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COVID-19-Related Stressors and the Role of Cognitive Assessment

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Abstract

Objectives: Determine the prevalence of various stress-related factors among a sample of the US adult population in order to ascertain the potential impact upon cognitive functioning during the COVID-19 pandemic.

Methods: A US census, age-balanced sample of adults was recruited through an online survey platform in June 2020. Participants, blinded to the survey sponsor, completed a 20-question survey regarding activity participation as well as experiences and perceptions prior to and since the onset of the pandemic.

Results: A total of 693 respondents were included, of which 23% (n=159/693) were ≥60 years of age. Most (93.2%; n=646/693) reported experiencing one or more stressors. The prevalence of lifestyle-related stressors was high, with 47.2% and 63.1% reporting poor diet and poor sleep, respectively; and a substantially greater proportion indicated a worsening of diet, sleep, and financial stress since the pandemic began. The overall prevalence of health-related stressors was also high, with 63.5% reporting anxious symptoms—of which 26.6% were new onset, and 51.7% reporting depressive symptoms—of which 21.1% were new onset. Overall, 20.8% (n=144/693) described a worsening of their cognitive health since the pandemic began, with a greater likelihood of such among those who also experienced worsening of a health-related issue.

Conclusions: The prevalence of stressors known to affect cognitive functioning has increased during the pandemic, underscoring the necessity of proactively establishing routine neurocognitive assessment in clinical practice in order to better mitigate the impending mental health crisis.

Keywords: Cognitive Test; Cognition; Stress; COVID-19; Brain Fog

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Introduction

The pandemic resulting from COVID-19, the disease caused by the highly transmissible severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has profoundly affected nearly every aspect of society. Information on COVID-19 continues to evolve rapidly, however many facets of the current and ongoing research effort have already yielded useful evidence that may be beneficial to multiple groups—patients with severe COVID-19, asymptomatic patients, healthcare professionals, or the general public. While the current pandemic context is tragic in every sense, an opportunity to more effectively manage one of the most common lingering effects of this disease nevertheless presents itself.

Cognitive impairment is a frequent and persistent issue among patients recovering from critical illness. It is associated with the post-surgical recovery period, ICU stay, specific procedures and conditions such as coronary artery bypass grafting (CABG) and acute respiratory distress syndrome (ARDS), as well as previous pandemics (SARS-1, Middle East respiratory syndrome [MERS]) [1-4], and now, COVID-19 [5,6]. Cognitive function is also a key determinant of functional recovery in a post-ICU setting, as such, failing to detect cognitive impairment at discharge can result in missed therapeutic opportunities for those who would otherwise benefit from targeted cognitive intervention [7].

Patients recovering from critical illness frequently experience other mental health and medical issues. Many ofthese issues are, in-turn, associated with cognitive impairment. Major depressive disorder (MDD), anxiety disorders, and post-traumatic stress disorder (PTSD) are common comorbidities among this patient population [1,8,9]. In addition, studies during the COVID-19 pandemic [10,11], as well as previous studies during the SARS and MERS pandemics [11-14], demonstrate the psychological impact of these infections on not only patients, but also clinicians, caregivers, family members, and the general public. In fact, psychological distress after natural disasters and health crises is common and often persistent [13,15]. There are many psychosocial factors at play during the pandemic which have the potential to cause psychiatric injury (Table 1) [16]. Public health crises such as the COVID-19 pandemic are also associated with the

Table 1: Pandemic-related psychosocial factors [16].

• Fear of infecting family members	• Economic hardships and insecurity, including social determinants of health (eg, food insecurity)
• Frequency/extent of exposure to individuals infected with the virus	• Shortages of available resources (eg, foods, paper products, and personal protective equipment)
• Diminished personal freedoms	• Increased workloads
• Physical distancing, home confinement, quarantining, and loneliness	• Inconsistent messages and directives regarding public health measures
• Lack of access to testing and medical care for COVID-19	• Continuous media reporting about the pandemic and uncertainty surrounding its eventual outcome

exacerbation of existing as well as recurrence of remitted mental health issues (eg, substance use disorders [SUDs]) [17].These psychiatric disorders have been associated with a wide range of negative effects including increased somatic illnesses and impaired cognitive function [18,19].

The direct impact of the pandemic on cognitive function and the indirect effects that result from the increased frequency and severity of psychiatric disorders emphasize the need for prospective monitoring and management of cognitive dysfunction. A quick and easy-to-use cognitive assessment tool would be highly beneficial. Indeed, a2020 UN policy brief urged swift action to prevent long-term impact on mental health both during and after COVID-19 due to the likely effects of the pandemic on brain health [20].

