and hundreds of thousands of survivors (<https://www.coronavirus.jhu.edu/map.html>). This tutorial reviews (a) what has been reported about neurological insults in cases of COVID-19 infection, (b) what is known from similar conditions in other disorders, and (c) how that combined information can inform clinical decision making.

Method: PubMed and the Cochrane Central Register of Controlled Trials were searched for COVID-19 or other coronavirus infections, cognitive impairment observed following critical care, and disorders for which intermittent or chronic hypoxia is characteristic. These were combined with searches relating to cognition, brain, and communication. All searches were conducted between April 8 and May 23, 2020. Meta-analyses and randomized clinical trials addressing other critical illnesses were also included to extend findings to potential cognitive communication outcomes following COVID-19.

Results: COVID-19 infection results in a combination of (a) respiratory infection with mechanical ventilation secondary to inadequate oxygenation, (b) inflammatory system reactivity, and (c) increased blood clotting factors. These affect central nervous system function incurring long-term cognitive communication impairment in a proportion of survivors. Diagnostic and intervention approaches for such impairments are discussed.

Conclusions: The existing literature on cognitive sequela of COVID-19 infection is small to date, but much can be learned from similar viral infections and disorders. Although COVID-19 is novel, the speech-language pathology approaches to evaluation and intervention of other populations of critical care patients are applicable. However, speech-language pathologists have not routinely been involved in these patients' acute care. As such, this is a call to action to speech-language pathologists to address the unprecedented numbers of patients who will need their services early in the disease process and throughout recovery.

Humans around the world are facing their first pandemic in a century. The climbing numbers of people testing positive for the severe acute respiratory syndrome coronavirus 2, the virus that causes the COVID-19 infection, are grabbing the attention of the populous, driving social distancing to “flatten the curve” (CDC.gov). High rates of infection are leading to the overcrowding of hospitals and intensive care units (ICUs) and shortages of ventilators for patients and of personal protection equipment for health care workers. There is known increased risk of COVID-19 in individuals with other serious health conditions and elderly individuals, particularly

those with comorbid health conditions (Richardson et al., 2020). Although the current concerns of the health care professions are on containing the spread of the virus and saving lives, there is growing evidence that those who survive the battle with the virus may have long-term neurological consequences (Needham et al., 2020; Pinna et al., 2020; Tsvigoulis et al., 2020; Wu et al., 2020). Thus, it is paramount that health care professionals and speech-language pathologists (SLPs), in particular, prepare to diagnose and treat the cognitive communication disorders that may arise as a result of those consequences in COVID-19 survivors.

The following tutorial provides background regarding the potential for cognitive communication impairment as a sequela of surviving critical, severe illness due to COVID-19 infection. Although data are emerging daily about survivors, this novel coronavirus is too new to provide direct knowledge for clinical decision making in speech-language pathology. For now, SLPs in the field are responding to each patient's symptoms, and referrals are largely for dysphagia,

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though there are reports in the ASHA Special Interest Group 2 forum and in the interim guidance from the World Health Organization (2020) about delirium in ICU patients with COVID-19. Thus, evidence from similar conditions can help to guide our practice in this pioneering age. This review will address (a) what has been reported about neurological insults in cases of COVID-19 infection, (b) what is known from similar conditions in other disorders, and (c) how that combined information can inform clinical decision making. What should become clear to the reader is that, although COVID-19 is new, the speech-language pathology approaches to evaluation and treatment of other populations of critical care patients are applicable. However, SLPs have not routinely been involved in these critically ill patients' acute care. As such, this is a call to action to SLPs to address the unprecedented numbers of patients who will need their services.

Method

This tutorial's purpose is to identify the potential for brain injury and cognitive communication impairment in survivors of COVID-19 infection as well as potential next steps for evaluating and treating such impairment. Because COVID-19 is a novel virus with limited published research on its disease process, the potential for cognitive disorders was also explored in other coronaviruses, as well as in similar disorders requiring critical care. Thus, to write this tutorial, database searches of PubMed and the Cochrane Central Register of Controlled Trials were conducted using the MeSH terms COVID-19 or other coronavirus infections, cognitive impairment observed following critical care ("critical care," "delirium," and "post-intensive care unit syndrome" [PICS]), and disorders for which intermittent or chronic hypoxia is characteristic (i.e., "chronic obstructive pulmonary disorder" [COPD], "chronic obstructive sleep apnea" [COSA], and "mechanical ventilation"). The root searches for each disorder were then combined with the following subtopic searches: "brain," "inflammation," "magnetic resonance imaging," "cytokines," "cognition," and "executive function." The role of SLPs in the evaluation and treatment of these disorders was also queried by including the terms *speech* and *language*. Results of the database searches were filtered to include only those involving human participants 18 years of age or older, published in English, and including experimental research studies and reviews. All searches were conducted between April 8 and May 23, 2020.

Results

Potential Neurological Consequences of COVID-19

Hospitalizations for individuals testing positive for COVID-19 (4.6% of all cases in the United States) have primarily been in those with cough, fever, and shortness of breath (each accounting for > 80% of cases) as well as with gastrointestinal symptoms (in approximately 20% of cases; Garg, 2020). Data from the origin of COVID-19

infections in Wuhan, Hubei Province, China, indicate that, of the 799 moderately to severely ill or critically ill patients admitted to Tongji Hospital between January 13 and February 12, 2020, 113 died and 161 recovered. On admission, most (64%) patients who died and only 12% of recovered patients had percutaneous oxygen saturations levels of < 93%, and all had abnormal chest radiographs with bilateral involvement in 100% of deceased and 94% of recovered patients (Chen et al., 2020). This is not surprising given that the first symptoms of COVID-19 identified in the critical care literature were respiratory distress and increased incidence of acute respiratory distress syndrome in COVID-19 patients (Chen et al., 2020). Disorders of consciousness at hospital admission were also reported in 2% of cases (Chen et al., 2020), suggesting possible central nervous system (CNS) involvement even in the early stages.

Currently, there are only a few reports of an overtly affected CNS in patients testing positive for COVID-19. In such cases, the damaged brain tissue is seemingly separate from the infection's effects on the lungs or other organs. For example, Poyiadji et al. (2020) reports on a woman in her late 50s, with severe presumptive COVID-19 presenting with cough, fever, and altered mental state. Following several radiological assessments, she was found to have acute necrotizing encephalopathy, a rare complication of influenza and viral infections. Acute necrotizing encephalopathy is associated with intracranial "cytokine storms" (immune system hyperinflammatory process; Mehta et al., 2020) that breakdown the blood-brain barrier and can result in symmetrical, multifocal lesions of medial temporal and thalamic cortex. Recently, severe acute respiratory syndrome coronavirus 2 also has been found in the cerebrospinal fluid in cases of COVID-19-related encephalitis (Moriguchi et al., 2020; Poyiadji et al., 2020). In fact, hypoxic encephalopathy was reported in 20% of deceased patients in Wuhan (Chen et al., 2020). Similar reports were seen following the Middle East respiratory syndrome coronavirus, with patients suffering severe respiratory infection, sepsis, organ damage, and blood clotting disorder (coagulopathy; Arabi et al., 2015; Mogi et al., 2017; Takanashi, 2009). Interestingly, some symptoms (i.e., delirium, seizures, altered consciousness) following Middle East respiratory syndrome coronavirus infections were described as "reversible" because they resolved within a month. Follow-up imaging and assessment of mental status or cognition after discharge have not been reported in those cases.

Other neurological consequences of COVID-19 may relate to co-occurring increases in coagulation factors (e.g., D-dimer and Fibrinogen levels), which are associated with poor prognoses (Panigada et al., 2020; Ranucci et al., 2020; Spiezia et al., 2020; Tang et al., 2020). This increase in the potential for blood clotting appears to be infection related, likely as a result of chronic inflammatory states and formation/deposition in the lungs of excess of fibrin (a protein activated when there is vessel wall injury to produce clotting to prevent blood loss; Weisel & Litvinov, 2017). These clotting factors appear to be spilling over into the circulatory system, as they do in chronic obstructive

pulmonary disease (Jiang et al., 2008) and normal aging (Weuve et al., 2011), increasing the risk for arterial and venous thrombi, myocardial infarctions, and cerebrovascular accidents.

Finally, COVID-19 infections may access the CNS via breakdown of the blood–brain barrier secondary to a cytokine storm or viral entry through the nasal mucosa. COVID-19 infection in other cells of the body (cf. Wadman et al., 2020) may trigger a *cytokine storm*, a term that was first popularized in another epidemic—the avian H5N1 influenza pandemic (“swine flu”) of 2009—that refers to a cascade of immune system responses (Guo et al., 2020). Although immune system activation in the face of infection is the body’s defense mechanism, cytokine storms risk damage to healthy tissue as a byproduct. Cytokine storms associated with a primary lung infection can circulate cytokines through the body, potentially leading to sepsis and multiple organ failure (Tisoncik et al., 2012)—a cause of death in the current COVID-19 pandemic (in 100% of deceased patients in the study of Chen et al., 2020). Furthermore, one consequence of increased cytokine activity is a breakdown of the blood–brain barrier, which allows the virus to enter the nervous system. Alternatively, it has been hypothesized that the unusual loss of the sense of smell (i.e., anosmia) in COVID-19 may be an indicator that the virus has accessed the CNS through the olfactory nerve in the nasal cavity (Wu et al., 2020).

