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The Impact of COVID-19 on Brain Stimulation Therapy

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KEYWORDS

• Electroconvulsive therapy (ECT) • Transcranial magnetic stimulation (TMS)
• Brain stimulation • COVID-19 • Access to care

KEY POINTS

- The COVID-19 pandemic severely restricted access to ECT and all but eliminated access to TMS.
- These changes occurred during a time when the availability of safe and effective psychiatric treatment was vital and, to some degree, may have been avoidable.
- ECT and TMS services have gradually begun to resume operations, but not without significant changes in practice.

INTRODUCTION

Among the far-reaching effects of the COVID-19 pandemic has been restricted access to safe and effective forms of psychiatric treatment. Focusing on electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS), we review the pandemic's impact on brain stimulation therapy by asking 3 fundamental questions—Where have we been? How are we doing? And where are we going?

WHERE HAVE WE BEEN?

The onset of the international COVID-19 pandemic in March 2020 taxed health care systems worldwide, and the impact on ECT services was severe. In France and Belgium, for example, half of ECT services suspended operations.[1,2] In the United States, the first 2 months of the pandemic reduced the number of ECT treatments delivered by 74%.[3] Eighty percent of US academic medical centers reported operating at less than half their typical ECT volume.[4] Among these institutions alone, restricted access to ECT care was linked to patient suicide and suicidal behavior.[4]

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There were 2 primary drivers of this harsh reality—supply and perception. During an ECT treatment, the need for muscle relaxation necessitates general anesthesia and positive pressure ventilation, thus making ECT an aerosolizing procedure. All such procedures require the use of personal protective equipment (PPE), including N-95 masks, eye protection, isolation gowns, and gloves for each member of the ECT team.[5] When the supply of PPE was limited, hospitals were faced with implementing practices that allowed extended use or limited reuse of PPE beyond that recommended by the CDC for aerosol-generating procedures.[6] Compounding this challenge was the scarce supply of space and anesthesia providers. Anesthesiologists were reassigned to clinical areas where supplemental staff were needed to manage the influx of patients with COVID-19. Hospitals also had to convert spaces such as postanesthesia care units, where ECT treatments are often performed, into hospital or intensive care beds. These factors combined to drastically reduce the number of surgeries and procedures performed. With inadequate PPE, limited COVID-19 testing, conversion of psychiatric beds to medical beds, and reduced availability of space in which to perform ECT safely, many hospitals suspended their ECT services.

The second key driver of restricted access to ECT was the perception of ECT as an "elective" or "nonessential" procedure. During the early phase of the COVID-19 pandemic, the value of such procedures was weighed against the estimated risks to those performing them as well as the "burn rate" of the facility's PPE. Such decisions involve important ethical considerations and are not made in isolation.[7] ECT providers were quick to proclaim that ECT is most certainly not an "elective" procedure, but a lifesaving one. During times of resource scarcity, such as during a pandemic, access to ECT is arguably even more essential. Professional societies reinforced this view[8–12] and implored the medical community to remember the life-saving effects of ECT, particularly for severely ill patients receiving an acute course of ECT, but also for patients receiving maintenance ECT, who are vulnerable to illness recurrence without continued treatment.[2,8] The pediatric population, especially individuals with autism and intellectual disability, were emphasized in such entreaties, especially given the heightened stress associated with loss of structure and programming[13] and increased risk of morbidity and mortality from COVID-19 itself.[14–16]

These advocacy efforts achieved variable success. Even ECT services that were able to continue operating were required to demonstrate exceptional circumstances or obtain formal leadership approval.[17] The following vignette illustrates the impact of delays in ECT care during the pandemic.

Vignette. A previously healthy 15-year-old girl with autism experienced acute onset of catatonia in December 2019. The patient underwent comprehensive serum and cerebrospinal fluid investigations, as well as brain imaging, to rule out any organic etiologies of catatonia, and all results were within normal limits. A lorazepam trial was begun with only mild improvement with dosages up to 14 mg daily. The patient was referred to ECT but was unable to access such for approximately 2 months because of a city-wide waitlist for ECT services resulting from the diversion of both anesthesia services and agents used in anesthesia induction to COVID-19 care settings. This youth required 24-h care including assisted feeding during the wait for ECT, and experienced ongoing psychosocial incapacitation as someone who was previously a diligent high school student and accomplished athlete. The patient demonstrated approximately 85% return to baseline functioning with the introduction of ECT, yet the benefit waned and was lost with cessation of such. When a second ECT course was recommended, there was no timely option for reintroduction of a thrice-weekly acute course of ECT as optimal treatment for catatonia; a maximum of once-weekly

therapy was available, and its usage did not confer benefit. Thrice-weekly ECT only became available once again a 3 month wait.