The effects of COVID-19 will be pervasive; therefore, it is imperative that prospective action be taken in an attempt to allay one of the persistent, and perhaps most debilitating, issues affecting patients recovering from COVID-19—"brain fog", which is generally characterized by memory and concentration deficits and extreme fatigue [21]. This issue may not be limited to patients recovering from severe COVID-19, as it has also been reported in those with mild infections. Ensuring accurate and consistent assessment of neurocognition for patients recovering from a critical illness such as COVID-19 is vital to the effective management of cognitive impairment.

The aims of the current survey were to determine the prevalence of various stress-related factors among a sample of the US adult population and to better understand their impact on cognitive function during the COVID-19 pandemic.

Methods

Design of the Survey

A survey was conducted online in June 2020 via the Survey Monkey® platform which draws a representative sampling from a diverse database consisting of more than 2.5 million individuals who had previously volunteered to participate in surveys concerning a variety of topics. Participant profiles on the platform include demographic information such as sex, age, and geographical region, as well as other targeting attributes (eg, cell phone usage, job type).

The survey included 20 questions overall, and included multiple choice or multi-part, Likert-format questions. Eightof the items were used to determine additional demographic characteristics and 12 were used to determine the respondent's experiences, activity participation, or perceptions prior to, and since, the onset of the COVID-19 pandemic.Responses for 19 of the 20 questions were required. All respondents were blind to the sponsor of the survey and all responses were completely anonymous.

Population Selection

Participants were US adults ≥18 years of age. The target sample size was N=500 and balanced by age according to the most recent US census data across all demographics and US states. The total number of completed surveys were oversubscribed, as the female demographic was fielded faster than the male, and the older age brackets were filled prior tothe younger age brackets. These additional respondents were included in the survey results.

Results

A total of 693 participants were included in the survey group, representing a broad cross-section of the US adult population. One-hundred fifty-nine (23%) respondents were ≥60 years of age. A greater proportion of respondents were female (53.7%), working full-time (49.2%), and had private coverage as their primary health insurance (58.9%) (Table 2). There was a marginal change in employment status with 15.3% (n=106/693) being unemployed pre-pandemic, and 23.5% (n=163/693) unemployed at the time of the survey. Overall, most respondents indicated that they were negative for, or unaware of having COVID-19. Only 7.5% (n=52/693) reported having tested positive; among whom approximately 60% were symptomatic.

The overall self-reported prevalence of individual stressors was high, and 93.2% (n=646/693) of respondents reported either an exacerbation or new onset of one or more factors associated with cognitive impairment. The proportion of respondents among the overall group who reported existing or new onset positive and negative lifestyle habits is shown in Table 3. Approximately 25% of respondents reported a poor diet prior to the COVID-19 pandemic, and another 22% reported poor diet since the pandemic began. For one issue, financial strain, more study participants reported it as a new onset issue rather than it being present prior to the pandemic. Rates of new onset issues reflect the prevalence at the time of the survey (Jun 2020), approximately 12 weeks after most US states issued stay-at-home directives.

The overall self-reported presence of various health-related stressors was also high, with anxiety, depression, and overweight being most common (Table 4). Since the COVID-19 pandemic began, 26.6% and 21.1% reported new onset of anxious and depressive symptoms, respectively, increasing the overall incidence of these stressors to 63.5% and 51.7%, respectively.

Among the subgroup of patients who had not reported the issue prior to the pandemic, the proportions of respondents who began experiencing a poor diet, poor sleep, or financial strain during the pandemic were 29%, 44%, and 42%, respectively. Similarly, and the proportion without prior anxiety or depression who had begun experiencing symptoms was 42% and 30%, respectively.

A substantially greater proportion of respondents rated their diet, sleep, and degree of financial strain as "worse" or "much worse" since the pandemic began compared to those who reported an improvement in those categories (Figure 1).

Since the pandemic began, most respondents with anxiety and depression felt that their symptoms had gotten worse (Figure 2). Approximately one-third of those suffering from diabetes or hypertension, and about half of those reporting being overweight

Table 2: Respondent demographics (N=693).

Characteristic	Respondents, n (%)
Age, y	
<20	31 (4.5)
20-39	283 (40.8)
40-59	220 (31.7)
60-79	151 (21.8)
≥80	8 (1.2)
Gender	
Female	372 (53.7)
Male	313 (45.2)
Do not identify with a gender	8 (1.2)
Education level	
Did not complete high school nor obtain GED	41 (5.9)
Completed high school or obtained GED	261 (37.7)
Completed college	270 (39.0)
Completed graduate school	121 (17.5)
Employment status, pre-COVID-19	
Working full-time	341 (49.2)
Working part-time	108 (15.6)
Unemployed, seeking work	52 (7.5)
Unemployed, not seeking work	54 (7.8)
Retired	94 (13.6)
Disabled, unable to work	44 (6.4)
Employment status, current*	
Working full-time	284 (41.0)
Working part-time	109 (15.7)
Unemployed, seeking work	87 (12.6)
Unemployed, not seeking work	76 (11.0)
Retired	92 (13.3)
Disabled, unable to work	45 (6.5)
Primary health insurance	
Private insurance	408 (58.9)
Medicare/Medicaid	209 (30.2)
Tricare	13 (1.9)
Other	11 (1.6)
None	52 (7.5)
COVID-19 status*	
Negative	641 (92.5)
Positive, symptomatic	31 (4.5)
Positive, asymptomatic	21 (3.0)

*As of 8 Jun 2020.