Common features can be observed across coronavirus infections, that is, COVID-19, SARS, and MERS. First, respiratory distress leads to intermittent or chronic hypoxia (reduction of oxygen delivery to the brain). Second, each has virus-related hypercoagulability that may cause strokes in major vessels. Third, the virus may affect the CNS directly, either by way of direct conveyance to brain tissue through the mucosal membranes in the nasal cavity or by blood–brain barrier breakdown via hyperimmune system activity. Each of these features may result in brain injury that can affect cognition, language, or speech functions in ways that are not yet evident in COVID-19 survivors (see Figure 1). As such, SLPs must understand the potential for brain injury in the thousands of U.S. cases so that they may prepare to provide appropriate services. To this end, the next section will focus on what is known about the effects of these three features on brain function, cognition, and cognitive communication as they are observed in other populations.

Critical Illness Factors Associated With Cognitive Communication Impairment

Prolonged Mechanical Ventilation

COVID-19 infection resulted in acute respiratory distress syndrome (ARDS) in 100% of deceased patients in Wuhan (Chen et al., 2020). ARDS is the rapidly progressing life-threatening respiratory failure associated with inflammatory fluids flooding the alveoli and limiting oxygen delivery to organs (Stam et al., 2020). ARDS, unrelated to COVID-19, has a mortality rate of 25%–40% (Mikkelsen

et al., 2012). Although ARDS was reported in fewer recovered than deceased patients, 16% of recovered patients in Wuhan were on mechanical ventilation during their hospital stay. Similar data are not yet available for deceased and recovered patients in the United States.

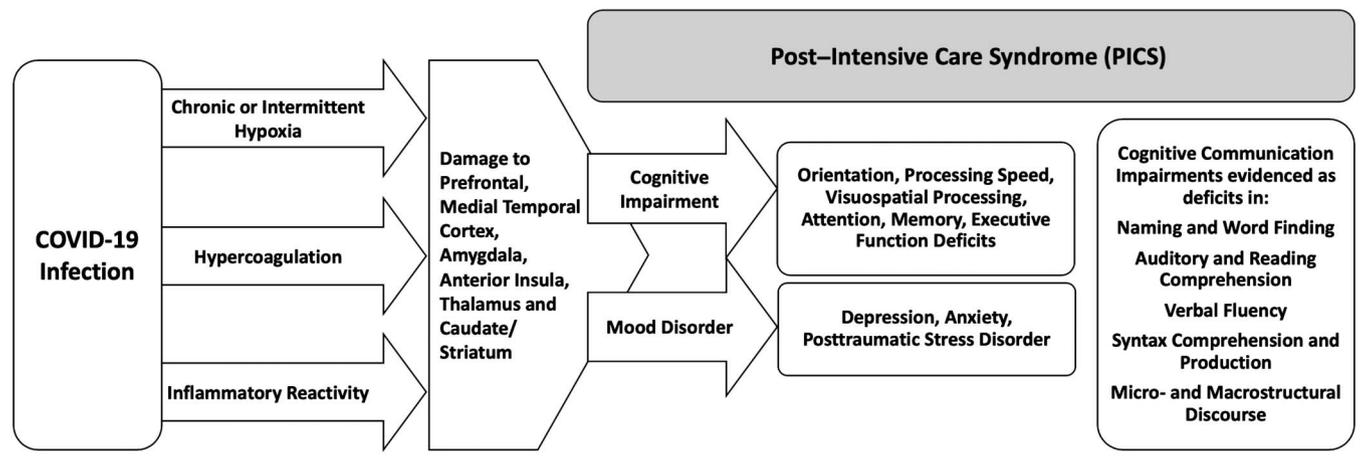
Cognitive dysfunction is often a consequence of ARDS, along with a host of other potential impairments resulting in reduced quality of life (Denke et al., 2018). In fact, cognitive impairment is estimated in 70%–100% of patients requiring mechanical ventilation and persists in approximately 20% of those 5 years later (Herridge et al., 2016; Wilcox et al., 2013). Impaired cognitive function may arise due to prolonged duration of hypoxia or mechanical ventilation (Mart & Ware, 2020). What remains unclear is whether the chronic reduction in oxygenated blood over the course of a COVID-19 infection, even in those not requiring mechanical ventilation, may also contribute. Thus, a look at other conditions with intermittent hypoxia may provide some clues about the potential outcomes.

Intermittent Hypoxia

Two conditions demonstrating cognitive impairment secondary to intermittent hypoxia are COPD and COSA. COPD is characterized by intermittent hypoxia with comorbid cardiovascular disease and low baseline oxygen saturation (< 88%, resting hypoxemia). Chronic hypoxemia can alter neurotransmitter function, and its presence is highly correlated with domain general cognitive deficits evidenced by performance on mental status screening (Thakur et al., 2018; Wen et al., 2018). Changes in neurological function are often observed in individuals with pulmonary edema or injured lungs, and vice versa, suggesting a synergistic relationship between these functions (Stevens & Puybasset, 2011). The severity of COPD and mental status impairment is associated with reductions in gray and white matter volume in prefrontal cortex, medial temporal lobe structures, thalamus, and caudate/striatum (Yin et al., 2019). However, these brain changes are not associated with arterial partial pressure of oxygen or blood oxygen saturation, suggesting that hypoxia alone may not be the cause.

COSA is also characterized by intermittent hypoxia, though the periods of inadequate oxygenation are brief. Apnea is defined as a reduction in respiratory amplitude of > 80% for 10 s or longer during overnight polysomnography (Ayalon et al., 2010; Harper et al., 2013; Kumar et al., 2014; Lutsey et al., 2016). Cognitive impairment is fairly common in untreated moderate-to-severe COSA, with particular deficits in attention, specifically vigilance, acquisition of new memories, visuospatial abilities, and executive functions (Otero et al., 2019). These deficits frequently co-occur with mood disorders. Changes in cognition and mood in COSA are associated with reductions or adaptations of gray and white matter brain tissue (cf. Castronovo et al., 2014; Joo et al., 2013; Kumar et al., 2014; Lin et al., 2016; Rosenzweig et al., 2016; Torelli et al., 2011) as well as alterations of task-related (Ayalon et al., 2010; Castronovo et al., 2009; X. Zhang et al., 2011) and resting-state (Park et al., 2016; Yaouhi et al., 2009;

Figure 1. The syndrome likely to be seen following critical care for COVID-19 infections, post-intensive care unit syndrome, is the result of chronic or intermittent hypoxia, hyper-immune system activity, and/or hypercoagulability as a result of the effect of the virus on the body. Each of these may cause damage to the parts of the brain that are associated with cognition and mood, which in turn may result in cognitive communication impairment, as described in more detail in MacDonald (2017).



Q. Zhang et al., 2015) brain function. A coordinate-based meta-analysis of brain imaging findings in COSA indicates a convergence of brain tissue changes in the right amygdala and anterior insula, which are integral to brain networks essential for sensory perception, emotion (anger, fear, happiness), interoception (air hunger [dyspnea], sexuality), and memory (Tahmasian et al., 2016).

Hypercoagulability

Virus-associated hyperinflammation is associated with risk for blood clotting or sepsis-induced coagulopathy in the lungs, legs, and brain (Hess et al., 2020). Venous and arterial thrombotic complications are estimated in as many as 31% of COVID-19 patients (Klok et al., 2020); therefore, an influx of critically ill stroke patients with this pandemic is likely. As in other instances of stroke, physicians treating COVID-19 cases are considering the use of tissue plasminogen activator and other anticoagulants (Klok et al., 2020) but are aware of the complexity of the cases given the two other features—hyperimmune activity and hypoxia.

Delirium

Delirium is a cytokine-mediated activation of microglia and astrocytes associated with acute brain dysfunction. It is characterized by quickly developing fluctuations in attention (focused, sustained, or shifting) and awareness (orientation) and may also involve cognitive disturbance (“The DSM-5 Criteria, Level of Arousal and Delirium Diagnosis,” 2014, p. 5). Importantly, this fluctuation is particularly characteristic of delirium and not seen in dementia or other forms of cognitive impairment (Hopkins & Jackson, 2006). Delirium occurs in up to 70% of critically ill older adults in ICUs (Wang et al., 2018), and its presence and duration is the strongest risk factor for the persistence of cognitive impairment following recovery. Its presentation

is often accompanied by myopathy or polyneuropathy due to long-term debilitation in an ICU, along with psychological comorbidities (anxiety, depression, and posttraumatic stress disorder [PTSD]; Mart & Ware, 2020). Premorbid cognitive impairment is associated with the likelihood of further impairment after delirium, but even in those with little or no impairment at baseline, delirium independently predicted poorer outcomes (Francis & Kapoor, 1992). Thus, the illness-related features that result in delirium likely alter brain function.

