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Guidelines for TMS/tES Clinical Services and Research through the COVID-19 Pandemic

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Et al.

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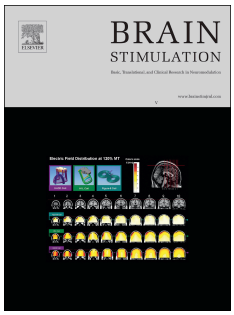

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Abstract

Background: The COVID-19 pandemic has broadly disrupted biomedical treatment and research including non-invasive brain stimulation (NIBS). Moreover, the rapid onset of societal disruption and evolving regulatory restrictions may not have allowed for systematic planning of how clinical and research work may continue throughout the pandemic or be restarted as restrictions are abated. The urgency to provide and develop NIBS as an intervention for diverse neurological and mental health indications, and as a catalyst of fundamental brain research, is not dampened by the parallel efforts to address the most life-threatening aspects of COVID-19; rather in many cases the need for NIBS is heightened including the potential to mitigate mental health consequences related to COVID-19.

Objective: To facilitate the re-establishment of access to NIBS clinical services and research operations during the current COVID-19 pandemic and possible future outbreaks, we develop and discuss a framework for balancing the importance of NIBS operations with safety considerations, while addressing the needs of all stakeholders. We focus on Transcranial Magnetic Stimulation (TMS) and low intensity transcranial Electrical Stimulation (tES) - including transcranial Direct Current Stimulation (tDCS) and transcranial Alternating Current Stimulation (tACS).

Methods: The present consensus paper provides guidelines and good practices for managing and reopening NIBS clinics and laboratories through the immediate and ongoing stages of COVID-19. The document reflects the analysis of experts with domain relevant expertise spanning NIBS technology, clinical services, and basic and clinical research – with an international perspective. We outline regulatory aspects, human resources, NIBS optimization, as well as accommodations for specific demographics.

Results: A model based on three phases (early COVID-19 impact, current practices, and future preparation) with an 11-step checklist (spanning removing or streamlining in-person protocols, incorporating telemedicine, and addressing COVID-19-associated adverse events) is proposed. Recommendations on implementing social distancing and sterilization of NIBS related equipment, specific considerations of COVID-19 positive populations including mental health comorbidities, as well as considerations regarding regulatory and human resource in the era of COVID-19 are outlined. We discuss COVID-19 considerations specifically for clinical (sub-)populations including pediatric, stroke, addiction, and the elderly. Numerous case-examples across the world are described.

Conclusion: There is an evident, and in cases urgent, need to maintain NIBS operations through the COVID-19 pandemic, including anticipating future pandemic waves and addressing

effects of COVID-19 on brain and mind. The proposed robust and structured strategy aims to address the current and anticipated future challenges while maintaining scientific rigor and managing risk.

Keywords: non-invasive brain stimulation, COVID-19, transcranial magnetic stimulation, transcranial direct current stimulation, transcranial alternating current stimulation, transcranial electrical stimulation

1. Introduction

COVID-19 was first recognized in December 2019 and within months evolved into a global pandemic declared by the World Health Organization (WHO) in March 2020. To avert its rapid spread, country-specific restrictions have been introduced spanning strict social/physical distancing measures, stay-at-home orders and even lockdowns, workplace closings and furloughs/layoffs, postponing of elective procedures in medical centers to preserve medical resources, suspending many in-person medical consultation and clinic visits, or substituting these face to face consultations with remote interventions, e.g. telecommunications. Measures to limit person-to-person contact affected institutions and researchers applying non-invasive brain stimulation (NIBS) operations. With the suddenness of COVID-19 emergence, operations at clinics and research centers administering NIBS were disrupted to varied degrees - from suspension of all activities, to limiting new enrollment or abbreviation protocols, to incremental accommodations - depending on regional restrictions and the nature of underling protocols (e.g. in-person treatment vs remote treatment). The means of maintaining (and even expanding) access to NIBS during the COVID-19 pandemic are strategically evolving. Considering that NIBS is a unique non-pharmacological tool, forms of which have been successfully established for treatment of a wide range of neurological and psychiatric disorders [1-7], often on moderately or even severely impaired patients unresponsive to conventional therapies [8, 9], the reestablishment of NIBS operations in the current era of COVID-19 pandemic as well as through future epidemics is of paramount importance.

Moreover, a further wave of mental health issues following this first outbreak of this virus is anticipated [10, 11]. Forms of NIBS are broadly applied and trials for mental health indications; thus, hold the potential to mitigate the psychological after-effects or comorbidities of the pandemic. This amplifies the urgent need for a roadmap of how to resume NIBS-based clinical and research activities in the face of the COVID-19 and also future pandemics.

This expert consensus paper aims to outline processes that could facilitate rapid, prudent, and coordinated re-establishment of operations at institutions providing NIBS treatments or using NIBS in research. We specifically focus on low intensity transcranial electrical stimulation (tES; encompassing transcranial direct current stimulation [tDCS], transcranial alternating current stimulation [tACS], transcranial random noise stimulation [tRNS]) and transcranial magnetic stimulation (TMS). However, our recommendations may be adapted to support the reestablishment of a broad range of device-based interventions. A session of the NYC

Neuromodulation 2020 Online Conference (20-22 April 2020) was dedicated to sharing experiences of NIBS researchers all over the world which inspired the plan to synthesize these opinions in the present document. Along with general guidelines and checklists, we provide an overview on the different strategies that have been introduced to mitigate the spread of the virus in NIBS procedures and NIBS laboratories. Additionally, we highlight new opportunities for NIBS regarding the current situation and discuss possible directions of research that could be taken considering the expected development of COVID-19-related diseases and disorders. The considerations presented here not only reflect the COVID-19 crisis but also prepares the NIBS community for potential future epidemics or pandemics.

In general, steps taken to support NIBS operations under any epidemic/pandemic conditions may span (a) reduction of unnecessary contact by judiciously removing protocol steps or transition to telemedicine approaches (which may include the intervention itself); (b) optimization of all at-center protocols based on sanitization (section 6.1), physical distancing (section 6.2), and streamlining procedures; (c) addition of protocols to manage risk such as COVID-19 or related symptom screening (section 6.3) or steps to support personnel affected by COVID-19 medically or professionally (section 5). These overarching principles apply with varied weights to the 3 phases of COVID-19 response (section 4) and are systematized through detailed guidance (section 4, section 5, section 6, section 9), our checklist (section 3.4), case examples (section 2, section 8) and consideration for specific clinical populations (section 7).

2. Results from Survey International Accommodations in Brain Stimulation Labs/Clinics to COVID-19

While strategies for the use of NIBS as a unique therapeutic tool through the COVID-19 crisis are currently developing, in the immediate aftermath of COVID-19 emergency many clinical trials and experiments involving neuromodulation around the world were severely disrupted or suspended - with the exception of those that employing remote at home tDCS treatments. In many cases, research activities were diverted to writing, reviewing and analyzing data remotely. Onsite clinical services were disrupted, in some cases with services limited to teleconsultations. Following initial disruption, several on-site services began to implement remediation measures (section 8, section 9). Clinical services and trials based around remote at-home tDCS through telemedicine, were generally able to proceed with minimal accommodations (section 8, section 9). This section focuses on immediate response as reflected in the survey of NIBS centers.

The survey addressing the impact of the COVID-19 pandemic was sent to institutions applying NIBS (research laboratories and NIBS clinics) across the world. Replies were received from 29 institutions representing 17 countries. These responses thus reflect the "situation on the ground" at the time of assessment with ongoing remediation methods addressed later in this paper. Mainly depending on the national and local restrictions in response to the COVID-19 outbreak and the nature of protocols (e.g. type of technology, trial stage, clinical population), there were substantial discrepancies in the extent to which neuromodulation operations were disrupted.

In February, preclinical and clinical research activities were interrupted in China and Iran. In Europe, the restrictions imposed by governments were implemented in an uncoordinated fashion; in Italy, Portugal, Denmark and the United Kingdom and the United States, restrictions were applied to clinic services and research labs beginning in the first half of March, while in Germany, Austria and Belgium, restrictions were applied in the second half of March. Switzerland and Brazil closed their labs in mid-March. Later, between the end of March and the beginning of April, clinics and research activities were suspended and labs were closed also in Canada, Russia, India, Australia, and Japan.

Globally, restrictions regarding hospitals often involved the interruption of all non-emergency services and the re-organization of routine activity focusing on handling COVID-19-related conditions. For many clinics where TMS and tES are used as treatment tools or involved in clinical research protocols, restrictions led to the suspension of non-urgent inpatient and outpatient services as well as all in-person activities. In some clinics, staff members have worked in rotation to minimize infection and provide only essential services. In Italy and the United Kingdom even home-based neuromodulation protocols were not immediately approved or feasible (Table 1).

Insert Table 1 about here

Examples of protocols without substantial disruption include the United States New York University (NYU) clinic and the Australia Black Dog Institute in Sydney using remote at-home tDCS treatments, which were largely able to continue operations with moderate accommodations and have even met an increased demand. Several centers providing in-patient NIBS treatment maintained at least some services, in the US including, Wake Forest (North

Carolina) and Medical University of South Carolina (MUSC), to help dampen the potential surge in psychiatric symptoms and illness resulting from the pandemic. Similarly, in Belgium at Ghent University COVID-19 sub-wards were established in the psychiatric clinic for the admissions of potential infected psychiatric patients. TMS has continued to be provided in both outpatient and inpatient programs in Australia although not in research protocols. At Ghent University in Belgium, electroconvulsive therapy (ECT) has been allowed only in selected cases depending on severity. The International Society for ECT and Neurostimulation published guidance on ECT during COVID-19 [12].

With limited exceptions, the restrictions limiting the routine and non-urgent clinical services and ceasing in-person activities have severely affected clinical research. Despite the guidance offered by agencies like the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) on how to manage clinical trials, clinical studies as well as single-center/multi-center trials are being impacted by the COVID-19 pandemic. In the immediate aftermath of COVID-19, research labs all over the world have been instructed to limit or stop most neuromodulation research that had direct person-to-person contact and was deemed non-essential. The timing of the closures varied, as well as the extent to which research was halted. Survey respondents report additional challenges arising from social/physical distancing measures, site closures, travel limitations for staff members and patients, interruption of suppliers' delivery, and considerations if personnel or subjects might be infected with the new coronavirus. Moreover, difficulties in meeting the required protocol-procedures, including the follow-up visits and laboratory/diagnostic testing resulted in a loss of data from ongoing trials, or in a delayed data acquisition, will continue until centers fully reopen and likely beyond (Table 2).

Insert Table 2 about here

Based on our survey, all other institutions stopped the enrollment of new subjects. In some cases, patient treatment studies were allowed to remain open to finish currently enrolled individuals, in other cases, institutions required investigators to determine if their research studies were addressing essential need and disruption of the intervention would lead to irreparable harm. It is possible that for some studies, new participants will need to be enrolled to compensate for these losses, which was not budgeted for across grants.

Even in early phases of COVID-19 responses, some centers report adapting NIBS clinical trials protocols to minimize in-person contact. Trials with remote home-based neuromodulation (tDCS and tACS) have largely continued, in some cases received updated approvals allowing for remote consenting (e-consent) and enrollment of new patients. For trials with in-center treatments, protocols are being implemented to allow for remote consenting, the remote collection of clinical data and the conduct of online cognitive tests, allowing some aspects of brain stimulation trials to continue even without home-based treatments.

Respondent to the survey reported teleworking is a central component of the overall response to the COVID-19 pandemic. While a challenge to the 'normal' culture way of working, tele-collaboration could represent an unexpected opportunity for researchers to re-analyze collected data, acquire new analysis and methods skills, design new experiments, pre-register scientific reports and brainstorm new ideas and projects. General tele-work practices and routines have also been introduced across NIBS centers to enable the remote working teams to maintain productivity, while monitoring and supporting the well-being, education, and professional development of staff (see section 5). For example, early career scientists and students concerned with the degree progress should, as appropriate, be offered additional support by adapting progress requirements (e.g. 3 months extensions concerning thesis submission deadlines) and providing them opportunities for online networking. Several respondents to our survey highlighted the opportunity to learn new skills online (through webinars, online lab meetings with guest speakers and online conferences). Responders are thus positive that the NIBS community could benefit from tele-work intellectual activities developed in the pandemic period (e.g. online conferences, papers, experimental designs, teaching materials, etc.) and the establishment of tele-communication tools should serve the NIBS community even beyond the pandemic period (e.g. project tracking and updates, new collaborations).

At present, the NIBS community is in the process of preparing for a return to either partial or full operational status in the coming months. While institutional regulations for restarting in person activities will vary, institutions surveyed consistently reported implementation of personal protective equipment (PPE) standards, social distancing approaches, plans to convert the consent process and assessments to tele-/video/online administration where possible, as well as sanitization procedures. A number of labs also indicated plans for COVID-19 testing and facilities modification to improve ventilation and social distancing procedures. At present a majority of sites surveyed do not have a definitive restart date. While the future is uncertain, labs

and clinics are preparing for eventual return to service with an eye toward implementation of plans to not only mitigate disruptions from the COVID-19 emergency, but also methods that will allow NIBS clinical and research services to weather future outbreaks of COVID-19 or similar events.

3. Response to COVID-19 Pandemic in NIBS Labs/Clinics: Past, Current, Future

A 3-phase model can describe responses to the COVID-19 pandemic in NIBS laboratories/clinics across the world, encompassing the immediate (Phase 0) to the COVID-19 emergency, the current (Phase 1) state of strategic responses within evolving COVID-19 restrictions (e.g. stay-at-home mandates), and planned activities (Phase 2) to optimize productivity through the COVID-19 pandemic, through potential future outbreaks, and the prolonged return to normal activities.

3.1 Phase 0: Past Measures in Immediate Response to Stay-at-Home Mandates from COVID-19.

In almost all cases, the rate and scale of impact from the initial COVID-19 outbreak created exigent circumstances that mandated rapid decisions. This commonly included cessation of all non-essential in-person research activities. However, institutional consideration was given in some cases for in-progress neuromodulation studies that involve the application of interventions addressing diagnoses such as depression, with some studies deemed essential and allowed to continue ongoing interventions with strict adherence to PPE for both researchers and participants. This determination was made by individual institutions with significant variability across sites. In response to stay-at-home mandates, entire study teams were faced with moving all activities to remote/tele continuation. For those involved in studies deemed “essential,” structured plans to allow study team members in labs/clinics and access to appropriate PPE were required. In addition, studies either already designed for remote administration of assessments and/or interventions were allowed to continue, with either minor or no modification to existing protocols.

In some cases, studies were able to modify their existing protocols to continue research efforts on a fully remote basis using tele-/online/video assessments or at-home brain stimulation procedures. However, many studies are incompatible with remote continuation and were required to stop. For those faced with remote/telework, documentation, reports of activity,

approvals, updates, online audits, online analysis, dissemination of results through manuscript development, online conferences and study team virtual meetings represented transitions requiring minimal effort to implement. However, for those requiring access to specialized hardware, specially protected data, or software, as a few examples, housed within the workplace, this transition either proved difficult or resulted in work stoppage. Regardless, an important element of the initial and ongoing response to COVID-19 across ongoing studies involved communication with all participants currently enrolled in ongoing studies to provide information regarding how their participation in the study would be impacted by stay-at-home mandates, as well as providing additional information for available local resources to address potential concerns for their welfare and well-being during the outbreak (e.g. tele-mental health services, community assistance programs, etc.).

