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Neurocognitive and Psychosocial Characteristics of Pediatric Patients With Post-Acute/Long-COVID: A Retrospective Clinical Case Series

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Abstract

Objective: Studies suggest a large number of patients have persistent symptoms following COVID-19 infection—a condition termed “long COVID.” Although children and parents often report cognitive difficulties after COVID, very few if any studies have been published including neuropsychological testing.
Methods: A retrospective chart review was completed for the first 18 patients referred for a neuropsychological evaluation from a multidisciplinary pediatric post-COVID clinic. The neuropsychological screening battery assessed verbal fluency and category switching, attention, working memory, processing speed, and verbal learning and memory. Patients’ caregivers also completed standardized questionnaires regarding day-to-day mood and behavior.
Results: At intake, the most common neurologic symptoms reported by caregivers were attention problems (83.3%), fatigue/lethargy (77.7%), sleep disturbance (77.7%), dizziness/vertigo (72.2%), and headaches (72.2%). On rating scales, most caregivers endorsed concerns for depressed mood and anxiety (14/15 and 12/15). A large proportion of patients had difficulties with attention (9/18) and depressed mood/anxiety (13/18) before COVID. On cognitive testing, the majority of the patients performed within or above broad average range ($\geq$16th percentile) across most domains. However, a little over half of the patients performed below average on auditory attention measures.
Conclusions: Within our clinically referred sample, children who reported lingering cognitive symptoms after COVID-19 often had a preexisting history of attention and/or mood and anxiety concerns. Many of these patients performed below average in attention testing, but it remains to be seen whether this was due to direct effects of COVID, physical symptoms, and/or preexisting difficulties with attention or mood/anxiety.

Keywords: Post-acute COVID syndrome; Long COVID; SARS-CoV-2; Attention; Neuropsychiatry; COVID-19

Introduction

As of January 1, 2022, over 53 million COVID-19 cases have been reported (Center for Disease Control and Prevention (CDC), 2021). The American Academy of Pediatrics (AAP) recently released a report that showed children represent approximately 15% of all cases of COVID-19 in the United States, totaling over 5 million affected youth (AAP, 2021). Relative to adults, there is generally a better prognostic outlook for children with COVID-19, as the disease course tends to be milder (Ding, Yan, & Guo, 2020), with lower rates of severe respiratory illness (Ludvigsson, 2020; Zhang, Peres, Silva, & Camargos, 2020) and hospitalizations (CDC, 2021), as well as fewer deaths (<0.5% of confirmed pediatric cases; AAP, 2021).

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However, growing evidence suggests that many affected adults and youth present with lingering or emergent neurologic, gastrointestinal, cardiac, pulmonary, or ear–nose–throat symptoms weeks or months after the infection when viral load is undetectable—a condition known as "long COVID." Specifically, the National Institutes of Health (NIH) and the CDC define long COVID as symptoms that are present more than 4 weeks after the initial infection (Datta, Talwar, & Lee, 2020). Interestingly, research suggests that long COVID symptomology is not typically associated with worse COVID-19 course severity (Goërtz et al., 2020). Long COVID has been reported at elevated rates among individuals with certain preexisting risk factors and those with mild acute disease course (Dennis et al., 2020).

Given challenges with initial COVID-19 testing availability, the true prevalence rate of long COVID within the United States remains unknown. Recent findings from the University of Washington suggest up to 30% of adults reported persistent symptoms 9 months after the disease course (Logue et al., 2021). Likewise, findings published from the Michigan COVID-19 Recovery Surveillance Study report approximately 35% of adults endorse lingering symptoms 60 days after the illness onset (Hirschtick et al., 2021). Epidemiological findings from other countries vary markedly, with estimates ranging from 22% at 5 weeks after infection to 87% at approximately 8 weeks (see review by Crook, Raza, Nowell, Young, & Edison, 2021).

Studies documenting rates of long COVID in the pediatric population are also emerging, albeit these are largely from international investigations. Data released by the UK Office of National Statistics (ONS) estimated that approximately 10–13% of children report at least one persistent symptom 5 weeks after testing positive for COVID-19 (ONS, 2021). In contrast, a more recent study that reported that about 4.4% of UK school-aged children who had COVID-19 symptoms continued to present with illness characteristics for over 28 days, but only about 2% of these children continue to show symptoms by 56 days (Molteni et al., 2021). A cross-sectional study in Italy observed more elevated estimates with nearly two thirds of children (66.7%) with positive polymerase chain reaction tests for COVID-19 presenting with at least one symptom 60–120 days after infection (Buonsenso et al., 2021). In a prospective cohort study of children who were hospitalized for COVID-19 in Russia, nearly 25% of these youth reported persistent symptoms up to 5 months after initial COVID-19 diagnosis (Osmanov et al., 2021). Among pediatric patients in France, approximately 17% of the cohort continued to show either persistent or newly emergent symptoms after infection, despite none of these children requiring hospitalization during disease course (Matteudi et al., 2021). Although rates are variable, these studies generally highlight the sizable proportion of adult and pediatric patients who have new or persistent symptoms well after initial infection.

In the first prospective study of adults with long COVID, common neurologic symptoms included brain fog, headaches, fatigue, and numbness/tingling (Graham et al., 2021). Relative to the US normative population, these patients also performed significantly worse on the NIH toolbox measures of attention and working memory. Performance in working memory was associated with higher levels of fatigue among the entire sample. Moreover, attention functioning was inversely related to fatigue severity among the subset of patients who had negative nasopharyngeal/antibody test results but prolonged clinical manifestations of COVID-19. It was suggested that adults with prolonged symptoms may experience a constellation of physical and cognitive symptoms similar to myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) or mild traumatic brain injury (mTBI). At present, the neurological and cognitive sequelae of children remain largely unknown, although recent case reports suggest affected youth and their parents similarly endorse complaints of fatigue, labored breathing, and attention/concentration difficulties (Brackel et al., 2021; Ludvigsson, 2021) in addition to sleep disturbances and memory difficulties (Borel et al., 2022). To our knowledge, most of these studies rely on self or parent report and there are no existing investigations on the cognitive sequelae of long COVID in youth based on objective cognitive test measures.