There are at least four subtypes of delirium (Girard et al., 2018) associated with separable mechanisms of action. These include the following:

1. hypoxic: secondary to chronic or intermittent hypoxia;
2. septic: secondary to cytokine-mediated organ and brain damage due to microglial activation;
3. metabolic: secondary to renal or hepatic dysfunction; and
4. sedative related: secondary to use of medications in critical care.

These causative mechanisms alter the brain in differing ways. For example, positive end-expiratory pressure-induced impairment of cerebral venous outflow and systemic return can result simultaneously in increased intracranial pressure and reduced blood flow to the brain (Sasannejad et al., 2019). Cytokine activation of microglia may result in increased permeability of the blood-brain barrier and accumulation of amyloid- β (Sasannejad et al., 2019). All four delirium subtypes may result in transient or permanent changes in brain function, resulting in cognitive impairment months and years later.

Delirium is further characterized by hyperactive, hypoactive, or mixed states. The hyperactive state is characterized by anxious or agitated behavior with increased psychomotor

activity, whereas the hypoactive state presents as depression or sedation with decreased psychomotor activity. Importantly, the more common hypoactive state may be easily missed or dismissed in the emergency department or ICU (Han et al., 2009). Delirium risk factors are largely weighted on premorbid and comorbid disease (e.g., visual or hearing impairment, cerebrovascular disease, terminal illness), though age, male gender, and previous alcohol or drug use or abuse increase the risk (Wilber & Ondrejka, 2016).

Presence and duration of delirium in critical illness are predictive of cognitive impairment 12 months after discharge. This persistence of cognitive symptoms, along with the inability to carry out activities of daily living, is termed *post-ICU syndrome* (PICS; Colbenson et al., 2019). PICS is seen in several critical illnesses and is associated with unmitigated delirium (Kotfis et al., 2020). A multicenter study of a large cohort of critically ill patients identified that hypoxic and sedative-related subtypes of delirium were associated with PICS, evidenced by poor performance on the global cognitive scores of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998) at 3 months and 1 year postdischarge (Girard et al., 2018). Septic delirium also predicted RBANS scores at the 1-year follow-up. Importantly, study participants tended not to have an isolated subtype of delirium. That is, a patient who is critically ill with COVID-19 infection may have systemic inflammatory activity with the potential for sepsis and may also be sedated during prolonged mechanical ventilation.

To date, there are not reports about cognitive outcomes in COVID-19 infection, but the other disorders with similar critical illness conditions reported here lend some predictive value. The common cognitive findings across the disorders reviewed above are slightly difficult to specify, as several of the investigations, particularly for COPD and delirium, have only screened cognitive function using either the Mini-Mental State Examination (Folstein et al., 1975) or the Montreal Cognitive Assessment (Nasreddine et al., 2005). These screens provide preliminary evidence of impairment but do not provide specific data about affected cognitive domains. Nonetheless, it is highly likely that, consistent with PICS, COVID-19 survivors will present with deficits in attention, memory, and executive function, as well as psychomotor or visuospatial performance.

Potential for Comorbid Psychiatric Conditions

Psychiatric comorbidities, including PTSD, anxiety, or depression, are known to influence cognitive function. Along with the cognitive and physical symptoms, PICS is also marked by the presence of mood disorders (Marra et al., 2018), which contribute to a person's well-being and, consequently, their cognitive ability. The interplay between mood and cognitive functioning is particularly mingled early in recovery, such that mood disorders may affect subjective measures of cognition as well as complaints of fatigue and perceptions of quality of life (Brück et al., 2019).

Furthermore, the presence of any mood disorder will make the diagnosis of delirium more complicated because individuals with depression or PTSD will present with cognitive symptoms associated with that mood disorder. For example, memory impairments in major depressive disorder are well documented (Ahern & Semkowska, 2017), as are attention and executive function deficits in PTSD (McKinnon et al., 2016), and intrusive memories are common in both populations (Payne et al., 2019). Although PTSD, anxiety, and depression are beyond an SLP's scope of practice, their potential impact on the presentation of cognitive communication impairment following COVID-19 infection is critical for SLPs to recognize. When these factors are suspected, referral to appropriate psychological services is warranted (Paul-Brown & Ricker, 2002). Although treatment for these mood disorders will not be a focus of speech-language therapy, the impact of these disorders on cognitive communication must be understood and addressed (cf. Ponsford et al., 2020).

Physical, financial, logistic, mood, and cognitive (McIntyre et al., 2020) concerns will likely plague those recovering from COVID-19 infection. Screening of mood disorders is warranted throughout the continuum of care. Though it may be under the purview of psychological services in some settings, the entire team should make observations and note symptoms (recommendations per Brück et al., 2019). As with many clinical populations, comorbid psychiatric conditions can hinder intervention outcomes when not addressed. The entire rehabilitation team should be mindful of the "whole person," and referrals should be made to address psychological well-being.

Clinical Recommendations for COVID-19 Cognitive Communication Impairment Following COVID-19

The potential cognitive outcomes for COVID-19 survivors are best characterized by PICS, along with the potential for comorbid stroke. PICS is expected to be present in an unprecedented number of COVID-19 survivors (Stam et al., 2020) who will need care early on and throughout their recovery. In fact, Stam et al. 2020 have initiated a call for action to rehabilitation professionals. Two essential elements in this call are (a) screening by an interprofessional team, beginning early in the intensive care stay, and (b) a reliance on systematic reviews of rehabilitation interventions for guidance. Stam et al. stress that it is "important to turn to...rehabilitation medicine and their multiprofessional teams who are equipped and experienced in providing the necessary interventions for mental, cognitive, and physical impairments of the consequences of intensive care and mechanical ventilation" (pp. 3-4).

In response to that call, SLPs are in a unique position to guide the treatment of cognitive communication deficits that may be present. This tutorial's descriptions of COVID-19's potential effects on the brain should illustrate that, although COVID-19 is novel, the cognitive and linguistic symptoms SLPs will observe in survivors are not

novel. Nonetheless, the abundance of patients in critical care units provides an opportunity for practicing SLPs to recognize and broaden their role. Although there is a dearth of evidence regarding cognitive communication impairments in the ICU, acute, or inpatient rehabilitation settings, evidence from outpatient settings can serve as a roadmap. Additional guidance may come from an emerging literature on post-traumatic amnesia/delirium and other cognitive communication symptoms often seen in traumatic brain injury, which centers on evaluation and intervention for such impairments (Ponsford et al., 2014; Steel et al., 2017).

The following recommendations address the cognitive communication impairment that may be present in COVID-19 survivors. Poststroke aphasia or communication disorders associated with right hemisphere are not specifically addressed, though a thorough evaluation of speech and language is recommended (see Ramsey & Blake, 2020; Vallila-Rohter et al., 2018, for suggestions). Even in the presence of aphasia or right hemisphere communication disorder, comorbid cognitive impairment or mood disturbances should be considered in evaluation and intervention, as these comorbidities negatively influence functional outcomes (Revet et al., 2019). Thus, SLPs are urged to evaluate cognition and its cumulative effects on communication in COVID-19–related stroke survivors.

A recent special section on COVID-19 and Physical Medicine and Rehabilitation in the *American Journal of Physical Medicine and Rehabilitation* (Frontera, 2020) highlights several recommendations—objective and subjective evaluation, interprofessional rehabilitation, patient and family education, and consideration of comorbid conditions—that are relevant to speech-language pathology practice. Below is a nonexhaustive set of suggestions for cognitive communication evaluation and intervention based on those recommendations, along with evidence from the literature for suggestions about implementation.

Prehabilitation Phase

The primary concern in the acute care setting, particularly in the ICU, is survival. In most cases, this will involve SLPs for swallowing and feeding. However, if the SLP in that setting also charts baseline cognitive function, communication, and mood, then the next level of care will be able to assess change. This is similar to that suggested as “prehabilitation” by Silver (2020), to have wide adoption of physical and psychological assessments to document onset and development of symptoms early in critical care. An example of implementing a common evaluation tool for language within a health care system in acute care is reported by Vallila-Rohter et al. (2018).

Evaluation. Administering objective and subjective measures of cognitive function is highly recommended throughout the stages of care—that is, pre- and rehabilitation (Brück et al., 2019). Subjective (self-report) measures may indicate an interaction between psychological and cognitive symptoms that could be predictive of mood disorders, whereas objective measures can indicate more accurately the presence of a cognitive impairment that could

be addressed in rehabilitation. Also, subjective measurements may indicate subtle or mild cognitive impairments not detected or found to be within normal limits on objective measures, but that nonetheless differ from premorbid function. Recommended sources for evaluation in the ICU and acute care settings include objective mental status screens, such as the Montreal Cognitive Assessment, or measures more specific to delirium in critical illness and could be administered, for example, the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU; Ely et al., 2001). Assessment of alertness and agitation may also be warranted, such as the Richmond Agitation and Sedation Scale (RASS) scores (Wassenaar, Rood, et al., 2018). A subjective measure to indicate the different aspects of cognitive function on subjective relative to objective assessments in delirium that has been used in the ICU is the Cognitive Failures Questionnaire (Broadbent et al., 1982; Brück et al., 2019; Wassenaar, de Reus, et al., 2018).