3.2 Phase 1: Current Response.

During the COVID-19-related stay-at-home mandate, critical consideration must be given to re-integration strategies and approaches for restarting studies and trials. The timing and details of re-integration procedures will vary significantly across institutions, as did study stoppage and stay-at-home procedures. Nonetheless, brain stimulation teams can begin planning for potential iterations of re-integration procedures. At present, commonly discussed strategies across institutions include a tiered return to institutions for study teams, potential split shifts for study team members to cover study activities, PPE for all participants and study staff, COVID-19 infection or antibody testing procedures, body temperature assessment of all staff and participants, redesign of lab procedures/space to minimize person-to-person contact, new facility and equipment sanitization procedures, among others (see also below, section 6). While institutional procedures will vary, advanced planning for how these procedures will impact study continuation is important. In addition, study teams will be faced with a backlog of participants that either missed planned follow-up visits or have upcoming follow-up visits, as well as a need to replace participants whose intervention schedules were interrupted by stay-at-home mandates. Study teams will likely be strained to perform all needed activities for study continuation upon return. Advanced planning for prioritization of study activities will be important for efficient transition back to in-person activity.

3.3 Phase 2: Future Response to COVID-19 and Subsequent Outbreaks.

We are also faced with the uncertain possibility of one or more recurrent waves of COVID-19 and similar epidemic/pandemic outbreaks in the coming months and years. Thus, careful

consideration of protective equipment to protect research participants and staff members, to disinfect tools and labs, and long-term planning for implementation of remote assessment and/or intervention procedures may prove critical for long-term continuation of studies should this become a reality. Further still, once rapid COVID-19 testing and antibody assays are proven to be reliable and widely available, we will have tools that may allow us to alter how we respond to future waves of COVID-19. If procedures for maximizing the safety of in-person study activities (modification of space for face to face visits, restructuring of waiting areas to separate participants/patients, stringent PPE procedures, etc.) can be implemented immediately following the current outbreak, these methods paired with new COVID-19 testing procedures may redefine how we respond to future COVID-19 pandemic events. For example, most TMS clinics around the world were shut down for depression treatment following the initial COVID-19 outbreak, preventing access to care needed by patients. If careful in our current and future response, different approaches for safely continuing such activities may be possible. We can consider developing institution specific standard operating procedures for the labs and orientation of all staff members to deal with future outbreaks. As such, we provide a summary of important considerations for response to COVID-19 as well as a checklist for adapting research and treatment practices to COVID-19 in Table 3.

Insert Table 3 about here

3.4 Recommendations (Checklist) for Adapting Research and Treatment Practices to COVID-19

Here we provide a list of recommendations for adapting research and treatment practices to COVID-19 pandemic.

1) Conduct a systematic updated risk-benefit analysis of each protocol to decide for each effort if it should continue and inform remaining steps; this may include contingency plans to changes in a given circumstance (e.g. if X happens the trial will need to wind down under these conditions), engaging all stakeholders in discussion (e.g. staff, program office, DSMB, etc.), and statistical consultation with respect to the power to make conclusions regarding protocol changes (e.g. change in dose, trials terminated prematurely) and associated changes in outcome reporting (e.g. feasibility instead of efficacy).

2) Transition as many study procedures as possible to electronic or video format (e.g. consent process, screening visit, assessment tools, switch to an established home-based techniques).

3) Remove non-essential steps in protocols that require in-person interactions.

4) Establish stringent safety and sanitization procedures for all required in-person interactions and train staff in execution of these procedures (with documentation of training completion). Ultimately, staff will have to follow regulatory and protection procedures adopted by specific research or clinical settings (e.g. nursing home setting) will have to follow COVID-19measures for that setting; or in-person visit at a patient's home will require compliance with COVID-19protection mandated for home care. Therefore, developing and updating protocol specific safety procedures requires research staff communication and coordination with institutional (clinical) leadership for the specific setting in which NIBS studies will be carried out.

5) Implement all institution required safety procedures (e.g. screening, PPE, COVID-19testing, etc.). Develop study-specific considerations for staff who recovered COVID-19.

6) Consider changes in intervention that do not impact trial integrity (e.g. number of visits, inclusion/exclusion) or consider changes that strategically change trial scope (i.e. still allow for meaningful publishable outcomes; e.g. changing to a pilot trial).

7) For in-person protocols, streamline the entire process from participant preparing to leave their home, to transportation, to arriving at clinic/lab, to leaving the clinic/lab to maximize social/physical distancing (including between patients and between staff) with special attention to neuromodulation steps; where possible, the clinical trial may provide support for car service for participants to avoid public transportation.

8) Add additional telemedicine steps (follow-ups) to adjust for changes in protocol; Add steps responsive to COVID-19 related concerns. This can include additional data collection that may impact immediate decisions (vii) or later analysis such as testing all subject temperature or surveying for COVID-19 related symptoms. Determine

protocol for identified COVID-19 positive patients, including if they are not critically ill or without symptoms.

9) Review explicit protocols / consideration for adverse events (related or not to the intervention) so that the decision tree (what to do, who makes the call, what needs to be reported) is mapped out beforehand (patient or caregiver has X symptoms leading to Y actions).

10) Obtain IRB approval for any applicable changes (e.g. all the above) in protocol including patient consent in regard to any new anticipated risks.

11) Take steps to share your plans, lessons, learned, and ongoing experiences with the broader community. Survey all stakeholders (e.g. building facilities, research personnel) to gauge comfort with planned activities.

4. Regulatory Factors

4.1 Trial Registry (e.g. ClinicalTrials.gov) Report Updating

All clinical trials registered with a database such as ClinicalTrials.gov should be appropriately updated to reflect the mitigation plan to limit risk of infection, a revised timeline for enrollment and any social/physical-distancing related adaptations to the protocol. Participants may be more willing to enroll knowing that precautions have been made.

4.2 Institutional Review Board/Ethics Review Board Approval

Some ethics boards may mandate withholding research recruitment for some period at peak of outbreaks. While pausing a study does not necessarily require notification to the IRB/Ethics Board, any protocol changes to the process of interaction, intervention or assessment of participants must be reviewed and approved by the resident ethics board. This includes but is not limited to modifications of the method of administration from in person to online, shifts to at-home neuromodulation procedures, change in participant payment method, etc. Study sponsors may have differing timelines for study restart than local institutions and ethics boards.

4.3 Converting to a Video/Online Consent Process

Many research groups are now converting their consent and screening visits to a tele-health/video-visit. The term most frequently used is “e-consent or e-consenting”. The

requirements for this vary by Institutional Review Board, but all contain the core features of providing the prospective participant with a copy of the Consent (e.g. via mail or email), going over the Consent remotely, and obtaining a signed copy of the Consent (e.g. mail or email) which the investigator countersigns on the date of receipt. Once the participant signs the consent, typically with either video observation or through a secure online signature process, this enables the investigator to proceed with the screening visit, which can be facilitated using electronic forms (e.g. RedCap, Qualtrics, ClinCapture). Such video/online consents and video/online-based screening visits lessen the risk of contracting the illness for everyone, and may provide a more effective means of performing a Consent visit involving all necessary safety precautions (masks, disinfection, etc.).

4.4 Communication with Funding Agencies and Data Safety Monitoring Boards

Study suspension and any revisions to procedures within funded studies should be discussed with the funding agency. In addition, for clinical trials with a standing data safety monitoring board (DSMB), study suspension and restart as well as changes in study procedures should be forwarded to the DSMB for approval.

4.4 Extensions of Funding for Research

In most places across the world, neuromodulation studies have been suspended, yet the costs associated with those experiments (e.g. salaries, animal housing and food costs) have continued. This placed a financial burden on these studies and will also delay the final results of the studies. Thankfully, several funding agencies, including the US National Institute of Health, Wellcome Trust and the Medical Research Council UK, and Swiss National Science Foundation have announced the ability to apply for an Administrative or grant Supplement to cover unforeseen COVID-19-related costs. They have also streamlined the process for getting approval for a No Cost Extension. These steps offer significant relief to researchers and increase the likelihood that the dedicated resources already invested in these projects will be fruitful.

5. Human Resources Considerations

Supporting our colleagues, particularly Early Career Researchers, is vital in this time of crisis. There are a number of issues that this period brings; here we will discuss some of the most pressing. This cannot be an exhaustive list, however, and it is vital that as a field we are sensitive to the additional needs of our colleagues. It is perhaps important to note that we are in

no way encouraging a decrease in the standards required for publication. Rather, an increase in understanding around the circumstances in which that work is done is called for.

Firstly, it is vital to recognize the additional anxiety the current situation will place on Early Career Researchers and PhD students. For students with only months of funding left with which to complete their degrees, this is a very stressful time, as it is for those more senior researchers with grant deadlines. It is to be hoped that this paper will provide helpful suggestions and contribute to the discussion for ways to ease the difficulties faced at this time, however, the inevitable anxieties associated with the current situation are real and should be explicitly acknowledged. We must work to address these and to support our colleagues through this difficult time.

Research groups around the world will be physically separate, indeed often spread across time zones if students choose to spend this unprecedented period at home. This will inevitably lead to psychological stress, something that has already been seen in China [13]. Maintaining group cohesion is vital and implementing explicit support structures is necessary, particularly for those isolating on their own with families elsewhere [14]. While online tools cannot replace face-to-face interactions, they are vital substitutes in current times. The vast majority of labs will have moved work meetings online already, but in addition to these it is important to recognize that for many work is also a social experience and now more than ever, an essential source of support. Scheduled coffee breaks, games nights, film nights, cocktail hours (with alcoholic or non-alcoholic drink of choice) and many other social events are all being implemented successfully across the world to create at least some of the social interactions so important to both our mental wellbeing and our lab cohesion. Explicitly matching group members in a buddy-scheme, where each lab member has a partner that they have to contact even briefly each day, is a way of providing a light touch method to flag potential mental health issues early. While we cannot prevent the inevitable increased rates of mental health problems in our community, making sure that we explicitly discuss the difficulties we all face in this pandemic, and the inevitable mental health repercussions, will hopefully allow those facing particular problems to speak out and receive the support they need [15].

It is necessary to act now to ensure that the current pandemic does not have long-lasting negative consequences on the field. NIBS has historically had a lack of female representation [16], something that leaders in the field have made a concerted effort to address in recent years

[17] with increasing success. However, the current crisis is likely to exacerbate the gap between women and men, and between carers and non-carers, in terms of available time and opportunities. The burden of care and responsibilities have fallen unequally in this crisis - for some this is a virtually unheard of period of quiet in which they have the time to produce as much, if not more, work than normal. However, for the field as a whole it is vital to recognize that for others this is a time where demands and anxieties have increased, and available time has shrunk considerably. The “room of one’s own in which to write” [18] is for some a daily reality and for others merely a distant dream. The real effects of this inequality across academia is already being spoken about anecdotally by editors, who report decreases in the number of submissions from women [19] and, possibly, increases in the number of submissions from men. How those trends continue will need to be carefully monitored.

While it is extremely difficult to judge what effect other responsibilities may have on our colleague’s productivity, it is timely to recognize that although individual circumstances vary substantially on average women still carry the majority of the burden of both caring responsibilities and household tasks even when both partners work [20] - something that can at the moment only exacerbate gender imbalances in the field. It must therefore, be the responsibility of all of us, particularly those in more senior positions, to acknowledge this and to challenge the potential prejudices of others and ourselves when making career-determining decisions, not just at the moment but in the months and years to come. Suggestions have already been made as to ways to tackle this, including explicitly treating this period as carers leave in future applications [21].

In the shorter term, the social/physical distancing measures in place around the world are not only limiting what we can do in terms of science, but limiting the opportunities for all of us, particularly the Early Career Researchers, to network and to meet potential advisors for the next stage of their careers. Initiatives such as on-line conferences are likely going to be the mechanism for sharing our science for at least the next few months and provide an essential opportunity for our ECRs to discuss their work. However, what is difficult to reproduce on-line is the informal chat over coffee with others in the field, which can often provide the start to a conversation that ends with a postdoctoral position or support for tenure-track applications.

Overcoming these restrictions will be difficult: by definition it is challenging to formally engineer informal discussions. We all have a responsibility to recognize this, and to be responsive to

unsolicited emails from researchers elsewhere. This is also a time to embrace the ability to invite speakers from around the world to give informal talks at lab meetings and small gatherings without the costs involved in travel. Not only does this broaden our horizons at a time when it is all too easy to reduce our interactions, it also has secondary benefits. Small lab talks provide excellent opportunity to interact with external researchers in a small group. Inviting senior researchers to speak can provide a route into discussions for ECRs, inviting ECRs to speak provides valuable experience for them.

In practical terms, many universities have relaxed the timescales required for PhD students, something that we must support and petition for. Many grant bodies around the world have already announced blanket extensions to current funding - as a field it is our responsibility to make these allowances as equitable as possible. A number of routes through the current crisis have been suggested in the rest of this article which will allow us to continue our research with disruption kept to a minimum. However, in the inevitable rush back to the lab, for the long-term sake of the field we must not forget to bring everyone with us.

6. General Guidance in Reopening Labs/Clinics

As with all COVID-19 safety procedures, regional and institutional guidances, applied judiciously to specific protocols considering changing conditions, will determine which procedures should be implemented and which can be abbreviated. Our recommendations below explain a range of existing procedures in the context of NIBS application and should not be considered necessary or sufficient for every situation.

6.1 Social/Physical Distancing Protocols

A critical factor in controlling and reducing the spread of SARS-CoV-2 and the associated COVID-19 has been so-called social/physical distancing, which means preventing physical contact especially of persons who otherwise would not have social contact. What is essential to understand here is that the terminology “social/physical distancing” may be somewhat misleading, as what matters in essence is the physical distancing. The latter in turn has mainly been recommended because one dominant way by which SARS-CoV-2 is transmitted is by airborne droplet infection. More specifically, aerosols emanating from the upper respiratory pathway housing the virus in high concentrations are thought to passively “travel” through the air and remain airborne for some time. While the exact travel distance and the amount of time that infectious materials maintain in the air are currently a matter of debate, most recommendations

suggest keeping (at least) 2 m (6 ft) distance to any other person and assuming that any unknown person could potentially be infectious [22]. Minimizing duration of contact is another strategy that may be considered based on study protocols, current federal and institutional guidances, and current scientific consensus on impact of briefer contact times (protocols) in reducing risk to operators and patients.

Social/Physical distancing parameters as defined by governments and regulatory authorities vary among countries, states and counties and change over time as a regional Covid-19 situation develops. The following procedures are therefore region and institute specific, and subject to ongoing risk-burden evaluation. As applicable, social distancing should be maintained in all offices. The allowed density of staff in given rooms should be considered along with the need for and mechanism of minimizing face-to-face interaction (e.g. by using chat, emails or telephones). As applicable to the specific time and protocol, it may be prudent to wear masks and maintain a recommended interpersonal distance. If and when patients should wear masks for necessary clinical treatments should be determined. For studies and therapies where wearing masks hinders the efficacy, transparent face masks could be considered.
During NIBS procedures, it is often not possible to maintain the recommended physical distance, at least for some amount of time. For instance, applying electrodes for tES or adjusting the position of TMS coils requires direct contact between the person applying NIBS and the person receiving NIBS. Robotic TMS provides some opportunity for TMS administration with operators further removed from participants (easily by 2 meters/ 6 feet except for brief localization to navigation, though the participant can be trained to do this). However, such devices will not be available to all labs and clinics. In these instances, protective measures are important to reduce the inhalation and expiration of aerosols, and the amount of time, during which the recommended physical distance cannot be complied with, should be restricted to a minimum possible.

6.2 Personal Protective Equipment (PPE)

PPE can take many forms such as wearing face masks that should cover both mouth and nose. There are different safety standards for these masks, and we recommend that medical and research personnel in constant contact with potentially infected persons (including participants and patients, but also co-workers) wear those with the highest safety standards (e.g. N95 masks). Importantly, the masks should be regularly changed (with maximal wear time differing as per the specific type and make of the mask) as otherwise they might even be

counterproductive due to the accumulation of viral material at the inner side of the mask. If appropriate, patients and participants may be provided with single use or disinfected multiple use masks by the neuromodulation labs.