Like its significant effect on ECT services, the onset of the COVID-19 pandemic brought TMS services essentially to a standstill. Barriers to TMS included suspension of "nonessential" procedures, staffing shortages, limited access to PPE and sanitization supplies, and clinics or offices ill-equipped to comply with social distancing recommendations. Both clinical patients and research participants proved difficult to retain because of fears of infection, loss of childcare, transportation difficulties, and a host of other pandemic-related psychosocial stressors. During the same time that access to TMS was reduced, rates of conditions for which TMS is indicated, including depression and cigarette consumption, were observed to climb.[18,19] To further compound patient burden, these psychiatric conditions have been associated with worse COVID-19 outcomes, including higher mortality rates.[18,20]

HOW ARE WE DOING?

As the supply of PPE and COVID-19 tests improved, and as the scientific community learned more about the new SARS-CoV-2 virus responsible for the pandemic, opportunity emerged for brain stimulation services to begin gradually resuming operations. By June 2020, half of the 20 academic medical centers belonging to the National Network of Depression Centers had ramped up to 75% of their typical ECT patient volumes.[4] In addition, case reports emerged of patients receiving ECT safely while also suffering from diagnosed COVID-19 illness.[2,21,22]

The resumption of ECT services was not universal and brought with it significant changes in practice, not only in the United States[23–26] but also in Belgium,[2] Brazil,[27] Canada,[17] France,[28] India,[29] Ireland,[30] Singapore,[31] and Spain.[32] These changes continue to evolve and vary geographically, but the focus remains on infection prevention and control (**Box 1**). Ongoing efforts to ensure access to ECT care are vital, particularly as data indicate a 44% relapse rate at 6 months among patients whose maintenance ECT was discontinued because of the pandemic. Of these individuals, 86% had to restart an acute course of ECT.[33] The following vignette illustrates the challenges of providing optimal ECT care to a patient with COVID-19 illness.

Vignette. A woman in her late 30s suffered from bipolar disorder and had a history of suicide attempts, episodes of catatonia, and multiple psychiatric hospitalizations. She also had obesity and received a kidney transplant in January 2020. She was domiciled with her husband and 6 children. Her bipolar disorder had stabilized with pharmacotherapy and ECT, and she was receiving continuation ECT after a recent psychiatric hospitalization. Her treatment interval was just being extended to every 3 weeks when the COVID-19 pandemic hit. As the pandemic was unfolding, and in the absence of diagnostic testing, shortage of PPE and even surgical masks and given patient's immunocompromised status, the ECT team classified her in a category where the treatment interval should first be extended and, if her symptoms remained stable, suspension of ECT could be considered. However, in the week before her scheduled appointment, she suffered a relapse of major depression with suicidal ideation and despite her immunocompromised status, required hospitalization, placing her at increased COVID-19 risk in the inpatient environment. She received 6 ECT treatments following a 3 times per week schedule, and her symptoms remitted. She was discharged home with continuation/maintenance ECT as an outpatient, which was provided without COVID-19 testing until June 2020 because of testing shortages. When testing became more widely available, she was tested within 3 days of each treatment. In September 2020, she tested positive for COVID-19 during routine

Box 1
Sample of changes in ECT practice due to COVID-19

Environment and scheduling
- Waiting areas restructured to allow social distancing. Families asked to wait in their car.
- Mandatory mask requirements for staff members, patients, and visitors.
- No visitors in the treatment/recovery areas.
- Plexiglass barriers at registration desk, recovery spaces, pre-ECT evaluation areas.
- Limited number of staff members inside the treatment room.
- Regular cleaning according to the institution's infection control guidelines.
- Patients scheduled in "batches," that is, patients from one location treated in the same batch.
- Staff scheduled in "pods" to keep the same staff working together as much as possible.
- Increase in the number of clinic days to accommodate for reduced operational efficiency.

