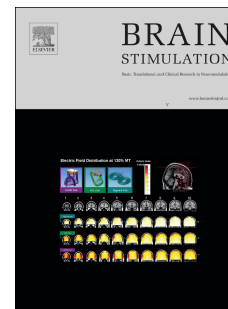


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Guidelines for TMS/tES Clinical Services and Research through the COVID-19 Pandemic

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

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97

98 **Abstract**

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

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

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

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

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

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

135

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

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140 **1. Introduction**

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

160
161 Moreover, a further wave of mental health issues following this first outbreak of this virus is
162 anticipated [10, 11]. Forms of NIBS are broadly applied and trials for mental health indications;
163 thus, hold the potential to mitigate the psychological after-effects or comorbidities of the
164 pandemic. This amplifies the urgent need for a roadmap of how to resume NIBS-based clinical
165 and research activities in the face of the COVID-19 and also future pandemics.

166
167 This expert consensus paper aims to outline processes that could facilitate rapid, prudent, and
168 coordinated re-establishment of operations at institutions providing NIBS treatments or using
169 NIBS in research. We specifically focus on low intensity transcranial electrical stimulation (tES;
170 encompassing transcranial direct current stimulation [tDCS], transcranial alternating current
171 stimulation [tACS], transcranial random noise stimulation [tRNS]) and transcranial magnetic
172 stimulation (TMS). However, our recommendations may be adapted to support the
173 reestablishment of a broad range of device-based interventions. A session of the NYC

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

183

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

194

195 **2. Results from Survey International Accommodations in Brain Stimulation Labs/Clinics** 196 **to COVID-19**

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

207

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

215

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

224

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

233

234

Insert Table 1 about here

235

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

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

249
250 With limited exceptions, the restrictions limiting the routine and non-urgent clinical services and
251 ceasing in-person activities have severely affected clinical research. Despite the guidance
252 offered by agencies like the Food and Drug Administration (FDA) and the European Medicines
253 Agency (EMA) on how to manage clinical trials, clinical studies as well as single-center/multi-
254 center trials are being impacted by the COVID-19 pandemic. In the immediate aftermath of
255 COVID-19, research labs all over the world have been instructed to limit or stop most
256 neuromodulation research that had direct person-to-person contact and was deemed non-
257 essential. The timing of the closures varied, as well as the extent to which research was halted.
258 Survey respondents report additional challenges arising from social/physical distancing
259 measures, site closures, travel limitations for staff members and patients, interruption of
260 suppliers' delivery, and considerations if personnel or subjects might be infected with the new
261 coronavirus. Moreover, difficulties in meeting the required protocol-procedures, including the
262 follow-up visits and laboratory/diagnostic testing resulted in a loss of data from ongoing trials, or
263 in a delayed data acquisition, will continue until centers fully reopen and likely beyond (Table 2).

264
265 **Insert Table 2 about here**
266

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

273

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

281
282 Respondent to the survey reported teleworking is a central component of the overall response
283 to the COVID-19 pandemic. While a challenge to the 'normal' culture way of working, tele-
284 collaboration could represent an unexpected opportunity for researchers to re-analyze collected
285 data, acquire new analysis and methods skills, design new experiments, pre-register scientific
286 reports and brainstorm new ideas and projects. General tele-work practices and routines have
287 also been introduced across NIBS centers to enable the remote working teams to maintain
288 productivity, while monitoring and supporting the well-being, education, and professional
289 development of staff (see section 5). For example, early career scientists and students
290 concerned with the degree progress should, as appropriate, be offered additional support by
291 adapting progress requirements (e.g. 3 months extensions concerning thesis submission
292 deadlines) and providing them opportunities for online networking. Several respondents to our
293 survey highlighted the opportunity to learn new skills online (through webinars, online lab
294 meetings with guest speakers and online conferences). Responders are thus positive that the
295 NIBS community could benefit from tele-work intellectual activities developed in the pandemic
296 period (e.g. online conferences, papers, experimental designs, teaching materials, etc.) and the
297 establishment of tele-communication tools should serve the NIBS community even beyond the
298 pandemic period (e.g. project tracking and updates, new collaborations).