As appropriate, in addition to masks, medical and research personnel may consider wearing transparent visors, or protective eye wear covering the upper parts of the face and especially the eyes, through which viral material can also easily enter the organism. Visors that cover the whole front of the face extending way down below the chin may supplement face masks for researchers and participants. In theory, the appeal of visors without masks is allowing better verbal communication, compared to face masks, which limit articulation and comprehensibility of speech sounds i.e., the “muffling” effect- b but such considerations are secondary to safety. The appropriateness of visors and other PPE (e.g. goggles, protective coats) in various social and clinical environments will ultimately depend on current regional and institutional guidances. In some regions and institutions, current recommendations are to use both a surgical mask and visor for direct interactions with patients.

Moreover, medical and research personnel should wear single use gloves when touching participants and patients, and the latter may also want to be provided with such gloves when touching apparel that will be touched by others, such as input devices, computer keyboards, desks, etc.

6.3 Facilities and Sanitization Procedures

As with all COVID-19 safety procedures, regional and institutional guidances, applied judiciously to specific protocols considering changing conditions, will determine which procedures should be implemented and which can be abbreviated. Our recommendations here thus index possible applicable procedures.

Besides body-worn protective measures, room dividers and transparent shields can be considered for installation in facilities that are not already designed for one-on-one visits. These devices constitute a physical barrier protecting spread of aerosols throughout the room from participants and patients to personnel and will be especially important at patient receptions. Provisions of hand washing opportunities, or hand sanitizers for patients and participants at the entrance to research and treatment premises are also generally recommended, and they should be provided in a way that they can be regularly and easily used by medical and research

personnel, after each new contact with a new person. Additional measures to minimize airborne particles being transmitted are regular ventilation of research and treatment laboratories, regular disinfection of surfaces, such as doorknobs, apparel, furniture, research equipment and visors as well as shields, ideally after each use by a new person, is highly recommended. Within elevators, covering all buttons with plastic membranes that are changed daily is advised. Tissue paper or small wooden pieces can be provided to push the button without skin contact.

Special consideration should be given for employing single-use equipment when possible. For example, within tES, a variety of single-use and multi-use electrodes is available. Maximizing the use of single-use devices that contact the participant/patient serves to minimize potential translocation of virally active material from one participant to the other. Where devices must be used across participants, antibacterial disinfection may not be sufficient. In all cases, all research equipment should be sanitized/disinfected before and after use. In this, special consideration as to which type of disinfectant is used needs to be applied, as the functionality of some electrodes may be negatively affected when disinfected with alcohol-based disinfectants. One potential alternative to alcohol-based disinfectants is the use of Hydrogen Peroxide. We recommend referring to manufacturer information to evaluate possible disinfection routines. All disposable supplies should be discarded in appropriate bio-waste repositories. Note that most of the considerations regarding sanitization protocols should not only be applied to laboratories and treatment facilities, but also for the off-site home use mentioned above in this paper.

The following disinfection and sanitization protocols are aiming to give research facilities some flexibility to re-start NIBS clinical services and research operations during the current COVID-19 pandemic and possibly similar outbreaks in the future for patients with non-COVID-19 needs or complex chronic disease management requirements.

- After the NIBS session is over, the environmental surfaces in the stimulation room should be sanitized using a 1% Hypochlorite solution, with a disposable antiseptic cloth [23]. Also, all the stimulation equipment, including magnetic coil (for TMS) stimulator, electrode/stimulator cables, EEG cap, tape measure, electrodes and sponge pockets should be sanitized. Follow manufacturer specific guidance on how to clean the stimulator. Furthermore, it is prudent to check for any leaked fluids from the participant on the stimulation chair.

- The stimulator trolley and treatment chair should be wiped with a permitted cleaning product (normally bacillocid is allowed, but it is better to check with the manufacturer).
- If an MRI/MEG□compatible stimulator is available for concurrent application of NIBS during the recording of neuroimaging or electrophysiological data, then the gantry and the RF coil should be sanitized with a permitted cleaning product. The MRI table also should be sanitized with any of the approved products. The coils need to be disinfected once again after the scanner room is thoroughly sanitized, then the next patient or participant may be taken [24]. It is necessary to ensure that the metal nose piece of surgical masks, if applicable, is not ferromagnetic [25].

6.4 Vulnerable Populations

An additional aspect that requires consideration is the inclusion of individuals that belong to high(er) risks groups, both on the side of the personnel and the research participants or patients. Currently, older age, a history of cardiovascular diseases and diseases affecting the respiratory system (e.g. asthma, smoking), but also diabetes, obesity and cancer or other diseases affecting the immune system directly or through immuno-depressant treatment (e.g. multiple sclerosis [MS]) are widely considered as major risk factors (see e.g. [26], for a meta-analysis). However, what constitutes a major risk to develop COVID-19 is still not definitely established scarce, and we thus recommend to closely monitor the accumulating scientific evidence in this respect (e.g. via [27]). For now, we recommend that individuals belonging to the groups mentioned, as well as individuals being in close regular contact with individuals belonging to such groups, should only enter studies or be treated under special circumstances and with utmost care.

A logbook of each lab and treatment room should be maintained, listing personal interactions that took place so that in case of an infection, all persons in contact with the infected person can be traced back and informed about a possible infection. In such cases, we strongly recommend swift reactions, including quarantining of the potential new carriers, exclusion from work premises, and rapid testing for SARS-CoV-2.

On a critical note, many of these measures are not based on concrete evidence on their effectiveness. There is still insufficient knowledge about which of them are necessary and sufficient to prevent further spread of the virus. However, to the best of our current knowledge, they can be expressed as strongly recommended. Another critical aspect is whether the measures can be implemented consistently. In many countries, for instance, masks but even disinfectants are still not available in the required quantities and using the limited number of protective measures for protection of healthcare workers treating COVID-19 patients should be given higher priority than using it for neuromodulation research.

6.5 Personnel, Participant and Patient Screening

Additional precautions are regular (self-)screening by personnel, patients and participants, for potential infections or contact with infected persons. This can be achieved by a symptoms checklist, which every person entering the research or treatment premises has to provide, as well as by temperature measurements at the entrance to the research facilities. All of the latter, however, may be of limited validity, as many persons infected by SARS-CoV-2 have been reported to be asymptomatic, and do not develop the associated disease (and thus will neither show symptoms, including fever). Many institutions have plans to implement either rapid COVID-19 testing and/or COVID-19antibody testing of faculty and staff prior to reentry into the workplace. In addition, some institutions are considering requiring all study participants to undergo rapid COVID-19 testing prior to in person study activity. Availability and implementation of these tests will vary across institutions.

The scientific basis for SARS-CoV-2-related immunity and reliability of antibody testing remains under development. Subject to ongoing scientific insight and respecting regional and institutional guidance, screening for antibodies in the blood of staff or participants could be one element supporting the basis for an “immunity passport” or “risk-free certificate” that would enable individuals to return to work or research assuming that they are protected against re-infection. In this respect it should be noted though that a previous infection and the development of immunity may not protect against another episode of infection, and development of the disease (see e.g. [28]). However, whether the immunity passport policy will apply systematically or not, there is value in specific protocols and based on broader COVID-19 situation factors in applying such tests during recruitment procedures to improve patient-clinician safety or trial integrity.

7. Specific Clinical Populations

7.1 Stroke Patients: Stroke survivors can experience a wide range of impairments and disabilities including motor deficits and the loss of ability to produce and/or to understand language (aphasia). Among other treatments, use of neuromodulation techniques has been proposed to enhance/facilitate stroke-recovery. Past studies have integrated centrally acting tDCS with peripherally acting intensive motor or language rehabilitation protocols [29-37]. Before COVID-19, there were several tDCS aphasia treatment protocols published with positive outcomes [38] but during the first half of March, the pandemic forced most of the labs involved in NIBS and stroke recovery to suspend clinical and research activities. COVID-19 has significantly increased the risk of social isolation and associated depression in people with aphasia. Indeed, language and cognitive problems limit the use of digital media (i.e. cellular and/or social network) to maintain social contact. Patients with motor symptoms have also been penalized as a result of COVID-19 since it might be more difficult for them to move or get around with limited caregiver and physical or occupational therapy support. Stroke patients being in an older age category increase the risk of contracting the virus and potentially having a worse outcome; thus, in order to contain the exposure, they will probably be forced to stay-at-home for a longer period than young people augmenting the possibility of psychological distress and depression. To address these mental health issues, researchers from the Aphasia research Lab at the IRCCS Santa Lucia Foundation in Rome have launched an online interview in the aphasic population to evaluate whether anxiety and fear towards COVID-19 contagion would discourage the restart of rehabilitation. One concern is that patients worried about COVID-19 may be deprioritizing their neurorehabilitation needs and may develop an attitude of resistance towards clinical research, deemed non-essential.

Assuming that regulatory agencies and medical centers will hopefully lift the research and clinical treatment suspensions in the coming months when appropriate mitigations plans are in place, it is important to consider that tDCS protocols for motor and/or aphasia rehabilitation will be hampered by the difficulty in maintaining an adequate safety distance during electrodes application and even more importantly by the mandatory use of masks. Indeed, for language and cognitive interventions, it is extremely important that both the therapist and the patient understand each other, being able to see their mouth's movements (i.e. 'lip-reading' is known to facilitate communication). Transparent face shields without masks might be a good alternative option here. However, these will not resolve the question of electrode application while keeping a safety distance. Another possibility is to develop remote, but supervised and controlled interventions at the patient's home using home-based tDCS devices. As appealing as this

sounds, considering that most patients have cognitive and physical limitations in applying the 'kit' and that NIBS approaches require a peripheral intervention (e.g. traditional speech therapy or physical-occupational therapies), it will be challenging to provide these combined approaches in a patient home. For stroke patients, there might be also an option to develop remote intervention in an outpatient clinical setting ensuring that there is enough separation and physical distance between the patient and the investigators. There is no doubt that requests will be made to regulatory agencies to allow for clinical research in stroke recovery to be conducted in a remote way or at the patient's home by integrating tDCS with other telerehabilitation techniques and digital interventions e.g. computer delivered rehabilitation. In this way, we may resolve the issue related to language distortion due to wearing a cover that, masking not only verbal communication but also facial expressions, would anyway hinder communication exchanges. Moreover, since some tDCS language protocols have already been validated, we might think of offering caps to the patient's family with the position of the electrodes already fixed to facilitate and standardized application. However, we must be mindful that by doing so we may be limiting the breath of patients we can study and the generalisability of our findings e.g. only those who have prior experience using digital technologies, with limited cognitive difficulties, who have family members that can monitor and assist putting on the 'home-kits would benefit from those treatments. We also have to consider the safety of the remote tDCS protocols. Patients might be at a risk of seizures after stroke and fatigue is an important factor which might interfere. So timing and careful monitoring of the remote interventions are additional variables to take into account. Considering past remote neuromodulation studies and current COVID-19-related problems, tDCS protocols either at home or in a remote location at a medical center (separating the patient from the clinician) may be an opportunity as well as a challenge in the future.

7.2 Pediatric Research: For over the last decade, neuromodulation has been safely integrated in pediatrics with myriad diagnoses and disorders and promising outcomes [39, 40]. Protocols have integrated TMS, rTMS, tDCS and theta-burst in varying age ranges from infancy through young adulthood. Although commenced in adult populations, pediatric tele-neuromodulation protocols have not yet been established. In response to COVID-19, the Pediatric Neuromodulation Laboratory in the Medical School at the University of Minnesota, in conjunction with physicians from Gillette Children's Specialty Healthcare, and Mayo-Rochester, have developed an online survey investigating the impact of COVID-19 and the stay-at-home mandate on family/child access to rehabilitation care for children with cerebral

palsy. Pediatric Investigators in our Department of Psychiatry are also integrating our protocol to run a parallel survey, for families of children with related psychiatric diagnoses. We are now commencing a novel pediatric telehealth NIBS study investigating tDCS in the home setting via remote/telehealth specifically for children with perinatal stroke and resultant cerebral palsy. This study is informed by our previous adult stroke neuromodulation telehealth studies, and previous established guidelines. The first phase of this study will investigate the feasibility and reliability of parents/caregivers in operating the device and positioning the electrodes. Phases thereafter will establish child tolerance and safety, along with administration and assessment of stimulation in conjunction with rehabilitation interventions.

7.3 Patients with Chronic Neurological Conditions: Neuromodulation is an appealing option for symptom management and rehabilitation for those living with chronic neurological conditions such as multiple sclerosis, Parkinson's disease (PD) and other disorders with cognitive or movement dysfunctions, with many positive signals from the literature and large controlled trials underway. Specific considerations with these patients include potential cognitive impairments, which may reduce the ability to understand and complete the required study procedures, as well as sufficient motor functioning to operate any study equipment from a remote (home) location. However, in our work to date, we have found that the majority of those living with MS, ages 18 to 80 years and with varying disability levels including wheelchair dependency and impaired upper limb motor functions, can complete our remotely supervised protocol with guidance from a tDCS technician and can also include caregiver training for support. It is important to include these patients with more advanced disease for full representation of the disease spectrum because they often have fewer treatment and rehabilitative options. Continuity of care for patients in research or clinical protocols is important, and ongoing communications serve as a connection to the clinic for those patients with stable disease who otherwise would not be in contact with their treatment teams during the current time period.

7.4 Addiction: The secondary effects of the COVID-19 pandemic (e.g. periods of lockdowns, closures of routine clinical services and forced self-isolation deriving) have uniquely challenged the health and welfare of people vulnerable to drug and alcohol addiction as well as those with behavioral addictions (gambling, gaming, compulsive eating, Internet and new technologies). Inpatient or residential treatments have been interrupted since the substantial risk of coronavirus spread with congregation of individuals in a limited space. Alcohol and

marijuana sales have also increased as, in many areas of the world, businesses that dispense/sell these products have been some of the few businesses to remain open as they are often deemed essential services. This suggests a burgeoning wave of drug and alcohol related problems will emerge in society, and highlights the need to return to delivery of clinical treatment research in this area. That said, a recent summary by the National Institute of Drug Abuse highlighted original research demonstrating that chronic smokers and opiate users are likely at higher risk for COVID-19 related morbidity associated with respiratory disease [41]. Data from the Chinese Center for Disease Control and Prevention have suggested that COVID-19 has an increased fatality in patients with chronic conditions, like respiratory and cardiovascular diseases [42]. An international group of experts on addiction medicine, infectious diseases, and disaster psychiatry has recently explored the possible raised concerns and nicely provided recommendations to a comprehensive healthcare response to COVID-19 in SUD [2]. To deal with the consequences of the COVID-19 on addictions, efforts will require joining partnerships and possibly unprecedented use of technology in which neuromodulation by NIBS would nicely fit, especially thinking in distance treatment with an online monitoring system.

7.5 Older Adults: It has become clear that older adults have the highest rates of morbidity and mortality associated with COVID-19. Consequently, older adults represent a vulnerable population and careful consideration should be made when bringing them into a research or clinical environment wherein they may be exposed to others that are infectious. Special consideration should be given in regard to lab/clinic activities with older adults that have comorbidities that further increase risk for poor COVID-19 outcomes, such as chronic obstructive pulmonary disease. While standard PPE, sanitization and minimization of person-to-person contact should be adhered to in all participants, it may be necessary to discontinue ongoing in-person research activities for those at the highest risk for infection and poor outcomes. In-home neuromodulation or treatment options in the daily care units for older people may be a particularly good option for these individuals. Regardless of comorbidities, labs/clinics working with older adults should adhere to the highest standard of safety for minimizing COVID-19 transmission when continuing in-person research activities.

Vulnerable sub-populations of older adults also include those with multiple chronic illness and low performance status, such as those receiving supportive services within the retirement communities (NORC) or community-based patients receiving specialist-level palliative care. At-

home tES paired with telehealth solutions has been shown feasible in these vulnerable sub-populations. With proper COVID-19 precautions, screening and PPE protection, non-invasive neuromodulation may provide an option for symptom management in home settings.