Table 3: Prevalence of self-reported lifestyle factors (N=693).

Characteristic	Pre-pandemic, n (%)	Since pandemic began, n (%)	Overall, n (%)
Poor diet	175 (25.3)	152 (21.9)	327 (47.2)
Poor sleep	234 (33.8)	203 (29.3)	437 (63.1)
Financial strain	142 (20.5)	232 (33.5)	374 (54.0)
Exercising	348 (50.2)	122 (17.6)	470 (67.8)
Socializing	474 (68.4)	41 (5.9)	515 (74.3)
Alcohol use	245 (35.4)	74 (10.7)	319 (46.0)
Recreational drug use	70 (10.1)	46 (6.6)	116 (16.7)
Cigarette smoking	83 (12.0)	40 (4.3)	113 (16.3)

Table 4: Prevalence of self-reported health factors (N=693).

Characteristic	Pre-pandemic, n (%)	Since pandemic began, n (%)	Overall, n (%)
Anxiety	256 (36.9)	184 (26.6)	440 (63.5)
Depression	212 (30.6)	146 (21.1)	358 (51.7)
Diabetes	95 (13.7)	33 (4.8)	128 (18.5)
Hypertension	166 (23.9)	51 (7.4)	217 (31.3)
Overweight	287 (41.4)	91 (13.1)	378 (54.5)
Hearing loss	86 (12.4)	28 (4.0)	114 (16.5)
Blurred vision	89 (12.8)	52 (7.5)	141 (20.3)

believed their condition had worsened. Hearing and vision impairment also worsened among many participants.

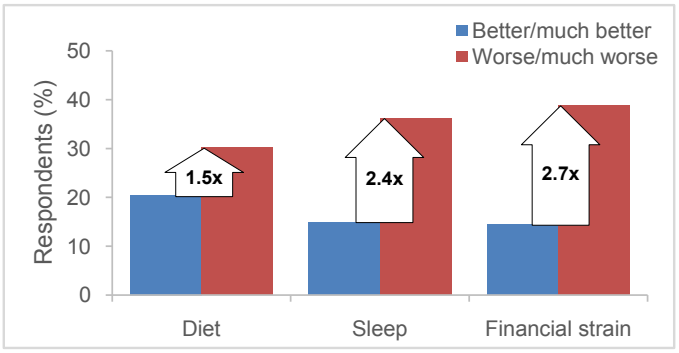

Figure 1: Current* rating of stressors among overall study group (N=693).
*As of 8 Jun 2020.

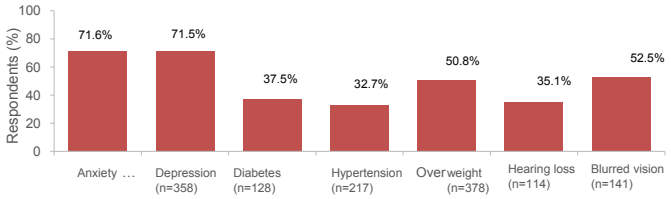

Figure 2: Proportion of respondents with specific health issue who reported it worsened since the COVID-19 pandemic began.

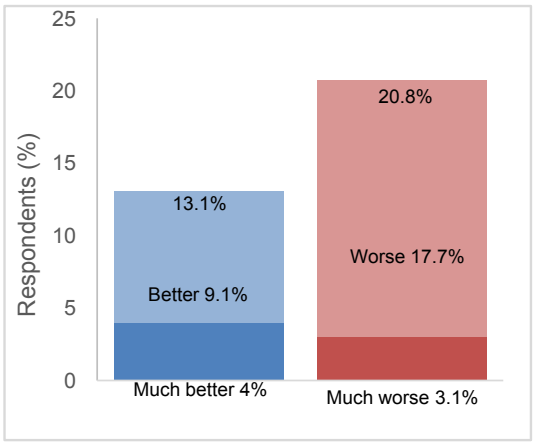

Figure 3: Self-rated cognitive health (N=693).

NOTE: This figure includes both those who reported the issue before the COVID-19 pandemic and rated it as "worse" or "much worse" since the pandemic began and all respondents with new onset of the issue since the COVID-19 pandemic began

Participation in certain activities was also markedly affected since the pandemic began compared with pre-pandemic participation levels. Many of respondents who reported exercising or socializing prior to the COVID-19 pandemic indicated a decreased level of participation since the pandemic began. An opposite effect was seen with alcohol, recreational drug, and tobacco use, which increased (data not shown).