299
300 At present, the NIBS community is in the process of preparing for a return to either partial or full
301 operational status in the coming months. While institutional regulations for restarting in person
302 activities will vary, institutions surveyed consistently reported implementation of personal
303 protective equipment (PPE) standards, social distancing approaches, plans to convert the
304 consent process and assessments to tele-/video/online administration where possible, as well
305 as sanitization procedures. A number of labs also indicated plans for COVID-19 testing and
306 facilities modification to improve ventilation and social distancing procedures. At present a
307 majority of sites surveyed do not have a definitive restart date. While the future is uncertain, labs

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

312

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

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

320

321 **3.1 Phase 0: Past Measures in Immediate Response to Stay-at-Home Mandates from** 322 **COVID-19.**

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

336

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

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

352

353 **3.2 Phase 1: Current Response.**

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

371

372 **3.3 Phase 2: Future Response to COVID-19 and Subsequent Outbreaks.**

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

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

392

393

Insert Table 3 about here

394

395 **3.4 Recommendations (Checklist) for Adapting Research and Treatment Practices to**

396 **COVID-19**

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

399

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

408

- 409 2) Transition as many study procedures as possible to electronic or video format (e.g.
410 consent process, screening visit, assessment tools, switch to an established home-
411 based techniques).
412
- 413 3) Remove non-essential steps in protocols that require in-person interactions.
414
- 415 4) Establish stringent safety and sanitization procedures for all required in-person
416 interactions and train staff in execution of these procedures (with documentation of
417 training completion). Ultimately, staff will have to follow regulatory and protection
418 procedures adopted by specific research or clinical settings (e.g. nursing home
419 setting) will have to follow COVID-19 measures for that setting; or in-person visit at a
420 patient's home will require compliance with COVID-19 protection mandated for home
421 care. Therefore, developing and updating protocol specific safety procedures requires
422 research staff communication and coordination with institutional (clinical) leadership
423 for the specific setting in which NIBS studies will be carried out.
424
- 425 5) Implement all institution required safety procedures (e.g. screening, PPE, COVID-
426 19 testing, etc.). Develop study-specific considerations for staff who recovered
427 COVID-19.
428
- 429 6) Consider changes in intervention that do not impact trial integrity (e.g. number of
430 visits, inclusion/exclusion) or consider changes that strategically change trial scope
431 (i.e. still allow for meaningful publishable outcomes; e.g. changing to a pilot trial).
432
- 433 7) For in-person protocols, streamline the entire process from participant preparing to
434 leave their home, to transportation, to arriving at clinic/lab, to leaving the clinic/lab to
435 maximize social/physical distancing (including between patients and between staff)
436 with special attention to neuromodulation steps; where possible, the clinical trial may
437 provide support for car service for participants to avoid public transportation.
438
- 439 8) Add additional telemedicine steps (follow-ups) to adjust for changes in protocol; Add
440 steps responsive to COVID-19 related concerns. This can include additional data
441 collection that may impact immediate decisions (vii) or later analysis such as testing
442 all subject temperature or surveying for COVID-19 related symptoms. Determine

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

445

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

450

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

453

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

457

458 **4. Regulatory Factors**

459 **4.1 Trial Registry (e.g. ClinicalTrials.gov) Report Updating**

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

464

465 **4.2 Institutional Review Board/Ethics Review Board Approval**

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

473

474 **4.3 Converting to a Video/Online Consent Process**

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

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

487

488 **4.4 Communication with Funding Agencies and Data Safety Monitoring Boards**

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

493

494 **4.4 Extensions of Funding for Research**

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

505

506 **5. Human Resources Considerations**

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

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

513

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

522

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

541

542 It is necessary to act now to ensure that the current pandemic does not have long-lasting
543 negative consequences on the field. NIBS has historically had a lack of female representation
544 [16], something that leaders in the field have made a concerted effort to address in recent years

545 [17] with increasing success. However, the current crisis is likely to exacerbate the gap between
546 women and men, and between carers and non-carers, in terms of available time and
547 opportunities. The burden of care and responsibilities have fallen unequally in this crisis - for
548 some this is a virtually unheard of period of quiet in which they have the time to produce as
549 much, if not more, work than normal. However, for the field as a whole it is vital to recognize that
550 for others this is a time where demands and anxieties have increased, and available time has
551 shrunk considerably. The “room of one’s own in which to write” [18] is for some a daily reality
552 and for others merely a distant dream. The real effects of this inequality across academia is
553 already being spoken about anecdotally by editors, who report decreases in the number of
554 submissions from women [19] and, possibly, increases in the number of submissions from men.
555 How those trends continue will need to be carefully monitored.

556

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

567

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

576

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

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

586
587 In practical terms, many universities have relaxed the timescales required for PhD students,
588 something that we must support and petition for. Many grant bodies around the world have
589 already announced blanket extensions to current funding - as a field it is our responsibility to
590 make these allowances as equitable as possible. A number of routes through the current crisis
591 have been suggested in the rest of this article which will allow us to continue our research with
592 disruption kept to a minimum. However, in the inevitable rush back to the lab, for the long-term
593 sake of the field we must not forget to bring everyone with us.