8 Examples of Best Practices in Brain Stimulation Labs/Clinics across the World

8.1 Example 1, NYU Remotely Supervised or RS-tDCS: In the Department of Neurology at NYU Langone Health in midtown Manhattan, a protocol for remotely supervised tDCS (RS-tDCS) [43-45] has been systematically developed and validated over the past five years with the goal of increasing access to treatments for larger sample sizes and to extend the number of treatment sessions. To date, using this protocol, >5,100 remotely supervised at-home sessions have been delivered to patients with MS [46, 47] and other neurological conditions such as PD [48] and cerebellar ataxia [49] and following ECT [50], targeting behavioral outcomes such as cognitive and motor functions and fatigue. While reducing patient time and costs was the original goal of the RS-tDCS protocol [51], the COVID-19 clinical research pause demonstrated the broad utility of remotely supervised at-home treatment for clinical trials. To date, there are two ongoing RCTs in MS participants, one pairing tDCS with cognitive training for 30 daily sessions over 6 weeks (National MS Society), and the other pairing tDCS with upper extremity motor exercises (US DoD) for 20 daily sessions.

The research team prepared lab computers in advance of the research pause to administer the video visits off-site. Research participants were able to continue their daily treatment sessions without interruptions. We then obtained IRB approval to obtain informed consent for these trials remotely and have continued to enroll new participants. We have coordinated shipping of study equipment in “kits” to our participants that includes a preprogrammed tDCS device, headset, single-use sponge electrodes, a preconfigured laptop computer for the video visits and survey administration for outcomes. In the motor training trial, equipment for the daily exercises and assessment measures is also included. Study materials preparation and shipping (incoming and outgoing) follow a checklist protocol for enforcement in the policy for cleaning and disinfecting of study materials with all equipment marked for visual confirmation of sanitization. A third ongoing study (National Institutes of Health, NIH) that required baseline and treatment end neuroimaging visits was able to continue the treatments for the current participants but with enrollment on hold until research neuroimaging visits are resumed.

Due to the high demand for access to tDCS from patients with MS (e.g. those who have had positive benefit in a clinical trial) as well as those with other chronic neurological conditions, we received institutional approval for a clinical tDCS service in December of 2019 as innovative care. This service was launched through the NYU Langone Virtual Health platform to provide video visits as telemedicine using our RS-tDCS procedures adapted for clinical use. Patients are loaned the tDCS device and headset, with a baseline clearance evaluation and then an intake visit with agreement forms and device orientation. The virtual visits operate directly through Epic [52] as is now system-wide throughout the NYU Langone Health system for implementation of telemedicine. Patients in the service currently include those with cognitive or motor symptoms of MS, mild cognitive impairment, and ataxia [49]. We also have provided the clinical treatment to patients with traumatic brain injury, post-stroke aphasia, and depression and cognitive impairment following ECT [50]. There has been no alteration of this clinical service during COVID-19 and we are able to see new patients through the outpatient telemedicine platform.

8.2 Example 2, University of Minnesota, Pediatric Transcranial Direct Current Stimulation: Similar to adults, tDCS has been found to be well tolerated by children and has promising clinical effects [53]. The challenge of pediatric in-home telemedicine methods includes safety and parental compliance [54]. Considering that neuromodulation performed remotely or in the home setting in children incorporates a vulnerable population and also involves parents/legal guardians, assessments of safety, reliability and adherence are expanded beyond the construct of adult studies, and the investigator's role in education and remote oversight pivotal.

For over a decade, our Pediatric Neuromodulation Laboratory has pioneered protocols incorporating neurorehabilitation and neuromodulation. The potentially devastating impact on access to rehabilitation therapies due to the COVID-19 stay-at-home mandate on families and children with disabilities has yet to be fully realized. Telerehabilitation, as an alternative means to access rehabilitation intervention, has been successfully and feasibly performed in diverse populations of children with disabilities and by diverse telerehabilitation strategies [54]. Considering the construct, telerehabilitation in children has been reported to initially involve face-to-face discussion and education for both the parents and the child [55]. Additionally, specific considerations are indicated for pediatric populations, and integration of parents. In a pediatric telerehabilitation study aiming to increase treatment opportunities in cognitive training for children, Corti et al. integrated assessments of the feasibility of interventions and the study

design in the home setting [55]. Key aspects of these assessments included ‘accessibility, training compliance, technical smoothness and training motivation’, along with assessments of recruitment, enrollment and retention. The authors found integration of the assessments to establish the study well-suited and remarkably high adherence to the protocol. Inherently, integrating tDCS with telerehabilitation would raise unique considerations, at the forefront-safety and reliability-with tDCS applications. To date there are no current publications surrounding pediatric tele-neuromodulation. Therefore, to adapt our current clinical research neuromodulation study to a tele-neuromodulation neuromodulation model with supervision for children who are diagnosed with stroke at or around the time of birth, we are currently integrating guidelines established by Charvet et al, [47, 56] and further work in adult stroke by Van de Winckel et al [57].

Our past studies have integrated repetitive transcranial magnetic stimulation (rTMS) and tDCS with intensive rehabilitation in the pediatric population with perinatal stroke and resultant cerebral palsy. Now with our latest study, ‘Single -Session tDCS in Cerebral Palsy’, [58] we are investigating the neurophysiology and behavioral outcomes surrounding tDCS in children with varying forms of circuitry. We had safely and feasibly completed sessions in 19 children with stroke by the time COVID-19 put our study on hold. However, from the commencement of this study, this study garnered local, national and international interest from families of children with stroke, many traveling great distances and incurring staggering related costs of travel to participate. The COVID-19 challenge has now encouraged us to consider how to potentially integrate tele-neuromodulation for children at home and could allow a broader catchment area of families previously unable to travel and enroll. Integrating accessibility and compliance in these unique teams of parents/children with cerebral palsy, our remote training and education laboratory ‘tDCS supervisors’ will incorporate training the ‘lay assistant’ (parent) as to tDCS delivery, and the ‘tDCS user’ (child). For ease of tDCS electrode placement, integration of a pre-marked skull cap with 10-20 electroencephalogram system electrode coordinates, indicating the C3 C4 locations to approximate the primary motor cortex will facilitate anode/cathode positioning based on the indicated montage. Assessments of reliability of set-up, and electrode placement, and prior to commencing the stimulation sessions and monitoring tolerance and impedance will be paramount, along with establishing a consistent and reliable method of remote communication (e.g. Zoom) during the set-up, stimulation session, and pre/post assessment trials.

Integrating a COVID-19 response to continue neuromodulation in the pediatric population with perinatal stroke and resultant cerebral palsy, as well as lack of access recruitment feedback garnered from our previous work with families nationally and internationally, this remote investigation will inform future larger externally-funded studies to remotely integrate children with mobility, financial, and access challenges (e.g. rural communities).

8.3 Example 3 NIBS at the University of Magdeburg, Germany: Most of the tDCS-tACS clinical trials were stopped in middle of March, 2020, there is one trial running with NeuroConn Mobile devices. The aim of this phase II study is to collect information about the efficacy of 10 Hz tACS in the treatment of glaucoma [59], using a domiciliary tACS. The number of possible stimulation sessions is fixed (34 during 14 weeks) which cannot be changed remotely –and at this stage will not be changed due to safety reasons. To the best of our knowledge, this is the longest stimulation duration that was ever applied in this patient group. Furthermore, none of the stimulation parameters can be changed during treatment, only by shipping a new stimulation module to the patients. Patients are required to document adverse events and side effects in a diary and the stimulation module is saving the parameters of each session, which t can be downloaded in the study center. Unfortunately, several patients were not able to visit the center at the end of the stimulation session, therefore the objective measurements (e.g. perimetry) are still missing. The state of the patients are followed by regular phone calls, two of them indicated to terminate the participation in the trial, due to high levels of personal stress.

8.4 Example 4, Example from a Multisite Definitive Phase III tDCS Trial at University of Florida and University of Arizona - Augmenting Cognitive Training in Older Adults: the ACT Trial: The ACT trial is a multisite definitive Phase III clinical trial that investigates the benefits of pairing tDCS with cognitive training in older adults to remediate age-related cognitive decline and potentially prevent onset of mild cognitive impairment and dementia [60]. ACT involves a 3-month cognitive training intervention paired with 20 in lab/clinic sessions of either active or sham tDCS. Participants undergo cognitive training and tDCS 5 days/week for the first two weeks, then complete cognitive training at home on a study supplied laptop 4 days per week with 1 day per week in lab/clinic for stimulation. At present, the ACT trial has randomized 307 of 360 older adults targeted for randomization in the trial. As this trial works with a population at high risk for poor COVID-19 outcomes, in-person study activities were stopped on March 13, 2020. At this time, 22 participants were actively in the intervention phase of the trial. As ACT is a definitive Phase III trial near its completion, a late phase change to at-home tDCS

procedures would significantly undermine trial integrity for evaluation of definitive benefits from tDCS paired with cognitive training, as only a small subset of participants would receive the alternative intervention approach. Even were the current COVID-19 outbreak to occur earlier in the trial, a significant change in intervention procedures would likely not be feasible for a Phase III trial. In addition, the primary outcome measure in the ACT trial is currently not available through telemedicine, further preventing continuation of trial activities through a fully remote process. In ACT, 22 participants whose interventions were interrupted will need to be replaced. In addition, approximately 40 participants will miss the timing of their final 1 year follow-up assessment and MRI visits as of the current date. Careful consideration with the trials data safety monitoring board and funding agency program office will need to be given regarding whether these 40 participants will need to be replaced in the trial as well. Pre-COVID-19, ACT was within 14 months of completion. With the loss of 22 participants, the study will likely not be completed for 24-26 months. Should the 40 participants missing their 1 year time point need to be replaced, trial completion could be delayed to 36 months or more. While the extent of delay is still to be determined, this serves as a poignant example of how COVID-19 is directly impacting the speed of progress in medical science. This example also further highlights the critical importance of advancing remotely supervised methods of neuromodulation administration. In ACT, participants complete cognitive training at home for a large portion of the trial. Were this initially paired with remote tDCS, the overall impact on ACT would be significantly reduced. However, lack of availability of primary outcome measures for remote online or tele-administration would have still led the ACT trial to pause activities. Thus, it is also important to note that there is a strong need for overarching work attempting to facilitate remote assessment activities for clinical trials.

9. NIBS New Opportunities

This section focuses on not simply accommodating the pandemic situation but using this period to update or enhance existing NIBS practices using techniques that have already been validated. We specifically consider telemedicine approaches using tDCS (9.1), accelerating in-clinic TMS procedures (9.2), and introducing new NIBS protocols to address existing and emerging COVID-19 morbidities (9.3).

9.1 Tele-neuromodulation (in home)

Considering past remote neuromodulation studies and current COVID-19 related challenges, ‘Tele-neuromodulation’ holds one of the greatest opportunities for innovation and growth in the

NIBS field right now [61]. Moreover, it is generally the case that administration of remote neuromodulation would allow those with limited accessibility (e.g. mobility issues, geographic location, financial barriers, limited access to communication technologies) to interventions not previously realized. Rapidly expanding investigations of tDCS in the home setting in adult populations have been well-tolerated and shown high compliance, and low drop-out rates in diagnoses such as depression [62], stroke [57], MS [44, 46, 47] PD [48], and amyotrophic lateral sclerosis [63], as well as in seriously ill multi-symptomatic palliative-care patients . Considering the acute challenges in neuromodulation access for all, an additional consideration is the expanding field of pediatric telemedicine, with implications for safe and feasible neuromodulation applications in the home setting [54, 64, 65].

As outlined in case examples (Sections 8.1, 8.2), for those centers already engaged in remote supervised tDCS, strategic and incremental protocols changes allow continuation (and even expansion) of protocols. For those centers exploring transition of in-center tDCS to remotely supervised tDCS, there are well established principles under the Remote Supervised rubric that allow home-based tDCS with compromising reproducibility [46] and detailed supporting documentation [45, 56, 65, 66].

For those protocols providing NIBS treatments that inherently require in-center application, notably TMS and ECT, and where COVID-19 related streamlining of in-center protocols is not practical (for specific patients), transition to home-based tDCS may be considered as a valid alternative option. There is evidence that tDCS can extend the benefit of TMS or ECT treatments [50, 67]. When ECT and TMS services are not available the operant decision is not the comparative efficacy of various NIBS techniques [68] but the risk/benefit ratio of trialing tDCS. The risk of tDCS is considered non-significant and safe, including across clinical populations [69-71] - indeed tDCS is broadly applied to healthy subjects (e.g. college students; [72]). Specifically for major depressive disorder, controlled trials [73-75], meta-analysis [68, 76, 77] and expert consensus [78] suggest tDCS is comparably effective with significantly less adverse events than drug therapy. Consideration for deploying remote-tDCS treatment should be based on the latest clinical trial data [56].

9.2 In-clinic Brain Stimulation

While the portability and cost of tES devices lend themselves to a relatively easy shift toward in-home usage and training, most TMS studies are currently tied to a fixed clinical or laboratory

location, which is often in a hospital environment. This is a challenge for researchers that are weighing the cost benefit ratio of restarting their therapeutic intervention trials in an environment wherein participants and staff members may be exposed to the COVID-19 virus. The balance is likely different for mechanistic TMS studies designed to characterize a disease or biology itself, without any anticipated therapeutic effect.

That said, there are several sites conducting therapeutic TMS clinical trials across the globe that have been allowed to remain open through the COVID-19 epidemic. Even more are resuming operations as universities, hospital systems, and countries at large begin to reopen clinical research operations (Section 2). In fact, while the majority of TMS research trials were put on pause during the COVID-19 period, clinical delivery of TMS continued in many U.S. states and a variety of countries for individuals with treatment' refractory major depression, often with modified clinical workflows to ensure safety related to COVID-19. Below we will outline topics that are common to many clinical services and trials that remained open (or are reopening) as well as some new areas for innovation and risk-reduction when performing TMS in the COVID-19 era.

9.2.1. Converting Consent, Screening, and Follow-Up Visits to Electronic, Voice, or Video Format. A common theme echoed in this manuscript is to shift any non-essential in-person visit to electronic/video format. For many research studies there is a Consent Visit, Screening Visit, and Follow-Up visits. One of the benefits of the COVID-19 crisis has been a widespread familiarity and increasing comfort with video conferencing software (e.g. Zoom, Webex, VSee). It is important to ensure the security of the videoconferencing platform when connecting with patients or study participants, however, with respect to institutional requirements for HIPAA compliant communications. Given that TMS studies often require at least one in-person intervention visit, transforming our protocols to embrace video techniques for all other visits would improve the risk benefit ratio for the staff and the participants. Additionally, research groups may want to consider adding "COVID-19-related illness" as an exclusionary criteria or as part of the risks for participating in a research study which relies on multiple in-person visits (should the institution deem this necessary).

9.2.2. Utility of Theta Burst Stimulation. Fixed frequency rTMS (e.g. 10 Hz) is the oldest and most established stimulation protocol and has been FDA-approved for use in treatment resistant major depressive disorder for many years. In recent years however, bursting frequency

protocols (e.g. theta burst stimulation (TBS)) have emerged as highly potent and temporally efficient forms of brain stimulation; that is, 600 pulses of intermittent TBS (iTBS) delivered over 45 seconds result in an elevation in cortical excitability comparable to 2000 pulses of 10 Hz TMS delivered over 15 minutes [79]. The effects of a single session last approximately 30 minutes, but repeated sessions have similar durability and efficacy as 10Hz rTMS [80] 34 and were first described in the motor cortex. Several recent, clinical trials applying TBS to the dorsolateral prefrontal cortex have demonstrated treatment outcomes with iTBS are comparable to treatment outcomes with traditional 10 Hz rTMS in major depressive disorder. Furthermore, these protocols have similar side-effects, safety, and tolerability profiles. The advantages of elevated potency and efficiency are coupled with a rigorous biologic foundation as theta is an endogenous neural rhythm associated with learning and memory. By using TBS, the number of patients treated per day with current rTMS devices can be increased several times without compromising clinical effectiveness or safety. In this COVID-19 era, one way to minimize the length of the time that a participant or patient has to be present in the room with a staff member would certainly be for investigators to consider using bursting frequency rTMS protocols which appear to be more efficient pulse-to-pulse. The shorter duration of the stimulation session also provides more flexibility when considering changes in workflow and schedules to ensure that patients do not overlap and thorough infection control measures are applied after every session.