This case series provides an overview of the neurologic, cognitive, and mood and behavior symptoms observed in a pediatric cohort with long COVID and cognitive or school difficulties. These patients were reporting symptoms or difficulties at least 4-week post-COVID disease onset and were referred for an outpatient neuropsychological evaluation from an outpatient multidisciplinary post-COVID clinic. In this case study, we describe subjective cognitive functioning as reported by the patients and their parents, performance-based cognitive functioning based on objective test measures, and mood and behavior based on rating scales. As such, this novel case series strives to develop a better understanding of the neurocognitive and psychological presentation of pediatric patients with long COVID who sought services from a dedicated specialty clinic.

Materials and Methods

Clinical Sample

This study involved a retrospective chart review of the first 18 pediatric patients (12 females; $M_{\text{age}} = 13.28$ years, $SD = 2.70$, range = 6–16) referred for an outpatient neuropsychological evaluation following the initial visit to a multidisciplinary pediatric post-COVID clinic at our institute. A subset of the patients reported here was also described in the outline of the multidisciplinary clinic model in Morrow et al., 2021. Our sample consisted of mostly non-Hispanic white patients (72.2% White, 11.1%

Black, 16.6% Unknown/Did not report; 72.2% not Hispanic, 27.7% Unknown/Did not report). Information regarding patient's insurance type (medical assistance vs. commercial insurance) was obtained as a proxy for socioeconomic status. Fifteen of the 18 patients had commercial insurance (83.3%). English was the reported preferred language of the entire sample.

All patients were diagnosed with COVID-19 either with nucleic acid test or serum antibody test (66.7%) or had an acute clinical presentation consistent with COVID-19 combined with known exposure to the illness (33.3%). Individuals with a clinical diagnosis of COVID-19 were included in the cohort given limited access to testing early in the pandemic, especially for pediatric patients with mild acute symptoms. All individuals in our pediatric cohort reported lingering or emergent neurologic, cognitive, and/or behavioral symptoms at least 4 weeks following initial COVID-19 diagnosis or symptom onset. The majority of these patients reported a mild acute course of illness with only three (16.6%) requiring brief hospitalization. None required mechanical ventilation during hospitalization. Based on caregiver report of positive diagnostic test results or clinical symptom presentation onset, this cohort completed the neuropsychological evaluation an average of 280 days after initial COVID-19 infection ($SD = 178$ days, range = 87–674). It is important to highlight that many of these patients sought rehabilitative services late after their infection as there were very limited multidisciplinary specialty clinics dedicated to serving pediatric long COVID patients until early 2021. Additionally, those with a longer time lapse between infection to the neuropsychological evaluation largely represent patients with clinical symptom presentation given lack of COVID testing at the time.

Neurologic complaints were screened at the initial multidisciplinary post-COVID clinic visit. As outlined in Table 1, the most common symptoms reported included: attention/concentration difficulties (83.3%), fatigue (77.7%), sleep disturbance (77.7%), dizziness/vertigo (72.2%), and headaches (72.2%). This research, which includes a retrospective chart review, has been approved under institutional review board at Johns Hopkins Medicine.

Procedures

As part of their clinical neuropsychological evaluation, patients and their caregivers were first interviewed regarding their COVID-19 illness course and general history including mood, anxiety, and attention concerns and history of behavioral and medication treatment (Table 1). Patients and caregivers were administered rating scales, using paper or online versions (see below). Subsequently, a semi-flexible brief neuropsychological screening protocol was administered to most patients (refer to Test Measures section for exceptions). The battery was designed to provide a brief assessment of multiple cognitive domains thought to potentially be affected by COVID-19. These domains include areas found to be impacted by ME/CFS and mTBI given initial findings of similar symptomatology. Our test battery was designed to be administered either in-person or via telehealth. The decision for an in-person/face-to-face versus tele-neuropsychological (teleNP) evaluation was made on a case-by-case basis based on factors such as patient's distance from clinic, medical history (e.g., seizures, strokes, etc.), developmental concerns, and sensory/motor deficits (for a review of the teleneuropsychology model applied in our clinic, review Pritchard, Sweeney, Salorio, & Jacobson, 2020). Given approximately half the patients resided out of state, the teleNP assessment modality offered a convenient opportunity to complete testing separate from their visit to the multidisciplinary pediatric post-COVID clinic. This approach was intentional as many patients reported significant fatigue as part of their long COVID symptomatology, raising concerns as to whether testing on the same day of the multidisciplinary clinic visit would drive overexertion. All but four patients completed the evaluation through the teleNP modality. Those who completed the neuropsychological evaluation through the telehealth model were tested through a Health Insurance Portability and Accountability Act compliant videoconferencing platform (Zoom) and were situated in a quiet room in their home alone on a laptop or computer. The neuropsychologists completing teleNP assessments with out of state patients obtained approval to practice telepsychology in states participating in the Psychology Interjurisdictional Compact (PSYPACT) and only completed teleNP assessments in those states. Prior to the availability of PSYPACT, the neuropsychologist only completed out of state telehealth appointments in states where telehealth licensure reciprocity or a temporary licensure waiver (due to COVID-19 public health emergency) was available.

Test Measures

The following cognitive domains were assessed: performance validity, verbal learning and memory, working memory, sustained auditory attention, processing speed, verbal fluency, and cognitive flexibility. As outlined in Table 2, the main neuropsychological screening battery included the Child and Adolescent Memory Profile List (ChAMP, Sherman & Brooks, 2015a), Wechsler Intelligence Scale for Children 5th Edition Digit Span (WISC-V, Wechsler, 2014), Wechsler Adult Intelligence Scale 4th Edition Digit Span (WAIS-IV, Wechsler, 2008), Oral Symbol Digits Modalities Test (SDMT, Smith, 1983), Test of Everyday Attention of Children Score (TEA-Ch Score, Manly et al., 2001), Delis Kaplan Executive Functioning System Verbal Fluency (D-KEFS, Delis, Kaplan, & Kramer, 2001), and Memory Validity Profile (MVP Verbal, Sherman & Brooks, 2015b).