Screening for delirium, likely conducted by physicians and nurses, is needed and often involves use of a rating scale (e.g., the Glasgow Coma Scale; Teasdale & Jennett, 1974; RASS). Additional screening for cognition is also necessary and may be conducted using mental status screeners and confusion assessments in the critical care setting (e.g., the CAM [Inouye et al., 1990] or the CAM-ICU [Ely et al., 2001]). Tracking change on such screens throughout the continuum of care will be beneficial in understanding the implications on cognitive impairment in recovery. Although the SLP is not likely the service provider administering these measures, the team of service providers (including the SLP) should agree upon and consistently acquire these measures to document for prehabilitation and to inform the rehabilitation effort.

Timing of intervention in the recovery process for cognition and communication is a primary consideration in evaluation of cognitive impairment in critical illness. As mentioned above, one source of delirium in the ICU is sedating and analgesic medications that can alter cognitive functions. Two of the seven studies reviewed by Deemer et al. (2020) staged cognitive intervention protocols based on the sedation levels of the participants using the RASS. That is, patients who were unarousable or deeply sedated were not treated, those who were moderately or lightly sedated took part in orientation exercises only, and those considered drowsy to alert took part in the complete intervention. This staging of the intervention protocol is reasonable, yielded appreciable improvement in cognitive outcomes, and provides a guide for clinicians across settings to begin employing diagnostics and intervention, similar to the utility of the Rancho Los Amigos Scale (Whyte, 2011) in traumatic brain injury.

These assessments provide common pieces of information that may be used across disciplines and setting and some data to discuss with the patient and family. Having the family/caregivers involved in the rehabilitation team will also be beneficial. For example, positive outcomes are emerging for the use of ICU diaries, completed by ICU staff and family/caregivers, that are used after discharge to

other units or to home, to help in clarifying for the patient the reality of the experience (Garrouste-Orgeas et al., 2017). These diaries have not been shown to reduce posttraumatic stress in ICU patients but could be utilized to support orientation and memory in intervention.

Intervention. Intervention approaches may be based, for example, on the recommendations of the International Cognitive Team (Ponsford et al., 2014; Togher et al., 2014) and more generally on those of Sohlberg and Turkstra (2011) for optimizing outcomes in cognitive communication intervention for SLPs. Although these recommendations are centered on service delivery in traumatic brain injury, the same principles generally apply for managing PICS. From the evaluation, the SLP should identify the individual's communication strengths and weaknesses, focusing on the modalities that are best understood (auditory or visual) and produced (verbal, written, gesture, pointing). Once the best mode for communicating is identified, the interprofessional team should be informed so that instructions can be routinely presented and elicited in the best modalities. This will optimize communication with the patient and will be a starting place for interprofessional intervention planning. For example, the intervention may focus initially on orientation to time, place, and person to reduce confusion. If a patient's best modality for communication is visual, then the SLP may develop orienting materials that can be placed prominently in the patient's room and used by all professionals and family members interacting in the patient's care. Spaced retrieval (cf. Hopper et al., 2005) may be used as an approach to strengthen memory for orientation facts and reinforced with all health care providers who visit a patient.

Rehabilitation Phase Evaluation

Once a COVID-19 patient is stable and able to engage in a longer diagnostic session, a self-report and/or informant report rating scale that assesses executive function, in particular in a person's day-to-day life, is warranted (e.g., Behavioral Rating Inventory of Executive Function–Adult; Roth et al., 2005). The Behavioral Rating Inventory of Executive Function–Adult provides the perspective of an informant (caregiver) who may have insight into the change in ability relative to pre-COVID-19 that may not be as clear to the patient yet. Next, a comprehensive cognitive communication battery will provide a glimpse into the nature of the cognitive impairment—executive function, memory, or attention—and how it is affecting communication (e.g., RBANS or Cognitive–Linguistic Quick Test; Helm-Estabrooks, 2018). Alternatively, the NIH Toolbox (Gershon et al., 2013) is a compendium of psychometrically sound standardized assessment tools with a large normative data set and is administered on an iPad. The NIH Toolbox Cognitive and Emotion batteries have published normative data (e.g., Akshoomoff et al., 2014) that are built in to the assessment that will provide results immediately.

At this point in recovery, consideration for social communication may also be important to determine if and how a cognitive communication impairment or mood

disorder may be affecting relationships. For this, the La Trobe Questionnaire (Douglas et al., 2000) is a standardized measure with extensive normative data that has been used in several neurogenic communication disorders. Although the La Trobe Questionnaire is primarily a social communication measure, it taps into several behaviors that are reliant on cognition and language (e.g., memory deficits, disinhibition/impulsivity, providing insufficient information, word-finding difficulty), as listed by the authors (Douglas et al., 2000).

Any of these assessments will provide data regarding potential deficits in attention and working memory, episodic memory, word list learning, visuospatial processing, and executive functions. They will provide vital information in determining strengths and weaknesses across cognitive domains that can guide decision making for cognitive communication intervention, as well as for advising modifications for other service providers. For example, the findings will inform the clinician about the information to provide for patient and family education, in which modalities to provide that information (verbal or written instruction), and the appropriate interventions.

Intervention: Need for Interprofessional Rehabilitation Approaches

Interprofessional rehabilitation, beginning early and continuing throughout the acute hospital stay, is essential in the care for individuals with PICS. Several randomized controlled trials are currently underway focusing on combinations of physical and cognitive training (cf. Fuke et al., 2018; Kondo et al., 2017; Wang et al., 2018), though most of these are being conducted by investigators in critical care medicine and not specific to the rehabilitation approaches that may be most advantageous over time. The data on interprofessional intervention approaches for delirium highlight the importance of early physical mobility to potentially improve at least the short-term physical concerns in PICS (Fuke et al., 2018; Kondo et al., 2017; Maheswaran et al., 2020). There are very few cognitive intervention trials for delirium or individuals in critical care in the literature (cf. for posttraumatic amnesia and cognitive communication impairment in Steel et al., 2017; Togher et al., 2014), with only seven reported in a recent systematic review (Deemer et al., 2020). That review concludes that there is insufficient evidence to indicate its use for PICS. Deemer et al. 2020 categorized the intervention strategies in these studies as either *training* (repeating standardized tasks), *stimulation* (group activities to enhance cognitive and social functioning), or *rehabilitation* (individualized approaches to improving functional abilities). Most of the studies were considered *stimulation* or a combination of *training + stimulation* and thus did not address *rehabilitation*. Furthermore, in all of these studies, there was poor description of the intervention procedures with lack of adequate experimental design to indicate generalizability/transfer of treatment effects. Nonetheless, the effects on outcome measures tended to be positive, providing support for the idea that early rehabilitation can reduce the incidence of delirium in critically ill patients.

Of concern is that, in all of the studies of cognitive interventions in PICS reviewed by Deemer et al., none involved SLPs. This is a shortcoming in the field that needs attention, particularly as COVID-19 is increasing the numbers of patients who will benefit from the unique knowledge and specialization in cognitive communication impairment that SLPs have.

Although the SLP referrals may be requested to assess postextubation effects on voice or dysphagia (Brodsky et al., 2020), it is imperative to recognize the potential for cognitive communication impairment and need for modifications of recommendations as part of the intervention plan. For example, if a patient has postextubation vocal trauma and has PICS, it may be that instructions and demonstrations utilized as part of the voice therapy will need to be written and practiced with high numbers of repetition, improving compliance to therapy procedures, or a patient may be more compliant with a medication schedule or exercise regimen if each is entered into a personal device with alarms as reminders with simple, written instructions. These modifications are reliant on the SLP identifying the modalities most effective for each patient. Last, rehabilitation should be continued in outpatient or at home—either in person or by telepractice (Lew et al., 2020).

Conclusions

With the COVID-19 pandemic comes a high likelihood of unprecedented numbers of survivors who may suffer from cognitive impairment. This is because the body's reaction to this novel coronavirus includes lung infection, which reduces the capacity of the lungs to provide sufficient oxygen for the organs, including the brain, to function optimally—dyspnea or hypoxia. The body also reacts to this infection with a hyperimmune response, creating a cytokine storm in which tissue, including brain tissue, may be damaged. Finally, the infection may result in increasing blood clotting factors in the body (hypercoagulation), which may result in emboli that can damage the brain in a consequent cerebrovascular accident. Importantly, these results are not unique to COVID-19 and are seen in many critical care illnesses, but the number of patients who will suffer these effects is unprecedented.