That said, there has been some concern that the response to theta burst stimulation is highly variable [80, 81]. Although there have been very few sham-controlled comparisons of fixed frequency versus theta burst frequency TMS, the largest study to directly compare these protocols (which was not sham controlled), did not find a difference in the variability or the durability of response to 20 sessions of iTBS compared to conventional 10 Hz TMS in patients with depression [80]. While the relative efficacy and durability of these protocols is an empirical question that remains unanswered, in the COVID-19 era it seems that greater investigation into the factors that increase theta burst efficacy are warranted.

9.2.3. Accelerated TMS Delivery. The development of novel, accelerated TMS dosing strategies is another opportunity for clinical researchers. Previous studies have demonstrated that delivering multiple TMS sessions per day has similar efficacy to a single TMS session per day when the total number of TMS administrations is equal [82-84]. Given that the total number of TMS sessions appears to be a critical factor in behavioral change, these concentrated dosing protocols would be attractive to both patients and providers. While these protocols are being

explored in research laboratories however, there is still a gap in our knowledge regarding the parameters that optimally balance efficiency with long-term efficacy. In one of the most concentrated TMS protocols to date Williams and colleagues (2018) recently published a study of 6 individuals with highly refractory depression (5 days, 10 sessions/day, 1800 pulses of iTBS/session, 50 minute inter-session interval) which demonstrated that this rapid dosing schedule was feasible and was effective as a rapid antidepressant [85, 86]. Galletly and colleagues (2010), for example, elegantly demonstrated that TMS delivered 3 times/week achieved overall similar outcomes to 5 times/week as long as the overall number of administrations was the same (18-20 administrations) [87]. While most accelerated TMS studies are being done in Major Depressive Disorder, they are also being used in many currently recruiting drug and alcohol treatment research trials [88-93]. These protocols reflect dosing schedules that are likely more tenable for patients who likely have job and family responsibilities (often 3 days per week versus the standard 5 days per week). They are being used by researchers around the world. By decreasing the number of times a participant or patient needs to come to the laboratory/clinic, accelerated TMS schedules will also minimize the number of days that individual spends out of the house, the number of times they use public transportation, and the number of other person-encounters they have over the course of their treatment (as 30 sessions of TMS could be given in as little as 3 or 6 days as has been tried at various institutions in the United States). On the other hand, although it reduces the total time of TMS treatment, patients need to stay longer in the TMS environment, from one or two hours mounting up to the entire day.

9.2.4. Other Technologies, such as Portable TMS. A few other techniques and opportunities for innovative TMS protocol adaptations include greater reliance on neuronavigation for reliable and fast TMS coil positioning (as described in previous sections of this manuscript) and the delivery of TMS in off-site community clinics wherein the participant may have less exposure to potential COVID-19 carriers in the hospital environment. Perhaps the most provocative (but still chimerical) opportunity is for increased investment and innovation in a portable means for TMS delivery. There are several patents currently for portable TMS devices (e.g. for the treatment of migraine attacks Starling et al. [94]) and several papers have recently been published describing personalized TMS helmet designs which stabilize the coil [95] and wearable TMS coil designs [96]. Currently, however, there are no devices being made for commercial use. The ability to distill the power of electromagnetic induction as a brain stimulation tool into a briefcase-sized device has the potential to revolutionize non-invasive neuromodulation as a

field. To see this materialize from a fantasy to a reality on the tails of the COVID-19 crisis could, in fact, be one of the biggest achievements the neuromodulation field may gain from this experience. It will, however, take talent, time, and investment to make this happen. One should also balance the safety balance of reducing exposure to the coronavirus with the exposure to the yet unclear risks of patient self-application of home-based TMS.

9.2.5. Consideration of tDCS as Alternative or Adjunctive Treatment. As discussed above (Section 9.1). tDCS can be deployed at home with no or minimal required in-person interactions. On a situation based, providing tDCS as an alternative to TMS or optimized the benefits of TMS (e.g. tDCS for maintenance of TMS therapy) can be considered [97, 98].

In conclusion many of the TMS treatment trials that were temporarily halted in March 2020 around the world have begun to put strategies in place to return to enrollment and execution. These decisions should be made with sensitivity to many factors including the potential risk of COVID-19 exposure to the participants and staff for in-person visits and the potential benefit to participants & patients of the intervention. Those trials involved structural or functional imaging remains restricted based on the opening of imaging facilities. Similarly, any TMS trials involving parallel in-person protocols (e.g. rehabilitation) are considered in totality. While there will be many factors that influence this decision for each TMS study, there are some common themes that will minimize risk (electronic visits when possible, accelerated treatment courses, shorter pulse sequences like theta burst, use of technological methods such as neuronavigation and scalp modeling to improve rigor and decrease contact) that not only improve the risk benefit ratio but will likely lead to a reimagination of the future of TMS delivery- perhaps even launching a new industry that merges the portability and affordability of tDCS devices with the benefits of electromagnetic induction as a mechanism of inciting brain change.

9.3 New Clinical Opportunities (Indications) with NIBS in the era of COVID-19

In response to the COVID-19 outbreak, initial psychological and emotional reactions such as elevated levels of anxiety, fear, stress or anger and behavioral responses like social/physical-distancing, stockpiling goods, PPE and disinfectants have been predicted based on previous experiences [99], and then reported during the COVID-19 outbreak [100-103]. However, precipitated psychological responses might progress into severe mental concerns which can easily outlast the pandemic. Sleep disturbances, somatization, stress-related illnesses, post-traumatic stress disorder (PTSD), anxiety disorders, depressive disorders and health risk

behaviors such as social isolation, substance abuse or suicide attempts might also surge [2, 102, 104]. Accordingly, depressive and post-traumatic symptoms have been constantly reported and found to persist even 2.5 years after epidemics [105]. Evidence that similar symptoms are present among health care professionals and the general population during the COVID-19 outbreak is already emerging from China, the epicenter of the outbreak [103, 106-108], and from Europe as well [109].

The consequences of COVID-19 might be more immense in terms of the number of affected and maybe in terms of symptom severity than previous outbreaks, not to mention its economic and political impact and their effects on an individual level. Apart from new cases with mental health issues, those already facing mental health problems or belong to a vulnerable population might experience their symptoms worsening [110, 111]. Increased risk of COVID-19 infection or potentially deteriorating mental health during the outbreak has been articulated concerning patients with cancer [112], dementia [113], PD [114], chronic pain [115], MS [116] and drug users [2].

In light of the potential surge of demand for mental health care, effective therapeutic options are critical. NIBS is a promising and versatile tool to consider. The administration of magnetic fields (i.e. TMS) or weak electrical currents (i.e. tES) induces long-term neuronal effects through modulating neuroplasticity [117]. One of the first and most successful areas of NIBS application is the use of HF-TMS over the left dorsolateral prefrontal cortex to alleviate depressive symptoms that now has a level A evidence (i.e. definite efficacy) [4]. Interestingly, promising results are emerging regarding the beneficial effects of NIBS on several clinical populations suggesting transdiagnostic opportunities. Level B (probable efficacy) recommendation has been proposed for the use of TMS in fibromyalgia, PD, MS, PTSD and stroke [5]. Evidence is less conclusive on tES; however, level B evidence supports the utility of tDCS in depression, chronic pain and fibromyalgia [6]. Moreover, prosperous results suggest the potential efficacy of NIBS in several other disorders e.g. in anxiety disorders [118], dementia [119], obsessive-compulsive disorder [120, 121] and pediatric attention-deficit hyperactivity disorder [122].

In an outbreak situation, adaptation skills and flexibility are essential to adjust behavior to the new regulations; thus, to mitigate the spread of the virus. Cognitive control is impaired in several conditions [114, 123]; however, NIBS has successfully ameliorated cognitive impairment in different patient groups [123-125]. Another important skill, emotion regulation has improved in patients with anxiety disorders with the effects being sustained for 3 months after TMS [126].

Depressive symptoms, anxiety and PTSD emerging or being accelerated by the COVID-19 pandemic [102] might also be successfully mitigated with NIBS based on previous research [4, 127, 128]. Furthermore, stress is also known to exacerbate disease-related symptoms such as the motor symptoms of patients with tic disorders or PD [114, 129, 130]. Preliminary evidence indicates the beneficial effects of TMS on motor performance as well [131, 132].

Recently, the possibility of COVID-19-associated nervous system diseases has also been clinically proven by detecting the ribonucleic acid (RNA) of the virus in the cerebrospinal fluid of a patient [133]. Neurological symptoms such as impaired consciousness, headache, dizziness and taste or smell impairment are not uncommon [134]. Therefore, the long-term follow-up and monitoring of severe cases of COVID-19 in terms of neurological symptoms is highly advised [135]. Through the enhancement of neural plasticity, some COVID-19-related neurological residual symptoms might be attenuated by NIBS. In a rat model, TMS has been found to reduce inflammation after focal brain injury [136] and to decrease the production of proinflammatory cytokines in patients with PD [137]. Moreover, patients with disorders of consciousness have shown neurobehavioral and electrophysiological gains after multiple sessions of NIBS [138-140]. Therefore, anti-inflammatory potential and neurological utilization of NIBS might also be investigated.

Finally, there may be opportunities to apply NIBS in the broader context of changing medical protocols. This could span changing methods and access to prescribed medications (e.g. ability to diagnose, monitor for adverse events) as well as any consideration of unexpected interactions between drugs (e.g. psychotropics) and antiviral medication. A general feature of NIBS is its non-drug non-systematic application nature, non-addictive nature, and ability to terminate or adjust dose (in clinic or remote for home-based treatment) and vice versa. Clearly, there is potential for NIBS as a unique treatment tool in the fight against the medical and psychological after-effects of the COVID-19 outbreak.

10. Conclusion

The COVID-19 pandemic, just like all crises, has yielded challenges for researchers, clinicians, participants and patients, but also lessons to learn from and new opportunities to pursue. By synthesizing the experiences of experts from all over the world, this consensus paper establishes practical recommendations to follow in operationalizing NIBS during COVID-19 pandemic, mitigating the risk of infections, and in preparing the NIBS community for any future

epidemic/pandemic. Indeed, as we emerge from the current pandemic, the number of people who require innovative treatments such as NIBS due to direct and indirect effects of COVID-19 onto the brain and mental health will significantly increase. This burden on the health care systems mandates broader investigation and adoption of therapeutic solutions such as the use of NIBS. For NIBS laboratories and clinics to contribute to the ease the burden of the pandemic, it is necessary to re-establish operation with prudent protocol modifications as soon as possible.

Maintaining ongoing and restarting operations at NIBS clinics and research institutions across the world requires accommodation to strict measures (namely social/physical distancing) introduced due to the COVID-19 outbreak The suddenness and severity of initial restrictions resulted in significant disruptions to ongoing clinical treatment and trials (spanning suspension recruitment of participants, interruption of ongoing treatment, to complete suspension of in-person activities). The degree of interruption varied; for example, in-person non-clinical (non-essential) work was largely halted while remote-tDCS clinical activity continued. Interruption of ongoing trials is compounded by overall operational and programmatic uncertainties e.g. the situation of students and early career scientists, financial concerns. The overarching concern is when and how specific clinical and laboratory work can be resumed and what precautions are to be adopted. This document provides guidelines for maintaining and resuming NIBS operations.

We distinguish three phases of procedural responses (immediate COVID-19 impact, current practices, and future preparation), with current reactions of the NIBS community to the COVID-19 pandemic largely in early phases with reactions aiming to limit disruption to ongoing protocols. However, streamlining and expanding NIBS services is now ongoing.

Based on the analysis of international experts with domain relevant expertise covering NIBS technology, clinical services, and human trials, we formed recommendations to ensure the safety of participants, researchers and staff members during the re-establishment of access to NIBS clinical services and research operations. Apart from the obvious preparations (e.g. sanitization and social distancing protocols and remote data acquisition where possible), recommendations are also made regarding protocol optimization, methodological good practices, the support of all stakeholders including early career scientists. To foster this process, a checklist is also provided in the article. Mitigation plans to reduce the risk of infection for subjects/participants and research/clinical staff are preeminent but should be based on the applicable national and institutional guidance and scientific understanding to avoid being

misdirected or unduly burdensome. Recommendation on precautions are also discussed considering pediatric research, older adults, patients with addiction, stroke, MS or other chronic neurodegenerative/inflammatory disorders.

As explicated through this document, appropriate safety protocols are crucial to provide NIBS for those who require mental health care regardless of, and also aggravated by, the outbreak. With well-coordinated and strategic responses, the NIBS community can play an expanding role in managing the burden related to the COVID-19 pandemic while continuing to generate clinical and scientific regarding the efficacy and underlying mechanisms of NIBS. As we have discussed above, expanding clinical trials with telemedicine-based NIBS are of high impact in the current situation and considering future outbreaks and longstanding need for vigilance. Since tES devices are more easily transportable and simple to use, the remote application of tES is more supported in contrast to TMS. Guidelines [46, 56] and empirical experience [140-142] regarding the at-home applications of tDCS are available. Experiences gained through this process as well as new perspectives gathered during the challenging era of COVID-19 might delineate new research and therapeutic goals and become invaluable when preparing for future outbreaks

The interest in telemedicine-based solutions has especially increased among the NIBS community [61] and the experiences gained from such studies conducted during the outbreak will be broadly valuable. Generally, remote NIBS solutions extend the availability of neuromodulation, and can reduce costs of increasing the trial sample sizes and treatment duration. The adaptation process of some in-clinic TMS solutions that sustained operation during the pandemic and protocols to reduce contact is addressed.

The NIBS community has faced varied degrees of disruption that has broadly challenged laboratories and clinics across the globe. By working around evolving restrictions and uncertainties, strategic (and not unduly burdensome) implementation of applicable safety procedures, and adaptation of protocol components to limit in-person activities, access to NIBS must be continued and re-established rapidly. In this article, approaches and practical recommendations have been provided. Indeed, if further outbreaks arise, the NIBS community will be better prepared for them.

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References

[1] Dhaliwal SK, Meek BP, Modirrousta MM. Non-Invasive Brain Stimulation for the Treatment of Symptoms Following Traumatic Brain Injury. Front Psychiatry 2015;6:119.

[2] Farhoudian A, Baldacchino A, Clark N, Gerra G, Ekhtiari H, Dom G, et al. COVID-19 and Substance Use Disorders: Recommendations to a Comprehensive Healthcare Response. An International Society of Addiction Medicine (ISAM) Practice and Policy Interest Group Position Paper. Basic and Clinical Neuroscience 2020:129-46.

[3] Fisicaro F, Lanza G, Grasso AA, Pennisi G, Bella R, Paulus W, et al. Repetitive transcranial magnetic stimulation in stroke rehabilitation: review of the current evidence and pitfalls. Ther Adv Neurol Disord 2019;12:1756286419878317.

[4] Lefaucheur J-P, Aleman A, Baeken C, Benninger DH, Brunelin J, Di Lazzaro V, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014–2018). Clinical Neurophysiology 2020;131(2):474-528.

[5] Lefaucheur J-P, André-Obadia N, Antal A, Ayache SS, Baeken C, Benninger DH, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). Clin Neurophysiol 2014;125(11):2150-206.

[6] Lefaucheur J-P, Antal A, Ayache SS, Benninger DH, Brunelin J, Cogiamanian F, et al. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Clin Neurophysiol 2017;128(1):56-92.