Overall, 144 respondents (20.8%) indicated a worsening of their cognitive health since the pandemic began, compared to only 9.1% and 4% who felt their cognitive health was "better" or "much better", respectively (Figure 3).

Cognitive health was more likely to be rated as "worse" or "much worse" among respondents who also experienced an exacerbation of

one or more of the specific health issues shown in Figure 2.Among those with anxiety or depression, more than twice as many respondents felt their cognitive health had deteriorated rather than improved (Figure 4). A similar, though less pronounced, effect was seen among those with hypertension (1.3x) or blurred vision (1.4x), but not among those with diabetes, who were overweight, or had hearing loss (data not shown).

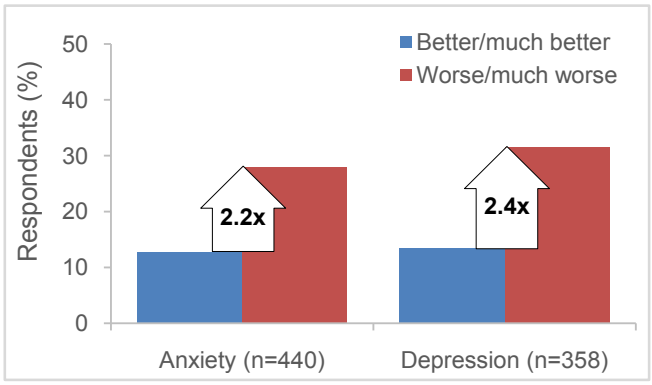

Figure 4: Current* ratings of cognitive health among respondents with anxiety or depression either prior to, or new onset during, the COVID-19 pandemic.
*As of 8 Jun 2020.

Discussion

During the COVID-19 pandemic, there have been reports of a rising incidence of common mental health disorders, such as major depressive disorder (MDD) and various anxiety disorders, as well as other comorbid health issues, many of which have well-documented associations with cognitive impairment. The increased likelihood of cognitive deficiencies is not limited to patients with severe infections, nor only those who are (or were) COVID-19 positive, but is being seen in the general population as a whole.

A large (n=336,525), US census sample analysis showed an approximately 3-times greater likelihood of a positive screen for anxiety (RR 3.76; 95% CI 3.57-3.96), depression (RR 3.56; 95% CI 3.36-3.77), or both (RR 3.26; 95% CI 3.12-3.41) during the period of April 23-May 4, 2020 compared to the first half of 2019 [22]. Such a substantial increase in prevalence aligns with our findings where the rates of self-reported anxiety and depression increased considerably from pre-COVID-19 to those reported at the time of the survey.

Stress Factors Associated with Changes in Cognition

The COVID-19 pandemic has had a profound effect on the daily life of the general population. There areimmediate and near-term consequences, but also long-term implications for the future mental health of those affected. Studies have documented increased rates of anxious and depressive symptoms [22,23], as well as poor dietary choices [24], substance use [10,17], sleep issues [23], and financial worry [25], among the general public during the pandemic. Declining rates of exercise [24], and socializing [23], have also been found. These issues are new to many people as a result of the pandemic [25], however, many others were experiencing one or more of the problems prior to the pandemic which have worsened since. This is confirmed by our findings, where the proportion of people reporting poor diet or poor sleep nearly doubled from the pre-COVID-19 rates.

Prior studies have established that patients with a mood disorder or anxiety disorder experience disproportionate rates of cognitive impairment [19,26]. The same is true for cardiovascular [27,28],and metabolic-related dysfunction [27-30], vision and hearing impairments [31], and poor sleep hygiene [32]. Many of these comorbidities have been exacerbated during the COVID-19 pandemic. Indeed, in our study cognitive health was more likely to have worsened among respondents who also reported a worsening of other issues such as depression or anxiety—disease states with symptoms overlapping those typical of "brain fog" [21].

Many people experience multiple stressors simultaneously, which compound the risks associated with other stressors. For example, not only does the presence of a mood disorder affect cognition [19], but it is also associated with poor nutritional choices and lack of adherence to an exercise regimen—both of which are also known to affect cognition [33].

Addressing lifestyle risk factors is important and doing so has been shown to be effective in improving cognition in a relatively short time-frame [34], therefore a brief review of the association between select factors and cognitive impairment follows.

Lifestyle Factors: Diet

Adults who report healthy dietary habits typically rate their cognitive status as very good [35]. Poor dietary choices, such as a high sugar intake, can increase the risk of neurocognitive impairment [32],whereas lower intake of saturated fats has been associated with improved cognitive performance [36]. Healthy diets, have been associated with improved cognitive functioning or decreased risk of developing Alzheimer's disease [36,37].