SLPs need to be aware of the potential for cognitive communication impairment and be a part of the rehabilitation team that is working to document and treat it. Diagnostic and intervention approaches should begin as early as possible in critically ill COVID-19 patients. That is, it should begin when patients are alert and only lightly sedated. Diagnostics should include objective and subjective measures of cognition as well as evaluation of mood. A primary focus of diagnostics is to document the presence or absence of impairment throughout the continuum of care, as well as to identify the level of impairment in each domain of cognitive functioning (orientation, processing speed, visuospatial processing, attention, memory, executive function) and how these affect the ability to communicate. This information will guide interactions with providers on

the health care team as well as aid in planning intervention. Importantly, SLPs are essential to identifying the effects of cognitive impairment on communication early in patient care, providing recommendations to the patient, family, and interprofessional team to optimize communication of patient education and therapeutic goals.

Author Contributions

Amy Ramage: Conceptualization (Lead), Formal analysis (Lead), Methodology (Lead), Writing – Original Draft (Lead), Writing – Review & Editing (Lead).

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References

- Ahern, E., & Semkowska, M. (2017). Cognitive functioning in the first-episode of major depressive disorder: A systematic review and meta-analysis. *Neuropsychology, 31*(1), 52–72. <https://doi.org/10.1037/neu0000319>
- Akshoomoff, N., Newman, E., Thompson, W. K., McCabe, C., Bloss, C. S., Chang, L., Amaral, D. G., Casey, B. J., Ernst, T. M., Frazier, J. A., Gruen, J. R., Kaufmann, W. E., Kenet, T., Kennedy, D. N., Libiger, O., Mostofsky, S., Murray, S. S., Sowell, E. R., Schork, N., . . . Jernigan, T. L. (2014). The NIH Toolbox Cognition Battery: Results from a large normative developmental sample (PING). *Neuropsychology, 28*(1), 1–10. <https://doi.org/10.1037/neu0000001>
- Arabi, Y. M., Harthi, A., Hussein, J., Bouchama, A., Johani, S., Hajeer, A. H., Saeed, B. T., Wahbi, A., Saedy, A., AlDabbagh, T., Okaili, R., Sadat, M., & Balkhy, H. (2015). Severe neurologic syndrome associated with Middle East respiratory syndrome corona virus (MERS-CoV). *Infection, 43*(4), 495–501. <https://doi.org/10.1007/s15010-015-0720-y>
- Ayalon, L., Ancoli-Israel, S., & Drummond, S. P. A. (2010). Obstructive sleep apnea and age: A double insult to brain function? *American Journal of Respiratory and Critical Care Medicine, 182*(3), 413–419. <https://doi.org/10.1164/rccm.200912-1805OC>
- Broadbent, D. E., Cooper, P. F., FitzGerald, P., & Parkes, K. R. (1982). The Cognitive Failures Questionnaire (CFQ) and its correlates. *British Journal of Clinical Psychology, 21*(1), 1–16. <https://doi.org/10.1111/j.2044-8260.1982.tb01421.x>
- Brodsky, M. B., Nollet, J. L., Spronk, P. E., & González-Fernández, M. (2020). Prevalence, pathophysiology, diagnostic modalities and treatment options for dysphagia in critically ill patients. *American Journal of Physical Medicine & Rehabilitation, Publish Ahead of Print*. <https://doi.org/10.1097/PHM.0000000000001440>
- Brück, E., Larsson, J. W., Lasselín, J., Bottai, M., Hirvikoski, T., Sundman, E., Eberhardson, M., Sackey, P., & Olofsson, P. S. (2019). Lack of clinically relevant correlation between subjective and objective cognitive function in ICU survivors: A prospective 12-month follow-up study. *Critical Care (London, England), 23*(1), Article 253. <https://doi.org/10.1186/s13054-019-2527-1>

- Castronovo, V., Canessa, N., Strambi, L. F., Aloia, M. S., Consonni, M., Marelli, S., Iadanza, A., Bruschi, A., Falini, A., & Cappa, S. F. (2009). Brain activation changes before and after PAP treatment in obstructive sleep apnea. *Sleep*, 32(9), 1161–1172. <https://doi.org/10.1093/sleep/32.9.1161>
- Castronovo, V., Scifo, P., Castellano, A., Aloia, M. S., Iadanza, A., Marelli, S., Cappa, S. F., Strambi, L. F., & Falini, A. (2014). White matter integrity in obstructive sleep apnea before and after treatment. *Sleep*, 37(9), 1465–1475. <https://doi.org/10.5665/sleep.3994>
- Chen, T., Wu, D., Chen, H., Yan, W., Yang, D., Chen, G., Ma, K., Xu, D., Yu, H., Wang, H., Wang, T., Guo, W., Chen, J., Ding, C., Zhang, X., Huang, J., Han, M., Li, S., Luo, X., . . . Ning, Q. (2020). Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study. *BMJ (Clinical Research Ed.)*, 368, m1091. <https://doi.org/10.1136/bmj.m1091>
- Colbenson, G. A., Johnson, A., & Wilson, M. E. (2019). Post-intensive care syndrome: Impact, prevention, and management. *Breathe*, 15(2), 98–101. <https://doi.org/10.1183/20734735.0013-2019>
- Deemer, K., Zjadewicz, K., Fiest, K., Oviatt, S., Parsons, M., Myhre, B., & Posadas-Calleja, J. (2020). Effect of early cognitive interventions on delirium in critically ill patients: A systematic review. *Canadian Journal of Anesthesia/Journal Canadien d'anesthésie*, 67, 1016–1034. <https://doi.org/10.1007/s12630-020-01670-z>
- Denke, C., Balzer, F., Menk, M., Szur, S., Brosinsky, G., Tafelski, S., Wernecke, K.-D., & Deja, M. (2018). Long-term sequelae of acute respiratory distress syndrome caused by severe community-acquired pneumonia: Delirium-associated cognitive impairment and post-traumatic stress disorder. *The Journal of International Medical Research*, 46(6), 2265–2283. <https://doi.org/10.1177/0300060518762040>
- Douglas, J. M., O'Flaherty, C. A., & Snow, P. C. (2000). Measuring perception of communicative ability: The development and evaluation of the La Trobe communication questionnaire. *Aphasiology*, 14(3), 251–268. <https://doi.org/10.1080/026870300401469>
- Ely, E. W., Inouye, S. K., Bernard, G. R., Gordon, S., Francis, J., May, L., Truman, B., Speroff, T., Gautam, S., Margolin, R., Hart, R. P., & Dittus, R. (2001). Delirium in mechanically ventilated patients: Validity and reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *JAMA*, 286(21), 2703–2710. <https://doi.org/10.1001/jama.286.21.2703>
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3), 189–198. [https://doi.org/10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)
- Francis, J., & Kapoor, W. N. (1992). Prognosis after hospital discharge of older medical patients with delirium. *Journal of the American Geriatrics Society*, 40(6), 601–606. <https://doi.org/10.1111/j.1532-5415.1992.tb02111.x>
- Frontera, W. R. (2020). *Special section on COVID-19* [Special issue] (Vol. 99). Wolters Kluwer.
- Fuke, R., Hifumi, T., Kondo, Y., Hatakeyama, J., Takei, T., Yamakawa, K., Inoue, S., & Nishida, O. (2018). Early rehabilitation to prevent postintensive care syndrome in patients with critical illness: A systematic review and meta-analysis. *BMJ Open*, 8(5), e019998. <https://doi.org/10.1136/bmjopen-2017-019998>
- Garg, S. (2020). Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019-COVID-NET, 14 states, March 1–30, 2020. *Morbidity and Mortality Weekly Report*, 69(15), 458–464. <https://doi.org/10.15585/mmwr.mm6915e3>
- Garrouste-Orgeas, M., Flahault, C., Fasse, L., Ruckly, S., Amdjar-Badidi, N., Argaud, L., Badie, J., Bazire, A., Bige, N., Boulet, E., Bouadma, L., Bretonnière, C., Floccard, B., Gaffinel, A., de Forceville, X., Grand, H., Halidfar, R., Hamzaoui, O., Jourdain, M., . . . Timsit, J.-F. (2017). The ICU-Diary study: Prospective, multicenter comparative study of the impact of an ICU diary on the wellbeing of patients and families in French ICUs. *Trials*, 18(1), Article 542. <https://doi.org/10.1186/s13063-017-2283-y>
- Gershon, R. C., Wagster, M. V., Hendrie, H. C., Fox, N. A., Cook, K. F., & Nowinski, C. J. (2013). NIH toolbox for assessment of neurological and behavioral function. *Neurology*, 80(11, Suppl. 3), S2–S6. <https://doi.org/10.1212/WNL.0b013e3182872e5f>
- Girard, T. D., Thompson, J. L., Pandharipande, P. P., Brummel, N. E., Jackson, J. C., Patel, M. B., Hughes, C. G., Chandrasekhar, R., Pun, B. T., Boehm, L. M., Elstad, M. R., Goodman, R. B., Bernard, G. R., Dittus, R. S., & Ely, E. W. (2018). Clinical phenotypes of delirium during critical illness and severity of subsequent long-term cognitive impairment: A prospective cohort study. *The Lancet: Respiratory Medicine*, 6(3), 213–222. [https://doi.org/10.1016/S2213-2600\(18\)30062-6](https://doi.org/10.1016/S2213-2600(18)30062-6)
- Guo, Y.-R., Cao, Q.-D., Hong, Z.-S., Tan, Y.-Y., Chen, S.-D., Jin, H.-J., Tan, K.-S., Wang, D.-Y., & Yan, Y. (2020). The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak—An update on the status. *Military Medical Research*, 7(1), Article 11. <https://doi.org/10.1186/s40779-020-00240-0>
- Han, J. H., Zimmerman, E. E., Cutler, N., Schnelle, J., Morandi, A., Dittus, R. S., Storrow, A. B., & Ely, E. W. (2009). Delirium in older emergency department patients: Recognition, risk factors, and psychomotor subtypes. *Academic Emergency Medicine*, 16(3), 193–200. <https://doi.org/10.1111/j.1553-2712.2008.00339.x>
- Harper, R. M., Kumar, R., Ogren, J. A., & Macey, P. M. (2013). Sleep-disordered breathing: Effects on brain structure and function. *Respiratory Physiology & Neurobiology*, 188(3), 383–391. <https://doi.org/10.1016/j.resp.2013.04.021>
- Helm-Estabrooks, N. (2018). Cognitive Linguistic Quick Test. In J. Kreutzer, J. DeLuca, & B. Caplan (Eds.), *Encyclopedia of clinical neuropsychology* (pp. 1–4). Springer. https://doi.org/10.1007/978-3-319-56782-2_9082-2
- Herridge, M. S., Moss, M., Hough, C. L., Hopkins, R. O., Rice, T. W., Biennu, O. J., & Azoulay, E. (2016). Recovery and outcomes after the acute respiratory distress syndrome (ARDS) in patients and their family caregivers. *Intensive Care Medicine*, 42(5), 725–738. <https://doi.org/10.1007/s00134-016-4321-8>
- Hess, D. C., Eldahshan, W., & Rutkowski, E. (2020). COVID-19-related stroke. *Translational Stroke Research*, 11(3), 322–325. <https://doi.org/10.1007/s12975-020-00818-9>
- Hopkins, R. O., & Jackson, J. C. (2006). Assessing neurocognitive outcomes after critical illness: Are delirium and long-term cognitive impairments related? *Current Opinion in Critical Care*, 12(5), 388–394. <https://doi.org/10.1097/01.ccx.0000244115.24000.f5>
- Hopper, T., Mahendra, N., Azuma, T., Bayles, K. A., Cleary, S., & Tomoeda, C. (2005). Evidence-based practice recommendations for working with individuals with dementia: Spaced-retrieval training. *Journal of Medical Speech-Language Pathology*, 13(4), xxvii–xxxiv.
- Inouye, S. K., van Dyck, C. H., Alessi, C. A., Balkin, S., Siegal, A. P., & Horwitz, R. I. (1990). Clarifying confusion: The confusion assessment method. A new method for detection of delirium. *Annals of Internal Medicine*, 113(12), 941–948. <https://doi.org/10.7326/0003-4819-113-12-941>