[7] Sagliano L, Atripaldi D, De Vita D, D'Olimpio F, Trojano L. Non-invasive brain stimulation in generalized anxiety disorder: A systematic review. Prog Neuropsychopharmacol Biol Psychiatry 2019;93:31-8.
[8] Gaynes BN, Lloyd SW, Lux L, Gartlehner G, Hansen RA, Brode S, et al. Repetitive transcranial magnetic stimulation for treatment-resistant depression: a systematic review and meta-analysis. J Clin Psychiatry 2014;75(5):477-89; quiz 89.
[9] Leggett LE, Soril LJ, Coward S, Lorenzetti DL, MacKean G, Clement FM. Repetitive Transcranial Magnetic Stimulation for Treatment-Resistant Depression in Adult and Youth Populations: A Systematic Literature Review and Meta-Analysis. Prim Care Companion CNS Disord 2015;17(6).
[10] Troyer EA, Kohn JN, Hong S. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. Brain Behav Immun 2020.
[11] Dutheil F, Mondillon L, Navel V. PTSD as the second tsunami of the SARS-Cov-2 pandemic. Psychol Med 2020:1-2.
[12] ISEN :: International Society for ECT and Neurostimulation.
[13] Cao W, Fang Z, Hou G, Han M, Xu X, Dong J, et al. The psychological impact of the COVID-19 epidemic on college students in China. Psychiatry Res 2020;287:112934.
[14] Zhai Y, Du X. Mental health care for international Chinese students affected by the COVID-19 outbreak. Lancet Psychiatry 2020;7(4):e22.
[15] Gunnell D, Appleby L, Arensman E, Hawton K, John A, Kapur N, et al. Suicide risk and prevention during the COVID-19 pandemic. Lancet Psychiatry 2020.
[16] Hoy K. Gender Imbalance at Brain Stimulation Conferences: We Have a Problem and It is Everyone's Problem. Brain Stimul 2017;10(1):155-6.
[17] George MS, Sackeim HA. Response to Hoy, 'Gender Imbalance at Brain Stimulation Conferences: We Have a Problem and It is Everyone's Problem'. Brain Stimul 2017;10(1):157.
[18] Woolf V, Hogarth P, R, Clark R, Women PP, Bloomsbury A. A room of one's own. London: Leonard and Virginia Woolf at the Hogarth Press; 1929.
[19] Early journal submission data suggest COVID-19 is tanking women's research productivity, https://www.insidehighered.com/news/2020/04/21/early-journal-submission-data-suggest-covid-19-tanking-womens-research-productivity.
[20] Yavorsky JE, Dush CM, Schoppe-Sullivan SJ. The Production of Inequality: The Gender Division of Labor Across the Transition to Parenthood. J Marriage Fam 2015;77(3):662-79.
[21] Minello A. The pandemic and the female academic. Nature 2020.
[22] Setti L, Passarini F, De Gennaro G, Barbieri P, Perrone MG, Borelli M, et al. Airborne Transmission Route of COVID-19: Why 2 Meters/6 Feet of Inter-Personal Distance Could Not Be Enough. Int J Environ Res Public Health 2020;17(8).
[23] Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect 2020;104(3):246-51.
[24] Mossa-Basha M, Meltzer CC, Kim DC, Tuite MJ, Kolli KP, Tan BS. Radiology Department Preparedness for COVID-19: Radiology Scientific Expert Panel. Radiology 2020:200988.
[25] Murray OM, Bisset JM, Gilligan PJ, Hannan MM, Murray JG. Respirators and surgical facemasks for COVID-19: implications for MRI. Clin Radiol 2020.
[26] Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect 2020.
[27] Coronavirus, https://www.who.int/emergencies/diseases/novel-coronavirus-2019.
[28] "Immunity passports" in the context of COVID-19, https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19.
[29] Marangolo P, Fiori V, Caltagirone C, Pisano F, Priori A. Transcranial Cerebellar Direct Current Stimulation Enhances Verb Generation but Not Verb Naming in Poststroke Aphasia. J Cogn Neurosci 2018;30(2):188-99.
[30] Campana S, Caltagirone C, Marangolo P. Combining Voxel-based Lesion-symptom Mapping (VLSM) With A-tDCS Language Treatment: Predicting Outcome of Recovery in Nonfluent Chronic Aphasia. Brain Stimul 2015;8(4):769-76.
[31] Fiori V, Nitsche MA, Cucuzza G, Caltagirone C, Marangolo P. High-Definition Transcranial Direct Current Stimulation Improves Verb Recovery in Aphasic Patients Depending on Current Intensity. Neuroscience 2019;406:159-66.

[32] Lindenberg R, Zhu LL, Schlaug G. Combined central and peripheral stimulation to facilitate motor recovery after stroke: the effect of number of sessions on outcome. Neurorehabil Neural Repair 2012;26(5):479-83.
[33] Lindenberg R, Renga V, Zhu LL, Nair D, Schlaug G. Bihemispheric brain stimulation facilitates motor recovery in chronic stroke patients. Neurology 2010;75(24):2176-84.
[34] Vines BW, Norton AC, Schlaug G. Non-invasive brain stimulation enhances the effects of melodic intonation therapy. Front Psychol 2011;2:230.
[35] Schlaug G, Marchina S, Wan CY. The use of non-invasive brain stimulation techniques to facilitate recovery from post-stroke aphasia. Neuropsychol Rev 2011;21(3):288-301.
[36] Wortman-Jutt S, Edwards DJ. Transcranial Direct Current Stimulation in Poststroke Aphasia Recovery. Stroke 2017;48(3):820-6.
[37] Feng W, Kautz SA, Schlaug G, Meinzer C, George MS, Chhatbar PY. Transcranial Direct Current Stimulation for Poststroke Motor Recovery: Challenges and Opportunities. PM R 2018;10(9 Suppl 2):S157-S64.
[38] Marangolo P. The potential effects of transcranial direct current stimulation (tDCS) on language functioning: Combining neuromodulation and behavioral intervention in aphasia. Neurosci Lett 2020;719:133329.
[39] Gillick BT, Gordon AM, Feyma T, Krach LE, Carmel J, Rich TL, et al. Non-Invasive Brain Stimulation in Children With Unilateral Cerebral Palsy: A Protocol and Risk Mitigation Guide. Front Pediatr 2018;6:56.
[40] Finisguerra A, Borgatti R, Urgesi C. Non-invasive Brain Stimulation for the Rehabilitation of Children and Adolescents With Neurodevelopmental Disorders: A Systematic Review. Front Psychol 2019;10:135.
[41] Volkow ND. Collision of the COVID-19 and Addiction Epidemics. Ann Intern Med 2020.
[42] Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020.
[43] Shaw M, Pilloni G, Charvet L. Delivering Transcranial Direct Current Stimulation Away From Clinic: Remotely Supervised tDCS. Mil Med 2020;185(Suppl 1):319-25.
[44] Kasschau M, Reisner J, Sherman K, Bikson M, Datta A, Charvet LE. Transcranial Direct Current Stimulation Is Feasible for Remotely Supervised Home Delivery in Multiple Sclerosis. Neuromodulation 2016;19(8):824-31.
[45] Shaw MT, Kasschau M, Dobbs B, Pawlak N, Pau W, Sherman K, et al. Remotely Supervised Transcranial Direct Current Stimulation: An Update on Safety and Tolerability. J Vis Exp 2017(128).
[46] Charvet L, Shaw M, Dobbs B, Frontario A, Sherman K, Bikson M, et al. Remotely Supervised Transcranial Direct Current Stimulation Increases the Benefit of At-Home Cognitive Training in Multiple Sclerosis. Neuromodulation 2018;21(4):383-9.
[47] Charvet LE, Dobbs B, Shaw MT, Bikson M, Datta A, Krupp LB. Remotely supervised transcranial direct current stimulation for the treatment of fatigue in multiple sclerosis: Results from a randomized, sham-controlled trial. Mult Scler 2018;24(13):1760-9.
[48] Dobbs B, Pawlak N, Biagioni M, Agarwal S, Shaw M, Pilloni G, et al. Generalizing remotely supervised transcranial direct current stimulation (tDCS): feasibility and benefit in Parkinson's disease. J Neuroeng Rehabil 2018;15(1):114.
[49] Pilloni G, Shaw M, Feinberg C, Clayton A, Palmeri M, Datta A, et al. Long term at-home treatment with transcranial direct current stimulation (tDCS) improves symptoms of cerebellar ataxia: a case report. J Neuroeng Rehabil 2019;16(1):41.
[50] Clayton AM, Howard J, Dobbs B, Shaw MT, Charvet LE. Remotely Supervised Transcranial Direct Current Stimulation After ECT Improves Mood and Cognition in a Patient With Multiple Sclerosis: A Case Study. J ECT 2018;34(1):e15.
[51] Shaw MT, Best P, Frontario A, Charvet LE. Telerehabilitation benefits patients with multiple sclerosis in an urban setting. J Telemed Telecare 2019:1357633X19861830.
[52] Mann DM, Chen J, Chunara R, Testa PA, Nov O. COVID-19 transforms health care through telemedicine: evidence from the field. J Am Med Inform Assoc 2020.
[53] Rivera-Urbina GN, Nitsche MA, Vicario CM, Molero-Chamizo A. Applications of transcranial direct current stimulation in children and pediatrics. Rev Neurosci 2017;28(2):173-84.

[54] Haimi M, Brammli-Greenberg S, Baron-Epel O, Waisman Y. Assessing patient safety in a pediatric telemedicine setting: a multi-methods study. BMC Med Inform Decis Mak 2020;20(1):63.
[55] Corti C, Poggi G, Romaniello R, Strazzer S, Urgesi C, Borgatti R, et al. Feasibility of a home-based computerized cognitive training for pediatric patients with congenital or acquired brain damage: An explorative study. PLoS One 2018;13(6):e0199001.
[56] Charvet LE, Shaw MT, Bikson M, Woods AJ, Knotkova H. Supervised transcranial direct current stimulation (tDCS) at home: A guide for clinical research and practice. Brain Stimulation 2020;13(3):686-93.
[57] Van de Winckel A, Carey JR, Bisson TA, Hauschildt EC, Streib CD, Durfee WK. Home-based transcranial direct current stimulation plus tracking training therapy in people with stroke: an open-label feasibility study. J Neuroeng Rehabil 2018;15(1):83.
[58] Single-session tDCS in Cerebral Palsy, https://ClinicalTrials.gov/show/NCT03635775.
[59] Gall C, Schmidt S, Schittkowski MP, Antal A, Ambrus GG, Paulus W, et al. Alternating Current Stimulation for Vision Restoration after Optic Nerve Damage: A Randomized Clinical Trial. PLoS One 2016;11(6):e0156134.
[60] Woods AJ, Cohen R, Marsiske M, Alexander GE, Czaja SJ, Wu S. Augmenting cognitive training in older adults (The ACT Study): Design and Methods of a Phase III tDCS and cognitive training trial. Contemp Clin Trials 2018;65:19-32.
[61] Caulfield KA, George MS. Treating the mental health effects of COVID-19: The need for at-home neurotherapeutics is now. Brain Stimul 2020;13(4):939-40.
[62] Alonzo A, Fong J, Ball N, Martin D, Chand N, Loo C. Pilot trial of home-administered transcranial direct current stimulation for the treatment of depression. J Affect Disord 2019;252:475-83.
[63] Sivaramakrishnan A, Datta A, Bikson M, Madhavan S. Remotely supervised transcranial direct current stimulation: A feasibility study for amyotrophic lateral sclerosis. NeuroRehabilitation 2019;45(3):369-78.
[64] Azizy A, Fayaz M, Agirbasli M. Do Not Forget Afghanistan in Times of COVID-19: Telemedicine and the Internet of Things to Strengthen Planetary Health Systems. OMICS 2020.
[65] Finkelstein JB, Nelson CP, Estrada CR. "Ramping up telemedicine in pediatric urology- Tips for using a new modality". J Pediatr Urol 2020.
[66] Borges H, Dufau A, Paneri B, Woods AJ, Knotkova H, Bikson M. Updated Technique for Reliable, Easy, and Tolerated Transcranial Electrical Stimulation Including Transcranial Direct Current Stimulation. J Vis Exp 2020(155).
[67] Wysokinski A. Successful replacement of electroconvulsive treatment (ECT) with transcranial direct current stimulation (tDCS) in severe, treatment-refractory catatonic schizophrenia: Case study. Schizophr Res 2020.
[68] Mutz J, Vipulananthan V, Carter B, Hurlemann R, Fu CHY, Young AH. Comparative efficacy and acceptability of non-surgical brain stimulation for the acute treatment of major depressive episodes in adults: systematic review and network meta-analysis. BMJ 2019;364:l1079.
[69] Moffa AH, Brunoni AR, Fregni F, Palm U, Padberg F, Blumberger DM, et al. Safety and acceptability of transcranial direct current stimulation for the acute treatment of major depressive episodes: Analysis of individual patient data. J Affect Disord 2017;221:1-5.
[70] Antal A, Alekseichuk I, Bikson M, Brockmoller J, Brunoni AR, Chen R, et al. Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines. Clin Neurophysiol 2017;128(9):1774-809.
[71] Bikson M, Grossman P, Thomas C, Zannou AL, Jiang J, Adnan T, et al. Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016. Brain Stimul 2016;9(5):641-61.
[72] Paneri B, Adair D, Thomas C, Khadka N, Patel V, Tyler WJ, et al. Tolerability of Repeated Application of Transcranial Electrical Stimulation with Limited Outputs to Healthy Subjects. Brain Stimul 2016;9(5):740-54.
[73] Brunoni AR, Valiengo L, Baccaro A, Zanao TA, de Oliveira JF, Vieira GP, et al. Sertraline vs. ELectrical Current Therapy for Treating Depression Clinical Trial--SELECT TDCS: design, rationale and objectives. Contemp Clin Trials 2011;32(1):90-8.
[74] Bares M, Brunovsky M, Stopkova P, Hejzlar M, Novak T. Transcranial Direct-Current Stimulation (tDCS) Versus Venlafaxine ER In The Treatment Of Depression: A Randomized, Double-Blind, Single-Center Study With Open-Label, Follow-Up. Neuropsychiatr Dis Treat 2019;15:3003-14.