While diet is a modifiable risk factor, many find it challenging to maintain a healthy diet [32,35,38]. The COVID-19 pandemic has increased this challenge; through disinclination to venture to a grocery store or financial insecurity due to job loss, access to affordable and nutritious foods may be limited. Further, patients with mental health disorders often make poor dietary choices [32]. Similarly, our survey showed that respondents had increased levels of depression and anxiety as well as poor diet during this pandemic, all of which can impact cognitive function.

Lifestyle Factors: Exercise

Physical exercise plays an important role in cognitive health [37], with an inactive lifestyle increasing the risk of cognitive decline [32,39-43]. Conversely, increased physical activity is associated with improved executive function and learning ability, a greater facilitation of neuroplasticity, increased peripheral brain-derived neurotrophic factor (BDNF) levels, increases in gray and white matter regions of the brain, and a reduced risk of dementia and mild cognitive impairment (MCI) [36].

One consequence of the COVID-19-associated stay-at-home orders is an overall reduction in available exercise options. As facilities such as gyms and yoga studios have closed their doors—some temporarily, some permanently—the public has been forced to find alternatives. However, not everyone has been either successful in doing so or has even chose to do so, as demonstrated by the 42.8% of respondents in our survey indicating a decrease in their exercise levels since the pandemic began.

Lifestyle Factors: Socializing

There is evidence from observational and longitudinal studies showing an association between a lack of social interaction and cognitive health [28,44-46].

Social connectedness confers substantial benefit by facilitating individual and group resistance to the negative effects on mental health [47-49]. Social participation has been shown to moderate the negative impact on cognitive decline after large-scale public crises [15,50].

Results from several studies in older adults underscore the importance of maintaining a moderate degree of socialization due to its protective effect on risk of cognitive decline [44-46]. Yet, the negative effects from a lack of social interaction are not limited to the chronic context often present among the elderly. In a six year, longitudinal study of 2,995 older adults, both chronic and transient deficiencies in socializing were associated with lower scores on the Mini Mental Status Exam (MMSE) [51]. As opportunities for in-person social engagement are understandably limited during the pandemic—a presumably transient context—the risk of cognitive impairment remains a concern. This was demonstrated in our survey, which showed that 83.1% of respondents reported a decrease in socializing.

Lifestyle Factors: Finances

The current pandemic has had a negative economic impact on a substantial portion of the general population. Lack of stable employment or increased financial strain increases the risk depressive symptoms, which can negatively affect cognition [52]. In our survey, 8.2% reported being newly unemployed and 42.5% reported either a worsening or new onset of financial stress since the pandemic began.

Further compounding direct economic issues such as job loss and financial insecurity during the COVID-19 pandemic, is the downstream effect of decreased access to healthcare due to the employer-based insurance model prevalent in the US. This loss of health insurance will undoubtedly negatively affect both physical and mental health—thus elevating risk of the cognitive-related consequences of the pandemic [52,53].

Lifestyle Factors: Substance Use

Excessive alcohol use, recreational drug use, and smoking are all factors known to exert a detrimental effect on neurocognition [37,54]. A large-scale analysis detailed the association between substance use and deficits in volume or thickness in numerous brain regions [55].

Additionally, the 2020 report from the Lancet Commission on dementia has identified both smoking and alcohol consumption (>21 units/week) as risk factors for dementia, with relative risks of 1.6 (95% CI 1.2-2.2) and 1.2 (95% CI 1.1-1.3), respectively [28]. Results from our survey highlight how such risk has increased, as approximately 26% of those who consumed alcohol and 40% of those who used recreational drugs or tobacco prior to the pandemic reported an increase in these harmful behaviors since the COVID-19 pandemic began.

Health Factors: Anxiety/Depression

Cognitive impairment is present in up to 80% of patients with depression [56]. In a large systematic review (249 studies) examining the prevalence and clinical associations of cognitive disorders, the majority of studies showed a strong relationship between depressive or anxious symptoms and the presence or severity of cognitive impairment [19]. Further, depressive symptoms are a recognized risk factor for dementia (RR 1.9; 95% CI 1.6-2.3) [27], as well asa more rapid decline of cognitive function [57].

Depressive disorders can affect cognition by reducing information processing speed and reducing cognitive reserves [58,59], and anxiety symptoms can impact verbal learning [58,60]. Studies in patients with a mood disorder have described abnormalities in many cognitive domains including executive function, working memory, attention, and psychomotor processing [18,61]. In our survey we found high rates of new onset (21.1%; n=146/693) and worsening (51.9%; n=110/212) depression, as well as new onset (26.6%; n=184/693) and worsening (51.2%; n=131/256) anxiety. among both of which a substantially greater proportion reported cognitive dysfunction(Figure 4).