- Jiang, R., Burke, G. L., Enright, P. L., Newman, A. B., Margolis, H. G., Cushman, M., Tracy, R. P., Wang, Y., Kronmal, R. A., & Barr, R. G. (2008). Inflammatory markers and longitudinal lung function decline in the elderly. *American Journal of Epidemiology*, *168*(6), 602–610. <https://doi.org/10.1093/aje/kwn174>
- Joo, E. Y., Jeon, S., Kim, S. T., Lee, J.-M., & Hong, S. B. (2013). Localized cortical thinning in patients with obstructive sleep apnea syndrome. *Sleep*, *36*(8), 1153–1162. <https://doi.org/10.5665/sleep.2876>
- Klok, F. A., Kruip, M. J. H. A., van der Meer, N. J. M., Arbous, M. S., Gommers, D. a. M. P. J., Kant, K. M., Kaptein, F. H. J., van Paassen, J., Stals, M. a. M., Huisman, M. V., & Endeman, H. (2020). Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thrombosis Research*, *191*, 145–147. <https://doi.org/10.1016/j.thromres.2020.04.013>
- Kondo, Y., Fuke, R., Hifumi, T., Hatakeyama, J., Takei, T., Yamakawa, K., Inoue, S., & Nishida, O. (2017). Early rehabilitation for the prevention of postintensive care syndrome in critically ill patients: A study protocol for a systematic review and meta-analysis. *BMJ Open*, *7*(3), e013828. <https://doi.org/10.1136/bmjopen-2016-013828>
- Kotfis, K., Williams Roberson, S., Wilson, J. E., Dabrowski, W., Pun, B. T., & Ely, E. W. (2020). COVID-19: ICU delirium management during SARS-CoV-2 pandemic. *Critical Care (London, England)*, *24*(1), 176. <https://doi.org/10.1186/s13054-020-02882-x>
- Kumar, R., Farahvar, S., Ogren, J. A., Macey, P. M., Thompson, P. M., Woo, M. A., Yan-Go, F. L., & Harper, R. M. (2014). Brain putamen volume changes in newly-diagnosed patients with obstructive sleep apnea. *NeuroImage: Clinical*, *4*, 383–391. <https://doi.org/10.1016/j.nicl.2014.01.009>
- Lew, H. L., Oh-Park, M., & Cifu, D. X., (2020). The war on COVID-19 pandemic: Role of rehabilitation professionals and hospitals. *American Journal of Physical Medicine & Rehabilitation*, *99*(7), 571–572. <https://doi.org/10.1097/PHM.0000000000001460>
- Lin, W.-C., Huang, C.-C., Chen, H.-L., Chou, K.-H., Chen, P.-C., Tsai, N.-W., Chen, M.-H., Friedman, M., Lin, H.-C., & Lu, C.-H. (2016). Longitudinal brain structural alterations and systemic inflammation in obstructive sleep apnea before and after surgical treatment. *Journal of Translational Medicine*, *14*(1), Article 139. <https://doi.org/10.1186/s12967-016-0887-8>
- Lutsey, P. L., Norby, F. L., Gottesman, R. F., Mosley, T., MacLehose, R. F., Punjabi, N. M., Shahar, E., Jack, C. R., & Alonso, A. (2016). Sleep apnea, sleep duration and brain MRI markers of cerebral vascular disease and Alzheimer's disease: The Atherosclerosis Risk in Communities Study (ARIC). *PLOS ONE*, *11*(7), e0158758. <https://doi.org/10.1371/journal.pone.0158758>
- MacDonald, S. (2017). Introducing the model of cognitive-communication competence: A model to guide evidence-based communication interventions after brain injury. *Brain Injury*, *31*(13–14), 1760–1780. <https://doi.org/10.1080/02699052.2017.1379613>
- Maheswaran, J., Fromowitz, J., & Goldfarb, M. (2020). Early mobilization interventions in the intensive care unit: Ongoing and unpublished randomized trials. *Critical Care Research and Practice*, *2020*, 3281394. <https://doi.org/10.1155/2020/3281394>
- Marra, A., Pandharipande, P. P., Girard, T. D., Patel, M. B., Hughes, C. G., Jackson, J. C., Thompson, J. L., Chandrasekhar, R., Ely, E. W., & Brummel, N. E. (2018). Co-occurrence of post-intensive care syndrome problems among 406 survivors of critical illness. *Critical Care Medicine*, *46*(9), 1393–1401. <https://doi.org/10.1097/CCM.0000000000003218>
- Mart, M. F., & Ware, L. B. (2020). The long-lasting effects of the acute respiratory distress syndrome. *Expert Review of Respiratory Medicine*, *14*(6), 577–586. <https://doi.org/10.1080/17476348.2020.1743182>
- McIntyre, M., Robinson, L. R., & Mayo, A. (2020). Practical considerations for implementing virtual care in physical medicine and rehabilitation: For the pandemic and beyond. *American Journal of Physical Medicine & Rehabilitation*, *99*(6), 464–467. <https://doi.org/10.1097/PHM.0000000000001453>
- McKinnon, M. C., Boyd, J. E., Frewen, P. A., Lanius, U. F., Jetly, R., Richardson, J. D., & Lanius, R. A. (2016). A review of the relation between dissociation, memory, executive functioning and social cognition in military members and civilians with neuropsychiatric conditions. *Neuropsychologia*, *90*, 210–234. <https://doi.org/10.1016/j.neuropsychologia.2016.07.017>
- Mehta, P., McAuley, D. F., Brown, M., Sanchez, E., Tattersall, R. S., & Manson, J. J. (2020). COVID-19: Consider cytokine storm syndromes and immunosuppression. *The Lancet*, *395*(10229), 1033–1034. [https://doi.org/10.1016/S0140-6736\(20\)30628-0](https://doi.org/10.1016/S0140-6736(20)30628-0)
- Mikkelsen, M. E., Christie, J. D., Lanken, P. N., Biester, R. C., Thompson, B. T., Bellamy, S. L., Localio, A. R., Demissie, E., Hopkins, R. O., & Angus, D. C. (2012). The adult respiratory distress syndrome cognitive outcomes study: Long-term neuropsychological function in survivors of acute lung injury. *American Journal of Respiratory and Critical Care Medicine*, *185*(12), 1307–1315. <https://doi.org/10.1164/rccm.201111-2025OC>
- Mogi, T., Toda, H., Tatsuzawa, Y., Fukutomi, T., Soga, S., Shinmoto, H., & Yoshino, A. (2017). Clinically mild encephalopathy with a reversible splenial lesion and nonconvulsive status epilepticus in a schizophrenic patient with neuroleptic malignant syndrome. *Psychiatry and Clinical Neurosciences*, *71*(3), 212. <https://doi.org/10.1111/pcn.12492>
- Moriguchi, T., Harii, N., Goto, J., Harada, D., Sugawara, H., Takamino, J., Ueno, M., Sakata, H., Kondo, K., Myose, N., Nakao, A., Takeda, M., Haro, H., Inoue, O., Suzuki-Inoue, K., Kubokawa, K., Ogihara, S., Sasaki, T., Kinouchi, H., ... Shimada, S. (2020). A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *International Journal of Infectious Diseases*, *94*, 55–58. <https://doi.org/10.1016/j.ijid.2020.03.062>
- Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, *53*(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>
- Needham, E. J., Chou, S. H.-Y., Coles, A. J., & Menon, D. K. (2020). Neurological implications of COVID-19 infections. *Neurocritical Care*, *32*(3), 667–671. <https://doi.org/10.1007/s12028-020-00978-4>
- Otero, L., Figueredo, M. d. C., Riveros-Rivera, A., & Hidalgo, P. (2019). Cognitive impairment and obstructive sleep apnea. *Updates in Sleep Neurology and Obstructive Sleep Apnea*. <https://doi.org/10.5772/intechopen.82756>
- Panigada, M., Bottino, N., Tagliabue, P., Grasselli, G., Novembrino, C., Chantarangkul, V., Pesenti, A., Peyvandi, F., & Tripodi, A. (2020). Hypercoagulability of COVID-19 patients in intensive care unit. A report of thromboelastography findings and other parameters of hemostasis. *Journal of Thrombosis and Haemostasis*, *18*(7), 1738–1742. <https://doi.org/10.1111/jth.14850>
- Park, B., Palomares, J. A., Woo, M. A., Kang, D. W., Macey, P. M., Yan-Go, F. L., Harper, R. M., & Kumar, R. (2016). Disrupted