Table 1. Clinical history of our pediatric long COVID cohort

Clinical history	Proportion of total patients ($N = 18$)
COVID-19 diagnosis	
Nucleic acid test or serum antibody test	12/18 (66.7%)
Clinical diagnosis and known exposure	6/18 (33.3%)
Hospitalization due to COVID-19	3/18 (16.6%)
Psychotropic medication	
Treatment prior to COVID-19	4/18 (22.2%)
Treatment at the time of testing∗	7/18∗ (38.8%)
Behavioral treatment or psychotherapy	
Treatment prior to COVID-19	6/18 (33.3%)
Treatment at the time of testing	7/18 (38.8%)
Domains of concern prior concerns prior to COVID-19	
Attention	9/18 (50.0%)
Anxiety/mood	13/18 (72.2%)
Anxiety/mood + attention jointly	7/18 (38.8%)
Developmental delay (language or motor)	4/18 (22.2%)
Decline in academic or school performance following infection	13/18 (72.2%)
Common neurologic symptoms at the time of the evaluation	
Attention/concentration difficulties	15/18 (83.3%)
Fatigue	14/18 (77.7%)
Sleep disturbance	14/18 (77.7%)
Dizziness/vertigo	13/18 (72.2%)
Headaches	13/18 (72.2%)
Anxiety	12/18 (66.6%)
Depression	10/18 (55.5%)
Dysgeusia	4/18 (22.2%)
Memory difficulties	4/18 (22.2%)
Anosmia	3/18 (16.6%)
Clinical information at testing	**Proportion of total patients ($N = 18$)**
Neurologic symptoms present during the evaluation	
Fatigue	7/18 (38.8%)
Headache	5/18 (27.7%)
Pain	1/18 (5.5%)
Dizziness	0/18 (0%)
Medication use during the evaluation	
Stimulants	3/18 (16.6%)
Antihistamine for anxiety	2/18 (11.1%)
Selective serotonin reuptake inhibitor	3/18 (16.6%)
Mood stabilizer	2/18 (11.1%)
Serotonin and norepinephrine reuptake inhibitors	2/18 (11.1%)
Selective alpha-2a adrenoreceptor agonist	1/18 (5.5%)

Note. (∗) At the time of the neuropsychological evaluation, seven patients were prescribed psychotropic medication to address anxiety, low mood, and attention deficit. One patient was not on psychotropic medication but was treated with Keppra due to seizures.

Most of the patients completed the same cognitive tests with the exception of two school-age patients who were administered different measures in processing speed and attention given developmental age and medical history and an adolescent who underwent a re-evaluation after infection. Specifically, an 8-year-old and a 6-year-old patients were administered the WISC-V given history of global developmental delay and seizures, respectively, and thus were given the Coding subtest rather than the SDMT. In addition, the latter was administered the NEPSY-II Auditory Attention subtest (Brooks, Sherman, & Strauss, 2009) rather than the TEA-Ch Score. A 15-year-old, who underwent a comprehensive neuropsychological re-evaluation, was administered the WISC-V Coding subtest, Continuous Performance Test 3rd Edition (CPT-3) (Conners, 2014), and California Verbal Learning Test Children's Version (CVLT-C) (Delis, Kramer, Kaplan, & Ober, 1994) instead of SDMT, TEA-Ch, and ChAMP, respectively, to allow direct comparison of performance pre- versus post-infection. Age-corrected norms were used across measures.

Parents completed rating scales regarding the patients' day-to-day attention, behavior, and psychosocial functioning. Specifically, caregivers were given the Conners Comprehensive Behavior Rating Scale (Conners CBRS) (Conners, 2008) or Conners

Table 2. Cognitive outcomes of pediatric long COVID patients on performance-based test measures

Cognitive domain	Tests administered	Total patients who completed the measure	Proportion of patients with below average performance
Verbal Learning and Memory			
Immediate Recall	ChAMP List or CVLT-C	18	1/18 (5.5%)
Delayed Recall		18	2/18 (11.1%)
Recognition		18	1/18 (5.5%)
Working Memory	WISC-V or WAIS-IV Digit Span	18	1/18 (5.5%)
Processing Speed	SDMT Oral or WISC-V Coding∗	18	2/18 (11.1%)
Auditory Attention	TEA-Ch Score, or NEPSY-II Auditory Attention∗	15	8/15 (53.3%)
Verbal Fluency			
Letter Fluency	D-KEFS Verbal Fluency	17	3/17 (17.6%)
Category Fluency		17	1/17 (5.8%)
Cognitive Flexibility			
Response Accuracy	D-KEFS Verbal Fluency, Category Switching	17	0/17 (0%)
Switching Accuracy		17	0/17 (0%)
Effort	MVP Verbal Subtest and Reliable Digit Span	15 15	All patients passed

Note. (∗) An 8- and a 6-year-old patients were administered the WISC-V given history of global developmental delay and seizures respectively, and thus, given the Coding subtest rather than the SDMT. The latter was administered the NEPSY-II Auditory Attention subtest (Brook et al., 2009) rather than TEA-Ch Score. One patient had a neuropsychological re-evaluation thus the WISC-V, CPT-3, and CVLT-C were administered for direct comparison of performance scores. For this patient, the CPT-3 Detectability was within the average range; however, this result was not included in the frequency above, as it measured visual rather than the auditory attention. Two 16-year-old patients were administered subtests comprising the Children's Memory Scale Attention Index, given they were out-of-range for TEA-Ch and NEPSY-II age norms. Although both performed at or above average, results were not included in the attention domain above, given the tests do not measure the same cognitive construct.
ChAMP = Child and Adolescent Memory Profile, CVLT-C = California Verbal Learning Test Children's Version, D-KEFS = Delis Kaplan Executive Functioning System, MVP = Memory Validity Profile, NEPSY-II = A Developmental Neuropsychological Assessment, SDMT = Symbol Digit Modalities Test, TEA-Ch = Test of Everyday Attention for Children, WAIS-IV = Wechsler Adult Intelligence Scale 4th Edition, WISC-V = Wechsler Intelligence Scale for Children 5th Edition

Early Childhood (Conners EC) (Conners & Goldstein, 2009), and Behavior Rating Inventory of Executive Function 2nd Edition (BRIEF-2) (Gioia, Isquith, Guy, & Kenworthy, 2015). Ratings on these measures yield T-scores, with higher T-scores reflecting more observed day-to-day problems within the domain. Scores of 60–69 indicate at-risk areas of concerns, whereas scores of 70 and above indicate clinically elevated concerns.