Health Factors: Cardiovascular/Metabolic Issues

Hypertension, obesity, diabetes, and metabolic syndrome have all been linked to an increased risk of cognitive decline or acceleration of the progression of MCI to dementia [27-29,37]. The 2020 report from the Lancet Commission on dementia noted relative risks of 1.6 (95% CI 1.2-2.2) for hypertension, 1.6 (95% CI 1.3-1.9) for obesity, and 1.5 (95% CI 1.3-1.8) for diabetes [27]. The present survey showed new onset rates of hypertension, obesity, and diabetes of 7.4%, 13.1%, and 4.8%, respectively; and among those reporting those conditions prior to the pandemic, 12.0%, 35.2%, and 15.8% reported them worsening.

Health Factors: Hearing/Vision Impairments

Hearing loss can negatively affect cognition by increasing cognitive load, requiring greater effort to understand speech, and slowing recall ability [62]. Ameta-analysis (36 studies; n=20,264) showed a significant association between audiological impairment and cognitive impairment (OR 2.00; 95% CI 1.39-2.89; p<0.001) or dementia (OR 2.42; 95% CI 1.24-4.72; p<0.01) [63].

Similar to earlier studies demonstrating the association between hearing impairment and cognition [31,64], two large longitudinal studies published in 2020 have reported a linear trend of significantly higher risk of cognitive function decline corresponding to degree of hearing loss. The relative risks for men with mild, moderate, or severe hearing loss were 1.30 (95% CI 1.18-1.42), 1.42 (95% CI 1.26-1.61), and 1.54 (95% CI 1.22-1.96), respectively [65]. The relative risks for women with mild, moderate, or severe hearing loss were 1.35 (95% CI 1.25-1.47), 1.39 (95% CI 1.24-1.56), and 1.40 (95% CI 1.21-1.75), respectively [66].

A 2019 report from the US Centers for Disease Control and Prevention (CDC) reported a greater prevalence of cognitive decline among individuals with impaired vision compared to those without (18% vs. 4%) [67]. Studies have shown an association between vision impairment and cognitive decline (OR 1.78; 95% CI 1.21-2.61) [31], with worsening visual acuity being associated with rate of worsening of cognitive function [68]. For those with both vision and hearing impairments, there is an even greater risk of cognitive decline (OR 2.19; 95% CI 1.26-3.81) [31]. In our survey, approximately 35% of respondents reported either new onset or a worsening of existing hearing loss, and approximately 53% reported either new onset or a worsening of existing vision impairment.

Health Factors: Sleep-Related Issues

Observational studies have reported an association between insomnia or sleep apnea and risk of cognitive decline [37]. Poor sleep hygiene is also associated with worse mental health [32]. The American Academy of Sleep Medicine consensus statements report that insufficient sleep (<7 hours per night)is associated with impaired performance, increased errors, and greater risk of accidents [69]. Data also suggests a causal link between circadian rhythm disturbances and the onset of neuropsychiatric disorders, such as Alzheimer's disease [32,36]. The current survey showed new onset of sleep issues in 29.3%

of respondents, and 21.4% of those reporting pre-pandemic sleep difficulties felt the issue had worsened since the COVID-19 pandemic began.

Exacerbation of stress factors

Quarantine measures during the COVID-19 pandemic have been associated with a greater level of mental distress [53,70], specifically an increased risk of acute stress disorder, and in younger patients, adjustment disorder [53]. The duration of quarantine has also been linked to an increased prevalence of PTSD and MDD [8,9].

The long-term effects of the additional or greater severity of various stressors on cognition during or after the pandemic is concerning. Early-life stress is associated with increased levels of cognitive impairment in later life [71,72]. The increased levels of stress that survey respondents attributed to the current pandemic environment, suggests impending widespread cognitive issues among the US population.

Severe Illness Associated with Changes in Cognition

The full scope of the acute and post-infectious neurological manifestations of COVID-19 has yet to be determined. Neurocognitive issues have been reported in COVID-19 cases and there is a substantial amount of data establishing the association between cognitive issues and post-intensive care syndrome (PICS), ARDS, and other critical illness. However, an indirect impact on cognition is also likely, as patients with COVID-19, PICS, or ARDS also experience greater rates of many of the previously discussed causal factors for cognitive impairment (i.e., depression, sleep-related issues) [1-3,6,73].

Direct Impact

Cognitive impairment is a common concern among post-surgical patients and those discharged from an ICU setting, and it is well established that ICU admission is associated with deficits in multiple cognitive domains [74,75]. Clinically, such patients are often referred to as "neuro-unfocused" as they frequently exhibit symptoms indicating one or more deficits in attention or language processing upon examination. Impairment is not limited to an inpatient setting, as a retrospective analysis (n=3,673) from the Mayo Clinic found ICU admission to be associated with significantly greater declines in global composite scores ($p<0.001$), memory ($p=0.002$), attention/executive ($p=0.016$), and visuospatial domains ($p=0.041$) over a median follow-up of 2.5 years [75].