- functional brain network organization in patients with obstructive sleep apnea. *Brain and Behavior*, 6(3), e00441. <https://doi.org/10.1002/brb3.441>
- Paul-Brown, D., & Ricker, J. H.** (2002). *Evaluating and treating communication and cognitive disorders: Approaches to referral and collaboration for speech-language pathology and clinical neuropsychology* [Technical report]. American Speech-Language-Hearing Association. <https://doi.org/10.1044/policy.TR2003-00137>
- Payne, A., Kralj, A., Young, J., & Meiser-Stedman, R.** (2019). The prevalence of intrusive memories in adult depression: A meta-analysis. *Journal of Affective Disorders*, 253, 193–202. <https://doi.org/10.1016/j.jad.2019.04.055>
- Pinna, P., Grewal, P., Hall, J. P., Tavarez, T., Dafer, R. M., Garg, R., Oosteraas, N. D., Pellack, D. R., Asthana, A., Fegan, K., Patel, V., Conners, J. J., John, S., & Silva, I. D.** (2020). Neurological manifestations and COVID-19: Experiences from a tertiary care center at the frontline. *Journal of the Neurological Sciences*, 415, 116969. <https://doi.org/10.1016/j.jns.2020.116969>
- Ponsford, J., Janzen, S., McIntyre, A., Bayley, M., Velikonja, D., Tate, R., & INCOG Expert Panel.** (2014). INCOG recommendations for management of cognition following traumatic brain injury, Part I: Posttraumatic amnesia/delirium. *The Journal of Head Trauma Rehabilitation*, 29(4), 307–320. <https://doi.org/10.1097/HTR.0000000000000074>
- Ponsford, J., Lee, N. K., Wong, D., McKay, A., Haines, K., Downing, M., Alway, Y., Furtado, C., & O'Donnell, M. L.** (2020). Factors associated with response to adapted cognitive behavioral therapy for anxiety and depression following traumatic brain injury. *The Journal of Head Trauma Rehabilitation*, 35(2), 117–126. <https://doi.org/10.1097/HTR.0000000000000510>
- Poyiadji, N., Shahin, G., Noujaim, D., Stone, M., Patel, S., & Griffith, B.** (2020). COVID-19-associated acute hemorrhagic necrotizing encephalopathy: Imaging features. *Radiology*, 296(2), <https://doi.org/10.1148/radiol.2020201187>
- Ramsey, A., & Blake, M. L.** (2020). Speech-language pathology practices for adults with right hemisphere stroke: What are we missing? *American Journal of Speech-Language Pathology*, 29(2), 741–759. https://doi.org/10.1044/2020_AJSLP-19-00082
- Randolph, C.** (1998). *Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) manual*. The Psychological Corporation. <https://doi.org/10.1037/t15149-000>
- Ranucci, M., Ballotta, A., Di Dedda, U., Bayshnikova, E., Dei Poli, M., Resta, M., Falco, M., Albano, G., & Menicanti, L.** (2020). The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. *Journal of Thrombosis and Haemostasis*, 18(7), 1747–1751. <https://doi.org/10.1111/jth.14854>
- Revet, M., Immerzeel, J., Voogt, L., & Paulis, W.** (2019). Patients with neuropsychological disorders short after stroke have worse functional outcome: A systematic review and meta-analysis. *Disability and Rehabilitation*, 1–20. <https://doi.org/10.1080/0963288.2019.1693642>
- Richardson, S., Hirsch, J. S., Narasimhan, M., Crawford, J. M., McGinn, T., Davidson, K. W., Barnaby, D. P., Becker, L. B., Chelico, J. D., Cohen, S. L., Cookingham, J., Coppa, K., Diefenbach, M. A., Dominello, A. J., Duer-Hefele, J., Falzon, L., Gitlin, J., Hajizadeh, N., Harvin, T. G., . . . Zanos, T. P.** (2020). Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA*, 323(20), 2059. <https://doi.org/10.1001/jama.2020.6775>
- Rosenzweig, I., Glasser, M., Crum, W. R., Kempton, M. J., Milosevic, M., McMillan, A., Leschziner, G. D., Kumari, V., Goadsby, P., Simonds, A. K., Williams, S. C. R., & Morrell, M. J.** (2016). Changes in neurocognitive architecture in patients with obstructive sleep apnea treated with continuous positive airway pressure. *EBioMedicine*, 7, 221–229. <https://doi.org/10.1016/j.ebiom.2016.03.020>
- Roth, R. M., Isquith, P. K., & Gioia, G. A.** (2005). *Behavior Rating Inventory of Executive Function—Adult Version*. Psychological Assessment Resources.
- Sasanejad, C., Ely, E. W., & Lahiri, S.** (2019). Long-term cognitive impairment after acute respiratory distress syndrome: A review of clinical impact and pathophysiological mechanisms. *Critical Care*, 23, Article 352. <https://doi.org/10.1186/s13054-019-2626-z>
- Silver, J. K.** (2020). Prehabilitation may help mitigate an increase in COVID-19 peripandemic surgical morbidity and mortality. *American Journal of Physical Medicine & Rehabilitation*, 99(6), 459–463. <https://doi.org/10.1097/PHM.0000000000001452>
- Sohlberg, M. M., & Turkstra, L. S.** (2011). *Optimizing cognitive rehabilitation: Effective instructional methods*. Guilford. <https://www.guilford.com/books/Optimizing-Cognitive-Rehabilitation/Sohlberg-Turkstra/9781609182007>
- Spiezia, L., Boscolo, A., Poletto, F., Cerruti, L., Tiberio, I., Campello, E., Navalesi, P., & Simioni, P.** (2020). COVID-19-related severe hypercoagulability in patients admitted to intensive care unit for acute respiratory failure. *Thrombosis and Haemostasis*, 120(6), 998–1000. <https://doi.org/10.1055/s-0040-1710018>
- Stam, H. J., Stucki, G., & Bickenbach, J.** (2020). COVID-19 and post intensive care syndrome: A call for action. *Journal of Rehabilitation Medicine*, 52(4), 1–4. <https://doi.org/10.2340/16501977-2677>
- Steel, J., Ferguson, A., Spencer, E., & Togher, L.** (2017). Language and cognitive communication disorder during post-traumatic amnesia: Profiles of recovery after TBI from three cases. *Brain Injury*, 31(13–14), 1889–1902. <https://doi.org/10.1080/02699052.2017.1373200>
- Stevens, R. D., & Puybasset, L.** (2011). The brain–lung–brain axis. *Intensive Care Medicine*, 37(7), 1054–1056. <https://doi.org/10.1007/s00134-011-2233-1>
- Tahmasian, M., Rosenzweig, I., Eickhoff, S. B., Sepehry, A. A., Laird, A. R., Fox, P. T., Morrell, M. J., Khazaie, H., & Eickhoff, C. R.** (2016). Structural and functional neural adaptations in obstructive sleep apnea: An activation likelihood estimation meta-analysis. *Neuroscience and Biobehavioral Reviews*, 65, 142–156. <https://doi.org/10.1016/j.neubiorev.2016.03.026>
- Takanashi, J.** (2009). Two newly proposed infectious encephalitis/encephalopathy syndromes. *Brain and Development*, 31(7), 521–528. <https://doi.org/10.1016/j.braindev.2009.02.012>
- Tang, N., Li, D., Wang, X., & Sun, Z.** (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal of Thrombosis and Haemostasis*, 18(4), 844–847. <https://doi.org/10.1111/jth.14768>
- Teasdale, G., & Jennett, B.** (1974). Assessment of coma and impaired consciousness. A practical scale. *Lancet (London, England)*, 2(7872), 81–84. [https://doi.org/10.1016/S0140-6736\(74\)91639-0](https://doi.org/10.1016/S0140-6736(74)91639-0)
- Thakur, E. R., Sansgiry, S., Petersen, N. J., Stanley, M., Kunik, M. E., Naik, A. D., & Cully, J. A.** (2018). Cognitive and perceptual factors, not disease severity, are linked with anxiety in COPD: Results from a cross-sectional study. *International Journal of Behavioral Medicine*, 25(1), 74–84. <https://doi.org/10.1007/s12529-017-9663-2>
- The DSM-5 criteria, level of arousal and delirium diagnosis: Inclusiveness is safer.** (2014). The DSM-5 criteria, level of arousal and