Results

Clinical History

Supplementary Table 1 includes patient-level clinical factors, parent reported concerns, and treatment history. Prior to COVID-19, per parent report, about half our cohort had attention/concentration problems (50%), and a large proportion had a history of anxiety or depressive symptoms (72.2%). Over a third of our sample also reported both attention and mood/anxiety concerns (38.8%). Two patients had a prior diagnosis of attention-deficit/hyperactivity disorder supported by neuropsychological testing completed before COVID-19 infection. Few patients underwent behavioral therapy (27.7%) or took psychotropic medication (22.2%) before COVID-19 infection. Four patients reported prior developmental concerns (e.g., language or motor functioning; 22.2%). Of these, two displayed persistent delays requiring some form of intervention (e.g., speech, occupational, and/or physical therapy) until services were disrupted by the pandemic. Two presented with early motor or speech delays that necessitated occupational, physical, or speech/language therapies in earlier childhood, but graduated from intervention services well before COVID-19 infection.

At the time of the neuropsychological evaluation, eight of the patients were in psychotherapy (44.4%) and seven were being treated with psychotropic medication (38.8%). Four patients out of our cohort had initiated medication after COVID-19 infection but before they were evaluated by our clinic (22.2%), and five began participating in therapy or reinitiated therapy during this interval (27.7%). At the time of evaluation, 13 of our cohort (72.2%) reported a decline in school performance following disease course.

Of note, five patients reported significant premorbid or preexisting medical history, which refers to medical conditions prior to COVID-19 infection. From this subgroup, five patients had a premorbid medical history significant for preterm birth ranging

Table 3. Caregiver report of day-to-day behavior and psychosocial functioning of pediatric long COVID patients

Psychological/Neuropsychological domain	Rating scale administered	Number of the 18 caregivers who completed the inventory	Proportion of the cohort with at-risk or elevated concerns
ADHD Predominantly Inattention	Conners CBRS or EC	15	12/15 (80%)
ADHD Predominantly Hyperactive/Impulsive		15	5/15 (33.3%)
Low mood (Major Depressive Episode on the Conners CBRS, Mood and Affect on Conners EC)	Conners CBRS or EC	15	14/15 (93.3%)
Anxiety (Generalized Anxiety Disorder on the Conners CBRS, Anxiety on the Conners EC)	Conners CBRS or EC	15	12/15 (80%)
Global Executive Functioning	BRIEF-2	11	4/11 (36.3%)

Note. Three caregivers did not complete the Conners CBRS and six did not complete or return the BRIEF-2. One patient was not administered the BRIEF-2, as this patient was seen prior to the clinic development of a semi-flexible screening battery. On the Conners CBRS, Conners EC, and BRIEF-2, at-risk to clinically significant refers to T-scores of 60 or above. The Conners EC provide combined ADHD index rather than subtypes; thus, significance on this composite was considered for both ADHD inattention and hyperactive/impulsive subtypes described previously. Likewise, the Conners EC does not yield Major Depressive Episode or Generalized Anxiety Disorder scales but rather Low Mood/Affect and Anxiety subscales. Significance in these latter two subscales were combined with the frequency count in Conners CBRS scales.

BRIEF-2 = Brief Rating Inventory of Executive Functioning 2nd Edition, Conners CBRS = Conners Comprehensive Behavior Rating Scales, Conners EC = Conners Early Childhood.

from 29 to 36 weeks gestation (i.e., Cases 2, 6, 7, and 8 of Supplementary Tables 1 and 2). One patient (Case 1) had a history of seizure disorder prior to COVID-19 infection. No other significant medical history was reported.

Cognitive Testing

Supplementary Table 2 outlines patient-level performance across cognitive domains. Almost a third of our sample presented with fatigue and headaches during the evaluation (see Table 1 for information regarding clinical observations and medication use during testing); however, test results were still felt to be valid. All patients passed a stand-alone performance validity measure (MVP) and an embedded measure of effort (reliable digit span; Welsh, Bender, Whitman, Vasserman, & MacAllister, 2012). Nearly all patients who were prescribed psychotropic medications were on these during testing, albeit a small proportion was on stimulants for attention.

Table 2 lists the proportion of respondents with below average performance across cognitive domains, which was defined as below the 16th percentile relative to children their age. Across most cognitive domains—including verbal learning and memory, working memory, processing speed, verbal fluency and cognitive flexibility—the majority of patients performed within the broadly average range or above. However, on a measure of auditory attention, 50% of patients performed below average. Of note, among the nine patients without preexisting attention concerns, two showed below average performance on attention measures, but one of these had persisting anxiety/mood concerns that may have contributed to these outcomes. Importantly, three of the nine patients with below average performance on attention measures had a history of preterm birth (one patient born at 33.5-week and two at 36-week gestation).

It should be highlighted that two of the four patients who completed in-person testing performed below the average range on attention testing; thus, difficulties in this domain were not solely seen on teleNP evaluations.

Caregiver-Reported Behavior Functioning

As outlined in Table 3, on parent rating scales, 80% of caregivers reported concerns with inattentive ADHD symptoms and anxiety and 93.3% reported problems with low mood (T-scores greater than 60) at the time of the neuropsychological evaluation. The majority of caregivers did not report concerns with executive functioning (70%), consistent with the absence of executive functioning deficits on objective testing described previously.