A cross-sectional study of patients (n=125) with COVID-19 showed 31% experienced acute alterations in behavior, cognition, consciousness, or personality [76]. Similar results were reported in both a smaller study (n=58) of patients hospitalized with ARDS due to COVID-19 where neuropsychological impairment was noted in 33% after discharge [5], and in a much larger study of 841 patients with severe COVID-19 which reported approximately 22.5% of the study population experienced one or more neuropsychiatric symptoms [77].

A 2020 systematic review and meta-analysis by Rogers JP, et al. (2020) [1], that assessed the neuropsychiatric presentations of coronavirus infections revealed that impairments to attention, concentration, and memory were relatively common symptoms during the acute phase (25 studies) of prior pandemics such as SARS and MERS, as well as the recovery phase (40 studies).

Many patients with severe disease will present with impaired neurological status, as shown in one cohort analysis (n=140) where 84.3% of those admitted to the ICU for ARDS due to COVID-19 had an abnormal neurologic examination [78]. And in another study, an increased incidence of altered mental status among patients hospitalized with COVID-19 was reported [76].

Abnormal neuropsychological evaluation has been associated with significantly longer durations of invasive mechanical ventilation($p=0.011$) and ICU stay ($p=0.017$), suggesting a worse prognosis if neurological issues are present [78]. Patients with severe COVID-19 are also more likely to experience PICS [53], which includes cognitive issues. An assessment by Helms J, et al. (2020) [5], has reported 33% of patients experienced dysexecutive syndrome after discharge from the ICU.

The systematic review and meta-analysis of SARS and MERS studies from Rogers JP, et al. (2020) [1], showed that severe viral infections can result in neuropsychiatric issues, including those affecting cognitive domains, such as confusion (incidence: 27.9%; 95% CI 20.5-36.0) and impaired memory (incidence: 34.1%; 95% CI 26.2-42.5) [1]. Cognitive issues are also common in patients who have suffered from ARDS, as longitudinal studies have shown impairments to memory, attention, and processing speed domains persisting up to five years post-discharge [2,3].

Results from arecent 3-month, prospective study showed micro-structural changes in the brains of patients recovering from COVID-19 [79], indicating potential for long-term effects on neurocognition. So, fittingly, researchers have highlighted the urgent need for prospective cohort studies to better understand the long-term impacts of COVID-19 on neurological function [80].

Indirect Impact

In addition to the direct effects of such conditions on cognition, patients with COVID-19, PICS, or ARDS may experience an exacerbation or new onset of some of the stress factors previously described (e.g., mood disorders, lack of exercise), where by indirectly contributing to cognitive impairment.

Data from the recent systematic review and meta-analysis by Rogers JP, et al. (2020) [1], show a point prevalence of PTSD, depression, and anxiety after severe coronavirus infections such as SARS or MERS of 32.2% (95% CI 23.7-42.0), 14.9% (95% CI 12.1-18.2), and 14.8% (95% CI 11.1-19.4), respectively [1]. Early results of follow-up studies in patients with COVID-19 suggest that lingering pulmonary effects will likely negatively impact physical exercise capabilities [81], a premise supported by studies of other pandemics [82,83]. And in an Italian study (n=103), more than 90% patients with COVID-19 also reported at least one neurological symptom, with sleep impairment being most common [6].

Also, of concern, is that a lack of contact with loved ones during quarantine or hospitalization in severe cases of COVID-19 may lead to increased psychological instability, and thus indirectly affect cognition. When one is prohibited from visiting with a hospitalized family member, the resultant stress is unquestionably increased [53]. Additionally, recent research has shown that anxiety is increased substantially when a relative has tested positive for COVID-19 (OR 3.00; 95% CI 2.38-3.80) [84,85].

Mental Health and Stress Management Considerations

Typically, care in most health systems is primarily reactive rather than proactive, often resulting in sub-optimal levels of interdisciplinary collaboration and inhibiting more timely access to appropriate services and therapies for patients [86].

This suggests the need for a more integrative, patient-centric model, one where routine cognitive assessment would be a beneficial component. Proposed models of multidisciplinary teams for patients recovering from COVID-19 have included cognitive rehabilitation—of which consistent assessment and monitoring of potential cognitive impairment would be a part [87,88]. Newly published consensus statements on post-COVID-19 rehabilitation recommend that plans be individualized according to the patient's needs and comorbidities with one aim being relief of psychological distress [73]. Detailed neuropsychological testing and follow-up may be required to determine the extent of cognitive dysfunction during the recovery phase of COVID-19 [89].