[75] Sampaio-Junior B, Tortella G, Borrione L, Moffa AH, Machado-Vieira R, Cretaz E, et al. Efficacy and Safety of Transcranial Direct Current Stimulation as an Add-on Treatment for Bipolar Depression: A Randomized Clinical Trial. JAMA Psychiatry 2018;75(2):158-66.
[76] Razza LB, Palumbo P, Moffa AH, Carvalho AF, Solmi M, Loo CK, et al. A systematic review and meta-analysis on the effects of transcranial direct current stimulation in depressive episodes. Depress Anxiety 2020.
[77] Brunoni AR, Moffa AH, Fregni F, Palm U, Padberg F, Blumberger DM, et al. Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. Br J Psychiatry 2016;208(6):522-31.
[78] Tortella G, Casati R, Aparicio LV, Mantovani A, Senco N, D'Urso G, et al. Transcranial direct current stimulation in psychiatric disorders. World J Psychiatry 2015;5(1):88-102.
[79] Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. Neuron 2005;45(2):201-6.
[80] Blumberger DM, Vila-Rodriguez F, Thorpe KE, Feffer K, Noda Y, Giacobbe P, et al. Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial. Lancet 2018;391(10131):1683-92.
[81] Jannati A, Block G, Oberman LM, Rotenberg A, Pascual-Leone A. Interindividual variability in response to continuous theta-burst stimulation in healthy adults. Clin Neurophysiol 2017;128(11):2268-78.
[82] Baeken C, Brem AK, Arns M, Brunoni AR, Filipcic I, Ganho-Avila A, et al. Repetitive transcranial magnetic stimulation treatment for depressive disorders: current knowledge and future directions. Curr Opin Psychiatry 2019;32(5):409-15.
[83] Fitzgerald PB, Hoy KE, Elliot D, Susan McQueen RN, Wambeek LE, Daskalakis ZJ. Accelerated repetitive transcranial magnetic stimulation in the treatment of depression. Neuropsychopharmacology 2018;43(7):1565-72.
[84] Holtzheimer PE, 3rd, McDonald WM, Mufti M, Kelley ME, Quinn S, Corso G, et al. Accelerated repetitive transcranial magnetic stimulation for treatment-resistant depression. Depress Anxiety 2010;27(10):960-3.
[85] Accelerated Intermittent Theta Burst Stimulation for Depressive Symptoms, https://ClinicalTrials.gov/show/NCT03601117.
[86] Williams NR, Sudheimer KD, Bentzley BS, Pannu J, Stimpson KH, Duvio D, et al. High-dose spaced theta-burst TMS as a rapid-acting antidepressant in highly refractory depression. Brain 2018;141(3):e18.
[87] Galletly CA, Clarke P, Carnell BL, Gill S. A clinical repetitive transcranial magnetic stimulation service in Australia: 6 years on. Aust N Z J Psychiatry 2015;49(11):1040-7.
[88] QuitFast: Evaluating Transcranial Magnetic Stimulation as a Tool to Reduce Smoking Directly Following a Quit Attempt, https://ClinicalTrials.gov/show/NCT04159571.
[89] Theta Burst Stimulation as a Tool to Decrease Drinking in Treatment-seeking Alcohol Users, https://ClinicalTrials.gov/show/NCT04154111.
[90] rTMS in Promoting Smoking Cessation and Preventing Relapse in Current Smokers, https://ClinicalTrials.gov/show/NCT03865472.
[91] Repetitive Transcranial Magnetic Stimulation for Opiate Use Disorder, https://ClinicalTrials.gov/show/NCT03538444.
[92] Transcranial Magnetic Stimulation for the Treatment of Veterans With Alcohol Use Disorders, https://ClinicalTrials.gov/show/NCT03191266.
[93] Theta-Burst Stimulation as a Treatment for Reducing Cocaine Use, https://ClinicalTrials.gov/show/NCT02927236.
[94] Starling AJ, Tepper SJ, Marmura MJ, Shamim EA, Robbins MS, Hindiyeh N, et al. A multicenter, prospective, single arm, open label, observational study of sTMS for migraine prevention (ESPOUSE Study). Cephalalgia 2018;38(6):1038-48.
[95] Badran BW, Caulfield KA, Lopez JW, Cox C, Stomberg-Firestein S, DeVries WH, et al. Personalized TMS helmets for quick and reliable TMS administration outside of a laboratory setting. Brain Stimul 2020;13(3):551-3.
[96] Lee S, Jang KI, Yoon S, Chae JH. The Efficacy of Miniaturized Repetitive Transcranial Magnetic Stimulation in Patients with Depression. Clin Psychopharmacol Neurosci 2019;17(3):409-14.

[97] Dell'Osso B, Altamura AC. Transcranial Brain Stimulation Techniques For Major Depression: Should We Extend TMS Lessons to tDCS? Clin Pract Epidemiol Ment Health 2014;10:92-3.
[98] O'Neill F, Sacco P, Bowden E, Asher R, Burnside G, Cox T, et al. Patient-delivered tDCS on chronic neuropathic pain in prior responders to TMS (a randomized controlled pilot study). J Pain Res 2018;11:3117-28.
[99] Goodwin R, Haque S, Neto F, Myers LB. Initial psychological responses to Influenza A, H1N1 ("Swine flu"). BMC Infect Dis 2009;9:166.
[100] Lee M, You M. Psychological and Behavioral Responses in South Korea During the Early Stages of Coronavirus Disease 2019 (COVID-19). International Journal of Environmental Research and Public Health 2020;17(9):2977.
[101] Cao W, Fang Z, Hou G, Han M, Xu X, Dong J, et al. The psychological impact of the COVID-19 epidemic on college students in China. Psychiatry Research 2020;287:112934.
[102] Shigemura J, Ursano RJ, Morganstein JC, Kurosawa M, Benedek DM. Public responses to the novel 2019 coronavirus (2019-nCoV) in Japan: Mental health consequences and target populations. Psychiatry Clin Neurosci 2020;74(4):281-2.
[103] Wang C, Pan R, Wan X, Tan Y, Xu L, McIntyre RS, et al. A Longitudinal Study on the Mental Health of General Population during the COVID-19 Epidemic in China. Brain Behav Immun 2020.
[104] Gunnell D, Appleby L, Arensman E, Hawton K, John A, Kapur N, et al. Suicide risk and prevention during the COVID-19 pandemic. The Lancet Psychiatry 2020;0(0).
[105] Mak IWC, Chu CM, Pan PC, Yiu MGC, Chan VL. Long-term psychiatric morbidities among SARS survivors. Gen Hosp Psychiatry 2009;31(4):318-26.
[106] Lai J, Ma S, Wang Y, Cai Z, Hu J, Wei N, et al. Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019. JAMA Netw Open 2020;3(3):e203976-e.
[107] Huang Y, Zhao N. Generalized anxiety disorder, depressive symptoms and sleep quality during COVID-19 epidemic in China: a web-based cross-sectional survey. medRxiv 2020:2020.02.19.20025395.
[108] Gao J, Zheng P, Jia Y, Chen H, Mao Y, Chen S, et al. Mental Health Problems and Social Media Exposure During COVID-19 Outbreak. Rochester, NY: Social Science Research Network; 2020.
[109] Veer IM, Riepenhausen A, Zerban M, Wackerhagen C, Engen H, Puhlmann L, et al. Mental resilience in the Corona lockdown: First empirical insights from Europe. PsyArXiv; 2020.
[110] Yao H, Chen J-H, Xu Y-F. Patients with mental health disorders in the COVID-19 epidemic. The Lancet Psychiatry 2020;7(4):e21.
[111] Yang Y, Li W, Zhang Q, Zhang L, Cheung T, Xiang Y-T. Mental health services for older adults in China during the COVID-19 outbreak. The Lancet Psychiatry 2020;7(4):e19.
[112] Fabiana G, Caliandro M, Surgo A, Carbonara R, Bonaparte I, Fiorentino A. Cancer patients in covid-19 era: swimming against the tide. Radiotherapy and Oncology 2020;0(0).
[113] Wang H, Li T, Barbarino P, Gauthier S, Brodaty H, Molinuevo JL, et al. Dementia care during COVID-19. The Lancet 2020;395(10231):1190-1.
[114] Helmich RC, Bloem BR. The Impact of the COVID-19 Pandemic on Parkinson's Disease: Hidden Sorrows and Emerging Opportunities. J Parkinsons Dis 2020;10(2):351-4.
[115] Shanthanna H, Strand NH, Provenzano DA, Lobo CA, Eldabe S, Bhatia A, et al. Caring for patients with pain during the COVID-19 pandemic: consensus recommendations from an international expert panel. Anaesthesia 2020.
[116] Brownlee W, Bourdette D, Broadley S, Killestein J, Ciccarelli O. Treating multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic. Neurology 2020.
[117] He W, Fong P-Y, Leung TWH, Huang Y-Z. Protocols of non-invasive brain stimulation for neuroplasticity induction. Neurosci Lett 2020;719:133437.
[118] Vicario CM, Salehinejad MA, Felmingham K, Martino G, Nitsche MA. A systematic review on the therapeutic effectiveness of non-invasive brain stimulation for the treatment of anxiety disorders. Neurosci Biobehav Rev 2019;96:219-31.
[119] Elder GJ, Taylor J-P. Transcranial magnetic stimulation and transcranial direct current stimulation: treatments for cognitive and neuropsychiatric symptoms in the neurodegenerative dementias? Alzheimers Res Ther 2014;6(9):74.
[120] Brunelin J, Mondino M, Bation R, Palm U, Saoud M, Poulet E. Transcranial Direct Current Stimulation for Obsessive-Compulsive Disorder: A Systematic Review. Brain Sci 2018;8(2).

[121] Cocchi L, Zalesky A, Nott Z, Whybird G, Fitzgerald PB, Breakspear M. Transcranial magnetic stimulation in obsessive-compulsive disorder: A focus on network mechanisms and state dependence. Neuroimage Clin 2018;19:661-74.
[122] Rubio B, Boes AD, Laganiere S, Rotenberg A, Jeurissen D, Pascual-Leone A. Noninvasive Brain Stimulation in Pediatric ADHD: A Review. J Child Neurol 2016;31(6):784-96.
[123] Nadeau SE, Bowers D, Jones TL, Wu SS, Triggs WJ, Heilman KM. Cognitive effects of treatment of depression with repetitive transcranial magnetic stimulation. Cogn Behav Neurol 2014;27(2):77-87.
[124] Chrysikou EG, Hamilton RH, Coslett HB, Datta A, Bikson M, Thompson-Schill SL. Noninvasive transcranial direct current stimulation over the left prefrontal cortex facilitates cognitive flexibility in tool use. Cogn Neurosci 2013;4(2):81-9.
[125] Nejati V, Salehinejad MA, Nitsche MA, Najian A, Javadi A-H. Transcranial Direct Current Stimulation Improves Executive Dysfunctions in ADHD: Implications for Inhibitory Control, Interference Control, Working Memory, and Cognitive Flexibility. J Atten Disord 2017:1087054717730611.
[126] Diefenbach GJ, Assaf M, Goethe JW, Gueorguieva R, Tolin DF. Improvements in emotion regulation following repetitive transcranial magnetic stimulation for generalized anxiety disorder. J Anxiety Disord 2016;43:1-7.
[127] Kedzior KK, Gellersen HM, Roth Y, Zangen A. Acute reduction in anxiety after deep transcranial magnetic stimulation (DTMS) in unipolar major depression- a systematic review and meta-analysis. Psychiatry Research 2015;230(3):971-4.
[128] Todder D, Gershi A, Perry Z, Kaplan Z, Levine J, Avirame K. Immediate Effects of Transcranial Direct Current Stimulation on Obsession-Induced Anxiety in Refractory Obsessive-Compulsive Disorder: A Pilot Study. J ECT 2018;34(4):e51-e7.
[129] Cohen SC, Leckman JF, Bloch MH. Clinical assessment of Tourette syndrome and tic disorders. Neurosci Biobehav Rev 2013;37(6):997-1007.
[130] Macht M, Brandstetter S, Ellgring H. Stress affects hedonic responses but not reaching-grasping in Parkinson's disease. Behav Brain Res 2007;177(1):171-4.
[131] Khedr EM, Rothwell JC, Shawky OA, Ahmed MA, Hamdy A. Effect of daily repetitive transcranial magnetic stimulation on motor performance in Parkinson's disease. Mov Disord 2006;21(12):2201-5.
[132] Mantovani A, Lisanby SH, Pieraccini F, Ulivelli M, Castrogiovanni P, Rossi S. Repetitive transcranial magnetic stimulation (rTMS) in the treatment of obsessive-compulsive disorder (OCD) and Tourette's syndrome (TS). Int J Neuropsychopharmacol 2006;9(1):95-100.
[133] Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. International Journal of Infectious Diseases 2020;94:55-8.
[134] Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol 2020.
[135] Paniz-Mondolfi A, Bryce C, Grimes Z, Gordon RE, Reidy J, Lednicky J, et al. Central Nervous System Involvement by Severe Acute Respiratory Syndrome Coronavirus -2 (SARS-CoV-2). J Med Virol 2020.
[136] Sasso V, Bisicchia E, Latini L, Ghiglieri V, Cacace F, Carola V, et al. Repetitive transcranial magnetic stimulation reduces remote apoptotic cell death and inflammation after focal brain injury. J Neuroinflammation 2016;13(1):150.
[137] Aftanas LI, Gevorgyan MM, Zhanaeva SY, Dzemidovich SS, Kulikova KI, Al'perina EL, et al. Therapeutic Effects of Repetitive Transcranial Magnetic Stimulation (rTMS) on Neuroinflammation and Neuroplasticity in Patients with Parkinson's Disease: a Placebo-Controlled Study. Bull Exp Biol Med 2018;165(2):195-9.
[138] He F, Wu M, Meng F, Hu Y, Gao J, Chen Z, et al. Effects of 20 Hz Repetitive Transcranial Magnetic Stimulation on Disorders of Consciousness: A Resting-State Electroencephalography Study. Neural Plast 2018;2018:5036184.
[139] Xia X, Bai Y, Zhou Y, Yang Y, Xu R, Gao X, et al. Effects of 10 Hz Repetitive Transcranial Magnetic Stimulation of the Left Dorsolateral Prefrontal Cortex in Disorders of Consciousness. Front Neurol 2017;8:182.
[140] Zhang Y, Song W. Transcranial direct current stimulation in disorders of consciousness: a review. Int J Neurosci 2018;128(3):255-61.
[141] Bystad M, Rasmussen ID, Grønli O, Aslaksen PM. Can 8 months of daily tDCS application slow the cognitive decline in Alzheimer's disease? A case study. Neurocase 2017;23(2):146-8.

[142] Palm U, Kumpf U, Behler N, Wulf L, Kirsch B, Wörsching J, et al. Home Use, Remotely Supervised, and Remotely Controlled Transcranial Direct Current Stimulation: A Systematic Review of the Available Evidence. Neuromodulation 2018;21(4):323-33.

Table 1. COVID-19 and International Accommodations in Brain Stimulation Clinic Setting.

Survey data were collected from April 30, 2020 to May 6, 2020. To date, data on 9 institutes have been collected from 7 countries. Phase 0 refers to the challenges that affected clinical activities with respect to COVID-19. Phase 1 refers to the activities that have been implemented in response to the pandemic. Phase 2 refers to the precautions planned or already implemented during the reopening of NIBS clinics.

Country	Name of the institution	Start date of restrictions	(Planned) date of easing the restrictions	Restrictions	Phase 0	Phase 1	Phase 2
Australia	Monash University and Epworth Healthcare	Beginning of April	To be decided, returning to campus is allowed after June 1, 2020	• Inpatient and outpatient treatment services are still allowed • Assessments are done via telehealth	• None mentioned	• Implementation of teleconsultation	• Screening system developed • Screening remotely and in person • Measuring body temperatures • Basic hygiene precautions*
Belgium	Ghent University	March 17, 2020	May 4 or May 11, 2020	• COVID-19 sub-wards • Non-urgent treatments and ambulatory consultation suspended • rTMS maintenance is allowed • ECT is allowed based on severity	• Interruption of VNS and DBS implantation • Mental deteriorations in some patients • ECT capacity is reduced	• Teleconference contacts, phone calls, or face to face contact (respecting the safety guidelines)	• To be decided
India	Kasturba Medical College, Manipal Academy of Higher Education	March 23, 2020	Not specified	• Interruption of non-emergency services • Rotating schedules to provide essential services	• Patients and staff under lockdown	• Implementation of tele-consultation for the follow-up of old patients	• Basic hygiene precautions*

Italy	Gallimberti & Partners (private addiction clinic)	March 9, 2020	May 18, 2020	• Interruption of clinical protocols • Only COVID-19 free patients are admitted	• Data loss from ongoing studies • Increase of psychological distress in addicted patients	• Implementation of teleconsultations (for psychological and medical support)	• PPE or transparent face shields • Rescheduling patients (only one at a time) • Measuring the temperature of patients
Italy	IRCCS Santa Lucia Foundation	March 9, 2020	May 18, 2020	• Interruption of clinical protocols	• Home-based protocols are not approved yet		• PPE or transparent face shields • Rescheduling patients (only one at a time) • Measuring the temperature of patients
Russia	National Medical Research Center for Psychiatry and Neurology, St.-Petersburg	March 26, 2020	Approximately mid-May 2020	• Interruption of all clinical activities	• None mentioned	• Teleconsultations for some patients	• To be decided
United Kingdom	Institute of Cognitive Neuroscience, University College London	March 6, 2020	To be decided, maybe January 2021	• Interruption of care services for community-based aphasic stroke patients • Interruption of remote outpatient and treatment services	• Redeployment of clinical staff to other units	• Teleconsultation (mainly for advising families)	• PPE • Home-based tDCS • Shift schedules for staff members • Social distancing measures

MA, USA	Beth Israel Deaconess Medical Center and Baystate Medical Center	March 20, 2020	May 18, 2020	• Interruption of all inpatient and outpatient visits • No visitors allowed in the hospital	• Interruption of research activities	• Implementation of teleconsultation	• Questionnaire or checklist to assess COVID-19 risk • Testing for COVID-19 • PPE • Remote or home stimulation
NY, USA	NYU Langone Health, New York NY	March 10, 2020	Approximately mid-May 2020	• Interruption of all outpatient visits	• Redeployed therapy staff to work remotely • Continued all ongoing tDCS treatments using virtual visits through the institution's telemedicine platform • Approved for new patient enrollment in service as telemedicine provision	• Continue treatments and enroll new patients to service remotely • Protocol for sanitation of equipment, including shipments (incoming and outgoing) of equipment to patients	• Continue treatments and enroll new patients remotely • Follow institutional guidelines for infection control for any onsite new patient evaluations • Shift schedules for staff members • Social distancing measures for clinical staff return to onsite

rTMS: repetitive transcranial magnetic stimulation; ECT: electroconvulsive therapy; tDCS: transcranial direct current stimulation; VNS: vagus nerve stimulation; DBS: deep brain stimulation; PPE: personal protective equipment.

basic hygiene precautions*: PPE, sanitization, social distancing

Table 2. COVID-19 and International Accommodations in Brain Stimulation Research Setting

Survey data were collected from April 30, 2020 to May 6, 2020. To date, data on 28 institutes have been collected from 17 countries. Phase 0 refers to the challenges that affected research activities with respect to COVID-19. Phase 1 refers to what activities have been implemented in response to the pandemic. Phase 2 refers to the precautions planned or already implemented during the reopening of NIBS labs.