Discussion

Our pediatric long COVID cohort showed a relatively high rate of attention difficulties, which were observed across both performance-based tests and parent report of day-to-day functioning. Many of these individuals also reported a history of attention problems prior to COVID-19 infection. Likewise, there was a high rate of depressive and anxiety symptoms in our sample; however, a majority of these patients had premorbid anxiety or mood concerns. Attention difficulties can be related to many factors, including but not limited to depression and anxiety, fatigue, and physical symptoms such as pain. Our data suggest that it is critical to consider preexisting attention, mental health, and medical conditions as part of the neuropsychological evaluation.

Potential Impact of COVID-19 Pandemic Stressors on Mental Health and Attention

Our findings are largely consistent with those observed in adult long COVID patients (Graham et al., 2021; Mazza et al., 2020) and suggest that those with long-term symptoms following COVID-19 infection are likely to report premorbid neuropsychiatric concerns. This is also consistent with research around prolonged symptoms after other conditions such as concussion (Iverson, Williams, Gardner, & Terry, 2020; Langer et al., 2021; Lumba-Brown et al., 2018).

It is possible that the stress associated with the pandemic—including school disruptions, isolation, access barriers to appropriate behavioral health services, increased family stress, and financial strain—may impact mental health (e.g., trigger onset of or exacerbate prior symptoms), and subsequently cognitive functioning (Golberstein, Wen, & Miller, 2020). Virtual learning may also contribute to the parent- and patient-reported difficulties with school, attention, and mood, as the format of instruction requires children to self-regulate in the home context without hands-on assistance from school staff and limits their access to peer support. Moreover, potential distractors in the home environment during remote learning may also contribute to greater day-to-day challenges with attention related to school.

Notably, children with premorbid depression and anxiety may struggle with social isolation related to the pandemic, anxiety about their health, and lower tolerance for distress to a greater degree than those without prior mental health concerns. Children with long COVID and a previous history of anxiety or low mood may show more functional impairment during the pandemic—a pattern generally observed in adults (Taylor et al., 2020). Given the lack of longitudinal data (i.e., repeated psychological assessment of mental health and cognitive functioning prior to and after COVID-19 infection), we are unable to identify this trend within our sample, albeit this gap in literature warrants further investigation. Regardless, future clinicians may consider monitoring mood symptomatology and adaptive functioning more closely among those with COVID-19 infection and a prior history of affective disorders (anxiety, depression).

It should be noted that a large proportion of our sample had no history of medication or behavioral intervention for premorbid mood, anxiety, and/or attention concerns. Clinicians working with youth recovering from COVID-19 should assess mental health history and pandemic-related stressors carefully and connect the patient to behavioral and clinical interventions as appropriate. Early behavioral intervention may serve as a protective factor to buffer these children from more severe anxiety/mood symptomatology, which may alleviate some symptoms associated with long COVID and indirectly reduce the risk of attention problems. Treatment plans should also incorporate strategies to help both the child and their caregivers to build resilience, support systems, and coping skills given the effect of pandemic stressors on family functioning (Feinberg et al., 2022).

Given the assorted symptoms associated with long COVID, which may represent multisystemic effects, partnerships between medical and mental health disciplines (e.g., neurology, rehabilitation medicine, neuropsychology), and across settings (e.g., medical, mental health, and school teams) will likely be integral in supporting patients' symptom management, well-being, and return to day-to-day functioning. Cognitive difficulties such as concentration difficulties are very commonly reported long after COVID illness as shown in our clinical sample and in prior case studies with children (Berg et al., 2022; Borch et al., 2022; Borel et al., 2022; Brackel et al., 2021; Ludvigsson, 2021). Because of their training in both the medical/neurological and psychological fields, neuropsychologists are uniquely poised to understand the many factors that might be contributing to these cognitive difficulties; communicate the identified brain–behavior relationships to patients, families, school personnel, and other providers; and tailor treatment and educational plans as appropriate.

Physical Symptoms of Long COVID and Effects on Mental Health and Attention

Alternatively, it is possible that attention and mood difficulties observed among children with long COVID are due to their physical symptoms such as fatigue, headaches, and dizziness (Crook et al., 2021). Prior literature suggests that deficits in attentional processes may also be seen in other conditions with overlapping symptomology including ME/CFS and postural orthostatic tachycardia syndrome, a disorder of the autonomic nervous system that commonly presents with lightheadedness, headaches, palpitations, and fatigue (Shanks et al., 2013). Consequently, to address these concerns with attention and concentration, integrating therapies to manage physical symptoms and mood should be considered. Indeed, recent consensus guidance statements to address cognitive symptoms of adult patients with long COVID incorporates multiple disciplines including neurology, speech/language pathology, physical therapy, and behavior psychology, as management of physical symptoms may indirectly improve cognitive functions (Fine et al., 2022). From a diagnostic standpoint, it is important for clinicians to fully assess current physical symptoms such as fatigue, headache, and pain, including on the day of testing, and consider how these symptoms might contribute to the patient's presentation.

To date, there are several proposed pathophysiological mechanisms through which SAR-CoV-2 affects the central nervous system (CNS) and subsequently neuropsychiatric and cognitive functioning (Crook et al., 2021; Kumar, Veldhuis, & Malhotra, 2021). Proposed hypotheses include viral entry of cells through binding to angiotensin-converting enzyme 2 (ACE-2) and inciting inflammatory processes across organs with ACE-2 receptors (Hoffmann et al., 2020; Hussman, 2020); CNS infection via neuronal pathway (i.e., olfactory pathway) (Kumar et al., 2021); activated immune system triggering neuroinflammation (Kempuraj et al., 2020); and breached blood–brain barrier (Wu et al., 2020). It remains unclear the mechanisms that underlie the neurocognitive sequelae of long COVID in pediatric patients given limited research with repeated measures design and/or more homogeneous samples. However, with more availability of COVID-19 testing and improved precision in early detection, a timely diagnosis of the infection is possible, which in turn affords detailed tracking of clinical features. Further characterizing the course trajectory of lingering or emergent symptoms post-COVID will be important to help discern if attention and anxiety/mood difficulties are risk factors for, byproducts of, and/or part of the long COVID symptomatology. These studies will be important to elucidate mechanisms for long COVID symptoms and inform long-term management or treatment approaches.