There is an increased need for attentive psychological support during the current pandemic across the general population, with an even more acute need among specific groups (e.g., healthcare workers) at greater risk for COVID-19-related stress [11,16,90].

The risk of viral exposure has been positively correlated with clinically significant psychological stress among healthcare workers (OR 1.74; 95% CI 1.50-2.03; p<0.001) [12]. Due to this increased stress and its negative consequences, some systems and facilities have established dedicated teams to provide mental health support specifically for these front-line workers [53,90]. Monitoring for changes in cognition is of even greater importance during a pandemic for groups predisposed to cognitive dysfunction, such as the elderly or patients with multiple sclerosis [53,91].

Options for Cognitive Testing and Monitoring

Mental health support systems should specifically include cognitive testing, and in light of the need for physical distancing, testing modalities should be used that do not require the face-to-face contact necessary for many traditional neuropsychiatric tests. A Lancet position paper stated that routine measurement of meaningful and valued outcomes related to service use may be beneficial in the arena of post-pandemic mental health [53]. The use of computerized neuropsychological assessment tools has also been suggested by Lancet [28].

RCT data demonstrate the efficacy of cognitive rehabilitation programs to improve cognitive performance and functional outcomes among post-ICU patients [92], as such, the routine assessment and monitoring of cognition would be an integral component. An easy and unencumbered process for doing so, would benefit both the patient and clinician.

The presence of stress disorders and related symptoms resulting from a public health emergency can persist in varying degrees well after the emergency has passed, therefore it is imperative that individuals suffering such distress be monitored long-term [13,93]. The same holds true for those recovering from COVID-19, as cognitive deficits can follow infection but not be evident until months later, and so prospective neuropsychiatric testing at various time points is recommended [11,73].

Should a patient who suffered from COVID-19 wish to go back to work, they may require certain accommodations. Cognitive testing can be helpful in determining the presence and extent of any cognitive changes, prior to requesting specific accommodations from an employer [94].

Studies have shown objective and comprehensive neurocognitive tests to be superior in detecting cognitive impairment. In a 2020 systematic review (46 studies) the mean prevalence of cognitive impairment was higher with objective assessment (54%; 95% CI 51-57) than with subjective assessment (35%; 95% CI 29-41) at 3 months follow-up [7]. The use of more comprehensive cognitive batteries was also associated with better detection of cognitive impairment than the MMSE at both 3 months and 12 months follow-up [7].

It can be a challenge to meet the increased demand for cognitive testing in the pandemic setting, since some tools, while validated for telephone administration(e.g., Montreal Cognitive Assessment [MoCA]), may require substantial adaptation to be of satisfactory utility during virtual encounters within a pandemic context [95]. Other limitations of traditional paper and pencil cognitive tests during the COVID-19 pandemic have included logistical challenges (e.g., personal protective equipment obscuring a wristwatch) and perceptual problems (e.g., speaking through a mask to patients with possible processing or hearing impairments) [96].

A quick and easy-to-use tool to objectively measure cognitive impairment, one not requiring a face-to-face interview between clinician and patient, could be of considerable utility. A portable computerized device to objectively measure cognition located in a private room, needing only basic instructions may help maximize physical distancing. The device could be disinfected after every use.

One limitation of the current survey is the self-reporting of anxious and depressive symptoms. Other analyses have utilized validated assessment tools (e.g., GAD-2, PHQ-2) to determine rates of anxiety and depressive disorders among survey participants [22]. Although such methods likely result in much lower incidence rates than those found in our survey, the trend of increasing rates of both disorders from before to during the current pandemic confirm the deterioration of mental health status. Another limitation is the possibility that some portion of the underserved population (low or no education, very low income) may be unaccounted for due to a lack of computer and/or internet access. However, there is no reason to believe the deterioration of mental and physical health would be less among that population. Additional limitations include the cross-sectional survey design which precluded determination of any potential causal relationships as well as the lack of objective measurement of both cognition and the worsening of health issues included in the survey. There are little data on whether the effects seen in the survey are transient, however this does highlight the need for ongoing, objective follow-up during and after this type of public health crisis.

Conclusions

The COVID-19 pandemic has devastated many aspects of everyday life—and continues to do so. The stressors arising from the current pandemic are pervasive, not only among those who have COVID-19 or are recovering from it, but also among those who care for such patients as well as the general population. This should serve as a warning for potential impending cognitive challenges. The inclusion of routine neurocognitive assessment within a patient-centric paradigm will facilitate the proactive provision of care. Furthermore, healthcare systems and facilities must take steps to avert a national and global mental health crisis. The routine assessment, and ongoing monitoring of, cognitive impairment in a quick and efficient manner is crucial to minimizing the ongoing psychological damage as well as the often unshakable pernicious brain-fog-like effects of the COVID-19 pandemic.

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