Treatment rooms
- Relocation and/or modification of the treatment room (eg, negative pressure).
- Enough time is allowed for aerosol to be cleared from the treatment room before bringing in the next patient.
- Air purification systems with high-efficiency particulate air (HEPA) filters can be installed in an individual treatment room to achieve higher air exchange rate and thereby lower air-exchange wait time between treatments.

PPE
- Extended use, selective use, and reuse of N95 masks.
- Reduced number of staff inside the treatment room.
- Face shield or eye protection, disposable gown, and gloves.

Anesthesia provision
- HEPA filter between the mask and tubing of the anesthesia circuit.
- Modifications in technique to reduce risks from aerosolization: supraglottic airway,[43] airway box,[32] preoxygenation and avoiding ventilation,[26] use of a plastic cover on the patient's head at the initiation of bag-mask ventilation,[23] use of hydrogen peroxide mouthwash and povidone-iodine nasal swabs to each nostril,[25] and apneic ventilation.[44]

Testing
- Frequently evolving requirements and approaches to preprocedure COVID-19 screening and testing, including the difficulty providers and patients experienced meeting such requirements for a procedure scheduled multiple times each week.

screening. She had denied symptoms or exposure at the time of testing but later admitted to having mild symptoms and being exposed to her infected son, who had returned sick from school. Her symptoms were limited to mild fatigue and muscle aches. Her course of ECT was suspended for 21 days. Upon reinitiation of ECT, she continued to test positive for COVID-19 during most of her visits for the subsequent 4 months and was considered "persistently positive." For that duration, she was scheduled as the last patient of the day or as the last patient of the shift, followed by terminal cleaning of the room. She continues to receive maintenance ECT every 2 weeks and at times has required rescue ECT treatments. She has received both doses of COVID-19 vaccine and plans to continue her course of maintenance ECT.

For TMS services, resuming operations was again like that of ECT. The Clinical TMS Society posted a rough outline of recommendations for how to continue operating clinical services under pandemic conditions, and a more formal framework for continuing clinical and research TMS was published a month later by an international group of experts.[34,35] **Box 2** lists modifications for continuing clinical and research TMS during the COVID-19 pandemic that were based on the aforementioned literature, Centers for Disease Control and Prevention (CDC) recommendations, and the

Box 2
Sample of changes in TMS practice due to COVID-19

Patient selection
- Patients triaged for suitability by weighing the risks of withholding TMS with the risks of potential SARS-CoV-2 infection.
- If treatment paused or withheld, referrals made to ensure continuity of care.
- Daily screening measures include a COVID-19 symptom checklist and exposure inquiry.
- COVID-19 testing, or documentation of COVID-19 vaccination before commencing any acute TMS course.
- CDC guidelines on quarantine and testing after COVID-19 exposure or symptom emergence for both patients and staff followed.

Distancing and PPE
- Waiting areas restructured to allow social distancing. Where possible, patients asked to wait in their car until called up for appointment and other visitors prohibited.
- Mandatory mask requirements for staff members, patients, and visitors.
- Plexiglass barriers between staff and patient at registration desk and other locations.
- Number of staff members inside the treatment room limited.
- Consultation and follow-up appointments performed via telemedicine whenever possible.
- Staff shifted to remote work where possible.
- In academic settings, number of students and trainees limited.
- Use of intermittent theta-burst stimulation to minimize in-person contact time.

Sanitization
- Regular cleaning according to the institution's infection control guidelines.
- Increased attention to hand sanitization before and after any patient/participant interaction.
- Use of disposable gloves considered when applying treatment coil.
- Sanitization supplies kept more readily accessible throughout clinics.
- Items touched by patients or research participants sanitized thoroughly between patients.
- Device-specific sanitization protocols followed per manufacturer's instructions.

Research
- Encourage telecollaboration across institutions for all meetings, conferences, and trainings.
- Review changes to study protocols or consents with the institutional review board.
- Modify budgets to allow for additional participants secondary to increased dropouts, additional costs associated with mitigating SARS-CoV-2 transmission.
- Ensure researchers working remotely have required access to appropriate hardware, software, secure databases, study forms, or any other sensitive or specialized tools.
- Mentoring and social support for researchers who may be negatively impacted by social isolation or lack of support during the pandemic.

clinical and research experience of the Brain Stimulation Service and Brain Stimulation Laboratory at the Medical University of South Carolina (MUSC).

WHERE ARE WE GOING?