- delirium diagnosis: Inclusiveness is safer. *BMC Medicine*, 12, Article 141. <https://doi.org/10.1186/s12916-014-0141-2>
- Tisoncik, J. R., Korth, M. J., Simmons, C. P., Farrar, J., Martin, T. R., & Katze, M. G.** (2012). Into the eye of the cytokine storm. *Microbiology and Molecular Biology Reviews*, 76(1), 16–32. <https://doi.org/10.1128/MMBR.05015-11>
- Togher, L., Wiseman-Hakes, C., Douglas, J., Stergiou-Kita, M., Ponsford, J., Teasell, R., Bayley, M., & Turkstra, L. S.** (2014). INCOG recommendations for management of cognition following traumatic brain injury, Part IV: Cognitive communication. *The Journal of Head Trauma Rehabilitation*, 29(4), 353–368. <https://doi.org/10.1097/HTR.0000000000000071>
- Torelli, F., Moscufo, N., Garreffa, G., Placidi, F., Romigi, A., Zannino, S., Bozzali, M., Fasano, F., Giulietti, G., Djonlagic, I., Malhotra, A., Marciani, M. G., & Guttman, C. R. G.** (2011). Cognitive profile and brain morphological changes in obstructive sleep apnea. *NeuroImage*, 54(2), 787–793. <https://doi.org/10.1016/j.neuroimage.2010.09.065>
- Tsivgoulis, G., Palaodimou, L., Katsanos, A. H., Caso, V., Köhrmann, M., Molina, C., Cordonnier, C., Fischer, U., Kelly, P., Sharma, V. K., Chan, A. C., Zand, R., Sarraj, A., Schellinger, P. D., Voumvourakis, K. I., Grigoriadis, N., Alexandrov, A. V., & Tsiodras, S.** (2020). Neurological manifestations and implications of COVID-19 pandemic. *Therapeutic Advances in Neurological Disorders*, 13, 1756286420932036. <https://doi.org/10.1177/1756286420932036>
- Vallila-Rohter, S., Kasparian, L., Kaminski, O., Schliep, M., & Koymen, S.** (2018). Implementing a standardized assessment battery for aphasia in acute care. *Seminars in Speech and Language*, 39(1), 37–52. <https://doi.org/10.1055/s-0037-1608857>
- Wadman, M., Couzin-Frankel, J., Kaiser, J., & Matacic, C.** (2020, April 17). How does coronavirus kill? Clinicians trace a ferocious rampage through the body, from brain to toes. *Science | AAAS*. <https://www.sciencemag.org/news/2020/04/how-does-coronavirus-kill-clinicians-trace-ferocious-rampage-through-body-brain-toes>, <https://doi.org/10.1126/science.abc3208>
- Wang, S., Hammes, J., Khan, S., Gao, S., Harrawood, A., Martinez, S., Moser, L., Perkins, A., Unverzagt, F. W., Clark, D. O., Boustani, M., & Khan, B.** (2018). Improving Recovery and Outcomes Every Day after the ICU (IMPROVE): Study protocol for a randomized controlled trial. *Trials*, 19(1), Article 196. <https://doi.org/10.1186/s13063-018-2569-8>
- Wassenaar, A., de Reus, J., Donders, A. R. T., Schoonhoven, L., Cremer, O. L., de Lange, D. W., van Dijk, D., Slooter, A. J. C., Pickkers, P., & van den Boogaard, M.** (2018). Development and validation of an abbreviated questionnaire to easily measure cognitive failure in ICU survivors: A multicenter study. *Critical Care Medicine*, 46(1), 79–84. <https://doi.org/10.1097/CCM.0000000000002806>
- Wassenaar, A., Rood, P., Boelen, D., Schoonhoven, L., Pickkers, P., & Boogaard, M. van den.** (2018). Feasibility of cognitive training in critically ill patients: A pilot study. *American Journal of Critical Care*, 27(2), 124–135. <https://doi.org/10.4037/ajcc2018467>
- Weisel, J. W., & Litvinov, R. I.** (2017). Fibrin formation, structure and properties. In D. Parry & J. Squire (Eds.), *Fibrous proteins: Structures and mechanisms* (pp. 405–456). Springer. https://doi.org/10.1007/978-3-319-49674-0_13
- Wen, X.-H., Li, Y., Han, D., Sun, L., Ren, P.-X., & Ren, D.** (2018). The relationship between cognitive function and arterial partial pressure O₂ in patients with COPD: A meta-analysis. *Medicine*, 97(4), e9599. <https://doi.org/10.1097/MD.00000000000009599>
- Weuve, J., Glymour, M. M., Hu, H., Sparrow, D., Spiro, A., Vokonas, P. S., & Litonjua, A. A.** (2011). Forced expiratory volume in 1 second and cognitive aging in men. *Journal of the American Geriatrics Society*, 59(7), 1283–1292. <https://doi.org/10.1111/j.1532-5415.2011.03487.x>
- Whyte, J.** (2011). Rancho Los Amigos Scale. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), *Encyclopedia of clinical neuropsychology*. Springer. https://doi.org/10.1007/978-0-387-79948-3_67
- Wilber, S. T., & Ondrejka, J. E.** (2016). Altered mental status and delirium. *Emergency Medicine Clinics of North America*, 34(3), 649–665. <https://doi.org/10.1016/j.emc.2016.04.012>
- Wilcox, M. E., Brummel, N. E., Archer, K., Ely, E. W., Jackson, J. C., & Hopkins, R. O.** (2013). Cognitive dysfunction in ICU patients: Risk factors, predictors, and rehabilitation interventions. *Critical Care Medicine*, 41(9 Suppl. 1), S81–S98. <https://doi.org/10.1097/CCM.0b013e3182a16946>
- World Health Organization.** (2020). *Clinical management of COVID-19: Interim guidance*. <https://apps.who.int/iris/handle/10665/332196>
- Wu, Y., Xu, X., Chen, Z., Duan, J., Hashimoto, K., Yang, L., Liu, C., & Yang, C.** (2020). Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain, Behavior, and Immunity*, 87, 18–22. <https://doi.org/10.1016/j.bbi.2020.03.031>
- Yaouhi, K., Bertran, F., Clochon, P., Mézenge, F., Denise, P., Foret, J., Eustache, F., & Desgranges, B.** (2009). A combined neuropsychological and brain imaging study of obstructive sleep apnea. *Journal of Sleep Research*, 18(1), 36–48. <https://doi.org/10.1111/j.1365-2869.2008.00705.x>
- Yin, M., Wang, H., Hu, X., Li, X., Fei, G., & Yu, Y.** (2019). Patterns of brain structural alteration in COPD with different levels of pulmonary function impairment and its association with cognitive deficits. *BMC Pulmonary Medicine*, 19(1), Article 203. <https://doi.org/10.1186/s12890-019-0955-y>
- Zhang, Q., Qin, W., He, X., Li, Q., Chen, B., Zhang, Y., & Yu, C.** (2015). Functional disconnection of the right anterior insula in obstructive sleep apnea. *Sleep Medicine*, 16(9), 1062–1070. <https://doi.org/10.1016/j.sleep.2015.04.018>
- Zhang, X., Ma, L., Li, S., Wang, Y., & Wang, L.** (2011). A functional MRI evaluation of frontal dysfunction in patients with severe obstructive sleep apnea. *Sleep Medicine*, 12(4), 335–340. <https://doi.org/10.1016/j.sleep.2010.08.015>