Premorbid Health History and Increased Risk for Attention Difficulties

Finally, as emphasized previously, patients' medical history may contribute to attention deficit following COVID-19 infection. Of the eight patients with below average attention performance in our cohort, three were born prematurely (37.5%), which has been linked to increased risk for attention problems (McCormick, Litt, Smith, & Zupancic, 2011). It is possible that increased academic difficulties following COVID in this subgroup of patients may represent preexisting weaknesses in attention that have begun to interfere with school functioning. Investigations with larger clinical samples and different comparison or control groups (e.g., children with long COVID with and without history of prematurity; children with low mood, chronic fatigue, and/or pain without a history of COVID-19) will be vital in illuminating whether the poor attention performance among these patients reflects an atypical neurodevelopmental course following preterm birth or other factors (independent of COVID-19), the direct viral infection on the CNS, or secondary effects of low mood or physical symptoms as noted previously.

Study Limitations and Future Directions

Given the nature of our clinical case series, there are several study limitations that should be carefully considered in prospective research. As our sample was clinically referred and our study was a retrospective chart review, we are not able to comment on the prevalence of long COVID in the greater population. Future investigations should consider including control groups, as noted previously, as well as comparison groups of individuals with anxiety and mood disorders without COVID infection history and patients with mTBI or ME/CFS given similar clinical presentation (Graham et al., 2021). Detailed characterization of symptom course following infection (e.g., symptom onset, peak of symptom severity, duration of symptom, interventions for symptom management) utilizing a repeated-measures study design will also be important to better understand whether cognitive and psychosocial concerns emerge secondary to select long COVID features. In a similar vein, examining the independent cognitive sequelae among those with long COVID following hospitalization and severe illness course (e.g., multisystem inflammatory syndrome in children) versus those without hospitalization will be important given the former clinical population may present with post-intensive care syndrome (Inoue et al., 2019). Family history of attention deficit, learning disorders, mood disorder, COVID infection, and long COVID may also increase risk for related symptoms, and thus should be closely examined. Our sample composition was largely of non-Hispanic white patients with commercial insurance and may represent those with more resources and access to clinical services. The clinical presentation of our sample may not represent the diverse population of patients with long COVID, particularly given those with low socioeconomic or disadvantaged background are at greater risk for more serious complications. Moreover, given our sample consists of those who sought a neuropsychological evaluation as part of their clinical care, a semi-flexible test battery was applied based on concerns reported by the patient and their parents. Subsequent clinical research with patients with long COVID should consider acute and serial testing while utilizing select fixed measures, which would afford better monitoring of the cognitive and psychosocial sequelae with the disease progression and recovery course.

It is worthwhile to note that the majority of our sample completed an evaluation via teleNP approach, as many participants seen in the multidisciplinary pediatric post-COVID clinic at our institute were from out of state. This service delivery model allowed families to receive assessment services without a costly extension of their visit (e.g., scheduling in person appointment across days that may require longer lodging), and to avoid overtaxing patients with long COVID who may have challenges with fatigue and pain. Although this clinical model increased accessibility of neuropsychological assessment services to families residing in rural settings or regions without a dedicated clinic for pediatric patients with long COVID, more research is needed to validate teleneuropsychology in pediatric samples with varying medical conditions and/or range of cognitive impairment. Within our sample, as noted previously, two of the four patients who completed in-person testing (50%) performed below average in attention testing, which was comparable to the 6 of the 11 patients who showed similar challenges via teleNP evaluation (55%). Although more research is necessary to provide support on the use of teleNP, our case series provides an example of how this assessment approach can be utilized in the context of a multidisciplinary clinic. It is also important to highlight that our sample largely represents non-Hispanic White patients with commercial insurance, which may reflect disparities in telehealth use and/or clinical services dedicated to manage long COVID. Clinics dedicated to long COVID care should consider strategies to expand services to afford access to the patients and families underserved, who are generally also at greater risk for COVID infection.

Finally, as new variants of COVID emerge and vaccinations are made available to younger children, subsequent investigations on children with long COVID should examine the different clinical characteristics that may be associated with viral mutations and prevention/treatment factors. Different COVID variants (e.g., alpha, delta, omicron) and vaccination status have been linked to varying clinical severity in adults (Lauring et al., 2022). Currently, the clinical presentations across variants and inoculation history among youth are unclear and have yet to be further explored. Clinics dedicated to long COVID care in pediatric populations are uniquely suited to engage in such research while providing interdisciplinary services to support affected individuals.

Conclusion

To our knowledge, this case series is the first study of pediatric long COVID patients to utilize a combination of clinical interview, performance-based cognitive tests, and standardized rating scales. Overall, a sizeable proportion of our heterogeneous clinical sample of children with long COVID showed difficulty on attention testing. It remains to be seen whether this is due to direct effects of COVID, physical symptoms, and/or to co-occurring attention, mood, or anxiety concerns. Findings highlight the importance of obtaining a detailed medical and mental health history in the assessment of cognitive functioning and in treatment considerations among affected individuals.

Conflicts of Interest

No potential conflict of interest was reported by the authors.

References

American Academy of Pediatrics (2021). *Children and COVID-19: State-level data report*. Accessed September 2, 2021. http://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/.

Berg, S. K., Nielsen, S. D., Nygaard, U., Bundgaard, H., Palm, P., Rotvig, C. et al. (2022). Long COVID symptoms in SARS-CoV-2-positive adolescents and matched controls (LongCOVIDKidsDK): A national, cross-sectional study. *The Lancet Child & Adolescent Health*, *6*(*4*), 240–248.