The COVID-19 pandemic has had a devastating effect on mental health worldwide. The magnitude of the challenge ahead is already apparent in the pediatric population, with escalating mental health emergencies and suicide attempts in the context of a medical system struggling to provide acutely needed pediatric mental health care.[36] As it becomes apparent that COVID-19 will not come to an abrupt and definite end, it will be necessary for mental health care providers to continue to adapt and advocate. A vital component of such efforts will be to ensure that brain stimulation therapy is safely, readily, and reliably accessible.

In the case of TMS, there was already enthusiastic interest in accelerated TMS protocols for depression before the emergence of COVID-19. During a pandemic,

potential reductions in time to response, treatment time, and overall days of treatment with accelerated intermittent theta-burst stimulation (aiTBS), in comparison to standard TMS protocols, may have exciting implications for mitigating viral transmission risk as well as for increasing treatment accessibility. To date, one small, open-label study found that 18 of 22 patients suffering from severe TRD met remission criteria with 50 high dose aiTBS sessions over 5 consecutive days.[37] Building on this work, Konstantinou and colleagues describe case reports of 2 patients with TRD whose symptom severity warranted ECT, but who instead received, and achieved remission from depression with aiTBS.[38,39] These cases along with the following vignette highlight the need for more research into the use of aiTBS as an alternative to ECT in cases where ECT is necessary but maybe unsafe or unavailable, such as during the early days of the COVID-19 Pandemic.

Vignette. A 40-year-old woman presented with a history of severe and recurrent major depressive disorder, rheumatoid arthritis, and migraines. Her medication history included adequate trials of citalopram, sertraline, fluoxetine, vortioxetine, desvenlafaxine, bupropion, aripiprazole, cariprazine, and dextroamphetamine. She had completed a standard course of rTMS treatments in October of 2019 and was considered a responder to that course of treatment. Despite medication changes, she experienced a relapse in depressive symptoms and returned to TMS in May of 2020. She completed an extended course of 50 TMS treatments with an FDA-cleared protocol, but this time did not respond to TMS treatment. Her outpatient psychiatrist started her on lithium, but she continued to struggle with worsening suicidal ideation. ECT was the next reasonable step in care, but the patient was not interested in pursuing ECT. A few months prior, ECT would not have been a treatment option because of a COVID-related hospital policy that restricted ECT to only immediately life-threatening cases. Two weeks after lithium was titrated to a therapeutic dose, in an attempt to avoid hospitalization, a course of aiTBS was proposed. Over 5 consecutive days, the patient received 50 aiTBS sessions in total. She had 10 sessions per day with 50-min intersession intervals, 1800 pulses per session in triplet 50 Hz bursts repeated at 5 Hz, train duration of 2 seconds, and an intertrain interval of 8 seconds, at 120% of the resting motor threshold over the left dorsolateral prefrontal cortex (DLPFC), localized with the modified BeamF3 method.[40] Her depression was monitored using the patient health questionnaire 9 (PHQ-9).[41] Her PHQ-9 ratings decreased from 19 on day 1 to 16 on day 5, and her affect appeared to improve. She reported a PHQ-9 of 15 1 week after her last treatment and 13 2 weeks after her last treatment. She reported stable and euthymic mood with full remission within a month of her last aiTBS session. She remained in reported remission for 6 months in the absence of any further medication changes. She tolerated treatments well with no reported side effects or adverse events. The patient's remission following a 5-day aiTBS protocol may have been multifactorial in nature, but her case does highlight the need for further research into aiTBS. The literature supporting aiTBS is limited, and there are still many questions to be answered regarding coil placement, dosing, optimal schedule, and durability.

How can brain stimulation services be allocated in unprecedented times? What is the acceptable threshold for clinical suffering? What can be done when treatments such as ECT are needed immediately, but simply not accessible? In some ways, this is not a new issue in the field of brain stimulation. In 2004, Ottoson and Fink found that ECT met all principles of medical ethics except for justice, as it was not universally and equally available to all in need.[42] Perhaps the experience of the COVID-19 pandemic offers a unique opportunity to consider solutions to remove barriers to access that have existed for decades.

DISCLOSURES

Dr M.J. Coffey has no relevant conflicts of interest to disclose; he reports receiving author royalties from UpToDate and MedLink Neurology. Drs S. Kerns, S. Sanghani, and L. Wachtel have no relevant conflicts of interest to disclose.

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