Country	Name of the institution	Start date of restrictions	(Planned) date of easing the restrictions	Restrictions	Phase 0	Phase 1	Phase 2
Australia	Monash University and Epworth Healthcare	Beginning of April	To be decided, returning to campus is allowed after June 1, 2020	• Interruption of ongoing preclinical studies • TMS studies suspended	• Data loss from ongoing studies • Interruption of data collection • Re-organization of tDCS studies for remote administration • Follow-up of recruited participants	• Implementation of teleworking • Data collection from remote studies	• Basic hygiene precautions*
Austria	University of Graz	March 11, 2020	Mid-May	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Staff working in rotations	• Implementation of teleworking • Implementation of teleconferencing • Online follow-up of patients • Strengthening collaboration across centers	• PPE • Sanitization protocols • Single-subject test sessions

Belgium	Université Libre de Bruxelles	March 15, 2020	To be decided	• All ongoing studies and in-person activities suspended	• Interruption of data collection	• Implementation of teleworking • Implementation of teleconferencing	• To be decided
Belgium	Ghent University	March 17, 2020	May 4, 2020 (under strict safety conditions)	• Interruption of research activities (preclinical and clinical)	• Interruption of data collection • Data loss from ongoing TMS studies	• Implementation of teleworking • Implementation of teleconferencing	• Continuation of teleconferencing • Basic hygiene precautions*
Brazil	Federal University of Espírito Santo	March 18, 2020	To be decided	• All ongoing studies and in-person activities suspended	• Interruption of data collection	• Implementation of teleconferencing	• Basic hygiene precautions* • Checklists for staff and patients • Rescheduled treatment sessions • Shift schedules for all professionals • Individualized devices and single-use packages for stimulation Immunity passports

Brazil	University of Sao Paulo	March 12, 2020	end of July	• All ongoing studies and in-person activities suspended	• Interruption of data collection	• Data mining • Computational modelling • Remote patient follow-up • Implementation of teleconferencing • Development of a questionnaire to measure COVID-19-related anxiety	• Basic hygiene precautions* • Checklists for staff and patients • Rescheduled treatment sessions • Shift schedules for all professionals • Individualized devices and single-use packages for stimulation • Immunity passports
Canada	University of Calgary	March 20, 2020	Likely May or June 2020	• Interruption of most clinical operations; continuation of urgent patients and acute care	• Interruption of data collection • Early career scientists losing time and opportunities	• Virtual clinics • Pooling data across labs for new analysis opportunities	• Priority to young early career scientists • Structured screening system
China	Shanghai Mental Health Center	Jan 29, 2020	May, 2020	• All ongoing studies and in-person activities suspended	• Interruption of data collection	• Implementation of teleworking • Implementation of teleconferencing • Re-analyzing previously collected data	
China	University of Science and Technology of China	February 1, 2020	May, 2020	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Regular meetings for Journal Clubs were stopped	• Implementation of teleworking • Implementation of teleconferencing	• Basic hygiene precautions* • Controlled entrance to campus

Denmark	Copenhagen University Hospital Bispebjerg	March 13, 2020	To be decided, treatment-related research is resumed after May 4, 2020	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Delays in projects • Potential depletion of project funding	• Implementation of teleworking • Implementation of teleconferencing • Daily updates on COVID-19	• Training for all researchers • Mitigation plan based on national and international standards • Reopening gradually • Screening patients • Rescheduling patients (only one at a time)
Denmark	Technical University of Denmark	March 12, 2020	To be decided, partial reopening with some lab activities and in-person work with patients after May 4, 2020	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Delays in projects • Potential depletion of project funding	• Implementation of teleworking • Implementation of teleconferencing	• Continuation of teleconferencing and remote work if possible • Sanitization protocols • Social distancing
Germany	Max Planck Institute for Human Cognitive and Brain Sciences	March 13, 2020	April 27, 2020 (with restrictions)	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Having to close a study without meeting the predefined sample size	• Implementation of teleworking • Implementation of teleconferencing	• PPE • Testing of patients
Germany	University Medical Center Göttingen	March 20, 2020	May 15, 2020	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Pause of recently started studies • Lower statistical power for studies terminated earlier	• Implementation of teleworking • Implementation of teleconferencing	• Shift schedule for all professionals • Rescheduled treatment sessions • Social distancing rules

India	Kasturba Medical College, Manipal Academy of Higher Education	March 23, 2020	Not specified	• Non-urgency activity suspended	• Interruption of data collection	• Implementation of teleworking • Implementation of teleconferencing	• Basic hygiene precautions*
Iran	National Brain Mapping Lab (NBML)	February 23, 2020	April 4, 2020	• Interruption of all preclinical experiments • Interruption of all in-person study activities	• Interruption of data collection • Decreased number of sessions and incoming projects	• Implementation of teleworking • Webinars	• Basic hygiene precautions* • Measuring the temperature of patients • Assessment by a doctor at the reception • Instructions for patients and staff
Italy	Novella Fronda Foundation	March 9, 2020	May 18, 2020	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Data loss from ongoing studies	• Implementation of teleworking	• PPE or transparent face shields • Rescheduling patients (only one at a time) • Measuring the temperature of patients
Italy	IRCCS Santa Lucia Foundation	March 9, 2020	May 18, 2020	• Interruption of ongoing research	• Interruption of data collection • Home-based protocols are not yet approved	• Implementation of teleworking	• PPE or transparent face shields • Rescheduling patients (only one at a time) • Measuring the temperature of patients
Japan	Nagoya Institute of Technology	April 10, 2020 Students are not allowed to access the University from March 9, 2020	Likely May 7, 2020	• All ongoing studies and lab activities suspended	• Financial burdens and uncertainties • Need to complete all preclinical research by the end of fiscal year after reopening	• Computational experiments remotely • Implementation of teleworking • Communication with collaborators	• Assessment of symptoms • Basic hygiene precautions* • Ventilation of the rooms

Portugal	University of Coimbra	March 9, 2020	Approximately mid-May 2020	• All ongoing studies suspended		• Conduction of online experiments later implemented in the lab's work • Implementation of teleworking	• PPE
Russia	National Medical Research Center for Psychiatry and Neurology, St.-Petersburg	March 26, 2020	Approximately mid-May 2020	• All ongoing studies suspended	• Interruption of data collection • Data loss from ongoing studies	• Implementation of teleworking	• To be decided
Switzerland	NCM lab, ETH Zürich	March 16, 2020	June 8, 2020 for low risk volunteers Unclear for vulnerable populations	• All ongoing studies and in-person activities suspended	• Interruption of data collection • Data loss from ongoing studies • Psychological effects of COVID-19 might influence the data	• Implementation of teleworking	• Basic hygiene precautions* • Remote data collection if possible • Scheduling office use • Measuring the temperature of participants • Ventilation of rooms • Switch to a round coil if possible
Switzerland	Zürich Center of Neuroeconomics, University of Zürich	March 16, 2020	May 15, 2020 (or sooner depending on authorization)	• All ongoing studies suspended	• Interruption of data collection • Decreased testing capacity due to safety precautions • Fewer healthy participants • Lower statistical power for studies terminated earlier	• Implementation of teleworking • New lab routines to keep staff motivated • Analysis of data from nearly complete studies	• Basic hygiene precautions* • Remote data collection if possible • Scheduling office use • Monitoring the infection of staff members • Measuring the temperature of participants

United Kingdom	Institute of Cognitive Neuroscience, University College London	March 9, 2020	To be decided, maybe January 2021	• Interruption of ongoing research	• Contacting patients is not allowed for remote research purposes • Illness of staff members (COVID-19 was not confirmed but symptoms were similar) • Support for junior lab members who live alone	• Implementation of teleworking • New lab routines to keep staff motivated • Collecting follow-up data remotely • Participation to online workshops	• PPE • Home-based tDCS • Shift schedules for staff members • Social distancing measures
United Kingdom	University of Oxford	March 13, 2020	To be decided	• Interruption of ongoing research (clinical and preclinical)	• Interruption of data collection	• Implementation of teleworking • Conducting modelling and in silico studies	• To be decided
FL, USA	University of Florida	March 13, 2020	TBD, tentatively June 1, 2020	• All ongoing studies and in-person activities suspended	• Data loss from ongoing studies • Interruption of data collection and recently commenced studies • Drop-out of subjects with interrupted protocol • Delayed completion of multisite clinical trials • Need to recruit new subjects when restarting the studies	• Implementation of teleworking	• Single-use sponges and head fixture devices for tES • Basic hygiene precautions* • Training for staff and students • Testing for COVID-19 • PPE for staff and participants
MA, USA	Beth Israel Deaconess Medical Center and Baystate Medical Center	March 20, 2020	May 18, 2020	• All ongoing studies and in-person activities suspended	• Data loss from ongoing studies • Interruption of data collection	• Implementation of teleworking	• Questionnaire or checklist to assess COVID-19 risk • Testing for COVID-19 • PPE • Remote or home stimulation

NY, USA	NYU Langone Health, New York NY	March 10, 2020	Approximately mid-May 2020	• Interruption of all outpatient visits outside of standard care or justified risk	• Redeployed research staff to work remotely • Continued all ongoing treatments using remote home-based tele-treatment (Remotely Supervised tDCS) • Received IRB approval for remote consenting and continued enrollment	• Continue tele-research program with home-based remotely supervised tDCS • Protocol for sanitation of equipment, including shipments (incoming and outgoing) of equipment to participants	• PPE • Shift schedules for staff members • Social distancing measures • Continue tele-research program with home-based remotely supervised tDCS
MN, USA	Pediatric Neuromodulation Laboratory University of Minnesota	March 17, 2020	'Sunrise Plan' Implementation In Process, TBD	• All studies considered 'non-essential operations' on immediate hold, which placed infant and child stroke studies on hold	• Data loss from studies in process and cancelled assessment and intervention sessions • Loss of participants with interrupted protocol, infants will now likely age out of the study dependent upon safety and date of reimplementation • Delayed completion of clinical trials • Continuous monitoring of inpatient pediatric census for return to research and new recruitment • Research staff/trainees established for secure at-home access and productivity	• Secured IRB approval for two COVID-19 related studies in feasibility/reliability of pediatric tele-neuromodulation and a Family Impact to Rehabilitation Access On-Line Survey • Protocol for training, safety and implementation of tele-neuromodulation in the pediatric population	• PPE • Shift schedules for staff/trainees • Social distancing measures with modifications for child/family interactions and infant positioning for neuromodulation • Continue tele-research program with home-based remotely supervised tDCS to advance from feasibility/reliability to efficacy • Testing for COVID-19 as per University protocols • PPE for staff /trainees and participants

tDCS: transcranial direct current stimulation; TMS: transcranial magnetic stimulation; tES: transcranial electrical stimulation; PPE: personal protective equipment.

basic hygiene precautions*: PPE, sanitization, social distancing

Table 3. Summary of Considerations for COVID-19 Response.

Initial

- Cessation of non-essential in-person research activities
    - Followed by determination of compatibility with continuation through valid remote assessment and/or intervention methods
- Movement of study teams to remote work to adhere with stay-at-home mandates
    - Special consideration required for remote access to resources (hardware, software, etc.)
- Potential continuation of patient studies defined as essential care (e.g., depression), institution-specific determination
- Allow reduced numbers of study team members to remain at work to continue essential study activities (e.g. shift or staggered working patterns)
- Communication with all participants currently enrolled in ongoing studies to provide information regarding how their participation in the study will be impacted by any stay-at-home mandates.
    - As applicable, communication to participants around any potential risk of COVID-19 transmission in relation to ongoing participation.
- Provide participants with additional information regarding available local resources (e.g. telemental health services, community assistance programs, etc.)
- Training specific staff or consider additional personnel resources for coordinating COVID-19 safety procedures

During

- Continue remote/teleworking activities such as analyzing data, manuscript writing, grant preparation, virtual meetings, adverse event follow-up, etc.
- Plan for study procedure changes to maximize participant safety and social/physical distancing (e.g., PPE and other safety procedures, facility and equipment disinfection)
- Plan for possible re-integration strategies (tiered, split, etc.) and how the team will adjust to accommodate institutional strategies
- Prioritize study activities that will occur in person once stay-at-home mandates are lifted to account for overburden of study teams due to prior missed visits, upcoming follow-up assessments, and need for new participants to replace those with interrupted and unrecoverable intervention schedules.
- Consider revision of ongoing studies to minimize person-to-person contacts through remote/online/teleassessment for questionnaires, self-report measures and other items not requiring in-person administration
- Consider necessary redesign of study space to minimize participant contact time during intervention delivery
- Further evaluation of feasibility for movement to remote assessment and intervention administration as a precaution for future COVID-19 related stay-at-home mandates.
- Consider procedures for implementation of rapid COVID-19 testing and antibody assays noting and depending on any limitations in current testing and antibody assays regarding sensitivity, specificity or established relevance to risk.
- Explore e-consenting procedures and e-questionnaires etc.

Future

- Consult reputable sources (IRB, CDC, FDA, etc.) for guidance on the timeline for study

restart.

- Devise a mitigation plan to limit exposure to Covid-19 or any other infectious agent for study subject/participant as well as research staff
- Immediate implementation of planned procedures and updated safety precautions (i.e. standard operating procedure documents), with appropriate staff training.
- If appropriate procedures for participant/patient safety (PPE, facility design, etc.) and other required procedures are implemented following the first wave of COVID-19, consider how the implementation of rapid COVID-19 testing and antibody assays may allow for the continuation of appropriate in-person activities that were immediately discontinued in the initial emergency response to the first COVID-19 outbreak. This decision will be institution specific.
- Consider creating a financial plan involving possible sources and a calculation on the costs in case of subsequent outbreaks (e.g. the acquisition of all necessary equipment)

Highlights

- We developed a framework for balancing the importance of NIBS operations with safety considerations, which facilitates the re-establishment of access to NIBS clinical services and research operations during COVID-19.
- The present consensus paper provides guidelines and good practices for managing and reopening NIBS clinics and laboratories through the immediate and ongoing stages of COVID‑19.
- The proposed robust and structured strategy aims to address the current and anticipated future challenges while maintaining scientific rigor and managing risk.

Author Conflict of Interest Declaration

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email from (hekhtiari@laureateinstitute.org).

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