Borch, L., Holm, M., Knudsen, M., Ellermann-Eriksen, S., & Hagstroem, S. (2022). Long COVID symptoms and duration in SARS-CoV-2 positive children—A nationwide cohort study. *European Journal of Pediatrics*, *181*, 1597–1602.

Borel, M., Xie, L., Kapera, O., Mihalcea, A., Kahn, J., & Messiah, S. E. (2022). Long-term physical, mental and social health effects of COVID-19 in the pediatric population: A scoping review. *World Journal of Pediatrics*, *18*, 149–159.

Brackel, C. L., Lap, C. R., Buddingh, E. P., van Houten, M. A., van der Sande, L. J., Langereis, E. J. et al. (2021). Pediatric long-COVID: An overlooked phenomenon? *Pediatric Pulmonology*, *56*(*8*), 2495–2502.

Brooks, B. L., Sherman, E. M., & Strauss, E. (2009). NEPSY-II: A developmental neuropsychological assessment. *Child Neuropsychology*, *16*, 80–101.

Buonsenso, D., Munblit, D., De Rose, C., Sinatti, D., Ricchiuto, A., Carfi, A. et al. (2021). Preliminary evidence on long COVID in children. *Acta Paediatrica*, *110*(*7*), 2208–2211.

Centers for Disease Control and Protection (2021). *COVID data tracker*. Accessed September 2, 2021. https://covid.cdc.gov/covid-data-tracker/#datatracker-home.

Conners, C. K. (2008). *Conners comprehensive behavior rating scales manual*. Toronto, ON, Canada: Multi-Health Systems Incorporated.

Conners, C. K. (2014). *Conners continuous performance test 3rd edition: Technical manual*. North Tonawanda, NY: Multi-Health Systems Incorporated.

Conners, C. K., & Goldstein, S. (2009). *Conners early childhood: Manual*. North Tonawanda: NY: Multi-Health Systems Incorporated.

Crook, H., Raza, S., Nowell, J., Young, M., & Edison, P. (2021). Long COVID—Mechanisms, risk factors, and management. *BMJ*, *374*, n1648.

Datta, S. D., Talwar, A., & Lee, J. T. (2020). A proposed framework and timeline of the spectrum of disease due to SARS-CoV-2 infection: Illness beyond acute infection and public health implications. *JAMA*, *324*(*22*), 2251–2252.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan executive function system*. San Antonio, TX: Psychological Corporation.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1994). *California verbal learning tests, children's version manual*. Boston, MA: Psychological Corporation.

Dennis, A., Wamil, M., Kapur, S., Alberts, J., Badley, A., Decker, G. A. et al. (2020). Multi-organ impairment in low-risk individuals with long COVID. *MedRxiv. [preprint]*..

Ding, Y., Yan, H., & Guo, W. (2020). Clinical characteristics of children with COVID-19: A meta-analysis. *Frontiers in Pediatrics*, *8*, 431.

Feinberg, M. E., A Mogle, J., Lee, J. K., Tornello, S. L., Hostetler, M. L., Cifelli, J. A. et al. (2022). Impact of the COVID-19 pandemic on parent, child, and family functioning. *Family Process*, *61*, 361–374.

Fine, J. S., Ambrose, A. F., Didehbani, N., Fleming, T. K., Glashan, L., Longo, M. et al. (2022). Multi-disciplinary collaborative consensus guidance statement on the assessment and treatment of cognitive symptoms in patients with post-acute sequelae of SARS-CoV-2 infection (PASC). *PM and R*, *14*, 96–111.

Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2015). *BRIEF: Behavior rating inventory of executive function*. Lutz, FL: Psychological Assessment Resources.

Goërtz, Y. M., Van Herck, M., Delbressine, J. M., Vaes, A. W., Meys, R., Machado, F. V. et al. (2020). Persistent symptoms 3 months after a SARS-CoV-2 infection: The post-COVID-19 syndrome? *European Respiratory Journal Open Research*, *6*(*4*), 00542–02020.

Golberstein, E., Wen, H., & Miller, B. F. (2020). Coronavirus disease 2019 (COVID-19) and mental health for children and adolescents. *JAMA Pediatrics*, *174*(*9*), 819–820.

Graham, E. L., Clark, J. R., Orban, Z. S., Lim, P. H., Szymanski, A. L., Taylor, C. et al. (2021). Persistent neurologic symptoms and cognitive dysfunction in non-hospitalized Covid-19 "long haulers". *Annals of Clinical and Translational Neurology*, *8*(*5*), 1073–1085.

Hirschtick, J. L., Titus, A. R., Slocum, E., Power, L. E., Hirschtick, R. E., Elliott, M. R. et al. (2021). Population-based estimates of post-acute sequelae of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (PASC) prevalence and characteristics. *Clinical Infectious Diseases*, *73*(*11*), 2055–2064.

Hoffmann, M., Kleine-Weber, H., Schroeder, S., Krüger, N., Herrler, T., Erichsen, S. et al. (2020). SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*, *181*(*2*), 271–280.

Hussman, J. P. (2020). Cellular and molecular pathways of COVID-19 and potential points of therapeutic intervention. *Frontiers in Pharmacology*, *11*, 1169.

Inoue, S., Hatakeyama, J., Kondo, Y., Hifumi, T., Sakuramoto, H., Kawasaki, T. et al. (2019). Post-intensive care syndrome: Its pathophysiology, prevention, and future directions. *Acute Medicine & Surgery*, *6*(*3*), 233–246.

Iverson, G. L., Williams, M. W., Gardner, A. J., & Terry, D. P. (2020). Systematic review of preinjury mental health problems as a vulnerability factor for worse outcome after sport-related concussion. *Orthopaedic Journal of Sports Medicine*, *8*(*10*), 2325967120950682.

Kempuraj, D., Selvakumar, G. P., Ahmed, M. E., Raikwar, S. P., Thangavel, R., Khan, A. et al. (2020). COVID-19, mast cells, cytokine storm, psychological stress, and neuroinflammation. *The Neuroscientist*, *26*(*5–6*), 402–414.

Kumar, S., Veldhuis, A., & Malhotra, T. (2021). Neuropsychiatric and cognitive sequelae of COVID-19. *Frontiers in Psychology*, *12*, 553.

Langer, L. K., Alavinia, S. M., Lawrence, D. W., Munce, S. E. P., Kam, A., Tam, A. et al. (2021). Prediction of risk of prolonged post-concussion symptoms: Derivation and validation of the TRICORDRR (Toronto Rehabilitation Institute concussion outcome determination and rehab recommendations) score. *PLoS Medicine*, *18*(*7*), e1003652.

Lauring, A. S., Tenforde, M. W., Chappell, J. D., Gaglani, M., Ginde, A. A., McNeal, T. et al. (2022). Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: Prospective observational study. *BMJ*, *376*, e069761.

Logue, J. K., Franko, N. M., McCulloch, D. J., McDonald, D., Magedson, A., Wolf, C. R. et al. (2021). Sequelae in adults at 6 months after COVID-19 infection. *JAMA Network Open*, *4*(*2*), e210830–e210830.

Ludvigsson, J. F. (2020). Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatrica*, *109*(*6*), 1088–1095.

Ludvigsson, J. F. (2021). Case report and systematic review suggest that children may experience similar long-term effects to adults after clinical COVID-19. *Acta Paediatrica*, *110*(*3*), 914–921.

Lumba-Brown, A., Yeates, K. O., Sarmiento, K., Breiding, M. J., Haegerich, T. M., Gioia, G. A. et al. (2018). Diagnosis and management of mild traumatic brain injury in children: A systematic review. *JAMA Pediatrics*, *172*(*11*), e182847–e182847.

Manly, T., Anderson, V., Nimmo-Smith, I., Turner, A., Watson, P., & Robertson, I. H. (2001). The differential assessment of children's attention: The test of everyday attention for children (TEA-Ch), normative sample and ADHD performance. *Journal of Child Psychology and Psychiatry*, *42*(*8*), 1065–1081.

Matteudi, T., Luciani, L., Fabre, A., Minodier, P., Boucekine, M., Bosdure, E. et al. (2021). Clinical characteristics of paediatric COVID-19 patients followed for up to 13 months. *Acta Paediatrica*, *110*(*12*), 3331–3333.

Mazza, M. G., De Lorenzo, R., Conte, C., Poletti, S., Vai, B., Bollettini, I. et al. (2020). Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. *Brain Behavior and Immunity*, *89*, 594–600.

McCormick, M. C., Litt, J. S., Smith, V. C., & Zupancic, J. A. (2011). Prematurity: An overview and public health implications. *Annual Review of Public Health*, *32*, 367–379.

Molteni, E., Sudre, C. H., Canas, L. S., Bhopal, S. S., Hughes, R. C., Antonelli, M. et al. (2021). Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. *The Lancet Child & Adolescent Health*, *5*(*10*), 708–718.

Morrow, A., Ng, R., Vargas, G., Jashar, D. T., Henning, E., Stinson, N. et al. (2021). Post-acute/long-COVID in pediatrics: Development of a multi-disciplinary rehabilitation clinic and preliminary case series. *American Journal of Physical Medicine & Rehabilitation*, *100*(*12*), 1140–1147.

Office for National Statistics United Kingdom (2021). *Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK*. Accessed September 2, 2021. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/alldatarelatingtoprevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk.

Osmanov, I. M., Spiridonova, E., Bobkova, P., Gamirova, A., Shikhaleva, A., Andreeva, M. et al. (2021). Risk factors for long COVID in previously hospitalised children using the ISARIC global follow-up protocol: A prospective cohort study. *European Respiratory Journal*, *59*(*2*), 2101341.

Pritchard, A. E., Sweeney, K., Salorio, C. F., & Jacobson, L. A. (2020). Pediatric neuropsychological evaluation via telehealth: Novel models of care. *The Clinical Neuropsychologist*, *34*(*7–8*), 1367–1379.

Shanks, L., Jason, L. A., Evans, M., & Brown, A. (2013). Cognitive impairments associated with CFS and POTS. *Frontiers in Physiology*, *4*, 113.

Sherman, E. M. S., & Brooks, B. L. (2015a). *Child and adolescent memory profile (ChAMP)*. Lutz, FL: Psychological Assessment Resources.

Sherman, E. M. S., & Brooks, B. L. (2015b). *Memory validity profile (MVP)*. Lutz, FL: Psychological Assessment Resources.

Smith, A. (1983). *Symbol digit modalities test*. Los Angeles, CA: Western Psychological Services.

Taylor, S., Landry, C. A., Paluszek, M. M., Fergus, T. A., McKay, D., & Asmundson, G. J. (2020). COVID stress syndrome: Concept, structure, and correlates. *Depression and Anxiety*, *37*(*8*), 706–714.

Wechsler, D. (2008). *WAIS–IV: Administration and scoring manual*. San Antonio, TX: Psychological Corporation.

Wechsler, D. (2014). *Wechsler intelligence scale for children–fifth edition (WISC-V)*. Bloomington, MN: Pearson Assessment.

Welsh, A. J., Bender, H. A., Whitman, L. A., Vasserman, M., & MacAllister, W. S. (2012). Clinical utility of reliable digit span in assessing effort in children and adolescents with epilepsy. *Archives of Clinical Neuropsychology*, *27*(*7*), 735–741.

Wu, Y., Xu, X., Chen, Z., Duan, J., Hashimoto, K., Yang, L. et al. (2020). Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain, Behavior, and Immunity*, *87*, 18–22.

Zhang, L., Peres, T. G., Silva, M. V., & Camargos, P. (2020). What we know so far about coronavirus disease 2019 in children: A meta-analysis of 551 laboratory-confirmed cases. *Pediatric Pulmonology*, *55*(*8*), 2115–2127.