594

595 **6. General Guidance in Reopening Labs/Clinics**

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

601

602 **6.1 Social/Physical Distancing Protocols**

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

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

618
619 Social/Physical distancing parameters as defined by governments and regulatory authorities
620 vary among countries, states and counties and change over time as a regional Covid-19
621 situation develops. The following procedures are therefore region and institute specific, and
622 subject to ongoing risk-burden evaluation. As applicable, social distancing should be maintained
623 in all offices. The allowed density of staff in given rooms should be considered along with the
624 need for and mechanism of minimizing face-to-face interaction (e.g. by using chat, emails or
625 telephones). As applicable to the specific time and protocol, it may be prudent to wear masks
626 and maintain a recommended interpersonal distance. If and when patients should wear masks
627 for necessary clinical treatments should be determined. For studies and therapies where
628 wearing masks hinders the efficacy, transparent face masks could be considered.

629 During NIBS procedures, it is often not possible to maintain the recommended physical
630 distance, at least for some amount of time. For instance, applying electrodes for tES or
631 adjusting the position of TMS coils requires direct contact between the person applying NIBS
632 and the person receiving NIBS. Robotic TMS provides some opportunity for TMS administration
633 with operators further removed from participants (easily by 2 meters/ 6 feet except for brief
634 localization to navigation, though the participant can be trained to do this). However, such
635 devices will not be available to all labs and clinics. In these instances, protective measures are
636 important to reduce the inhalation and expiration of aerosols, and the amount of time, during
637 which the recommended physical distance cannot be complied with, should be restricted to a
638 minimum possible.

639

640 **6.2 Personal Protective Equipment (PPE)**

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

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

650

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

662

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

667

668 **6.3 Facilities and Sanitization Procedures**

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

673

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

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

687

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

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

- 705
- 706 • After the NIBS session is over, the environmental surfaces in the stimulation
707 room should be sanitized using a 1% Hypochlorite solution, with a disposable
708 antiseptic cloth [23]. Also, all the stimulation equipment, including magnetic coil
709 (for TMS) stimulator, electrode/stimulator cables, EEG cap, tape measure,
710 electrodes and sponge pockets should be sanitized. Follow manufacturer specific
711 guidance on how to clean the stimulator. Furthermore, it is prudent to check for
any leaked fluids from the participant on the stimulation chair.

- 712 • The stimulator trolley and treatment chair should be wiped with a permitted
713 cleaning product (normally bacillocid is allowed, but it is better to check with the
714 manufacturer).
- 715 • If an MRI/MEG-compatible stimulator is available for concurrent application of
716 NIBS during the recording of neuroimaging or electrophysiological data, then the
717 gantry and the RF coil should be sanitized with a permitted cleaning product. The
718 MRI table also should be sanitized with any of the approved products. The coils
719 need to be disinfected once again after the scanner room is thoroughly sanitized,
720 then the next patient or participant may be taken [24]. It is necessary to ensure
721 that the metal nose piece of surgical masks, if applicable, is not ferromagnetic
722 [25].

723

724 **6.4 Vulnerable Populations**

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

737

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

743

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

752

753 **6.5 Personnel, Participant and Patient Screening**

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

765

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

777

778 **7. Specific Clinical Populations**

779 **7.1 Stroke Patients:** Stroke survivors can experience a wide range of impairments and
780 disabilities including motor deficits and the loss of ability to produce and/or to understand
781 language (aphasia). Among other treatments, use of neuromodulation techniques has been
782 proposed to enhance/facilitate stroke-recovery. Past studies have integrated centrally acting
783 tDCS with peripherally acting intensive motor or language rehabilitation protocols [29-37].
784 Before COVID-19, there were several tDCS aphasia treatment protocols published with positive
785 outcomes [38] but during the first half of March, the pandemic forced most of the labs involved
786 in NIBS and stroke recovery to suspend clinical and research activities. COVID-19 has
787 significantly increased the risk of social isolation and associated depression in people with
788 aphasia. Indeed, language and cognitive problems limit the use of digital media (i.e. cellular
789 and/or social network) to maintain social contact. Patients with motor symptoms have also been
790 penalized as a result of COVID-19 since it might be more difficult for them to move or get
791 around with limited caregiver and physical or occupational therapy support. Stroke patients
792 being in an older age category increase the risk of contracting the virus and potentially having a
793 worse outcome; thus, in order to contain the exposure, they will probably be forced to stay-at-
794 home for a longer period than young people augmenting the possibility of psychological distress
795 and depression. To address these mental health issues, researchers from the Aphasia research
796 Lab at the IRCCS Santa Lucia Foundation in Rome have launched an online interview in the
797 aphasic population to evaluate whether anxiety and fear towards COVID-19 contagion would
798 discourage the restart of rehabilitation. One concern is that patients worried about COVID-19
799 may be deprioritizing their neurorehabilitation needs and may develop an attitude of resistance
800 towards clinical research, deemed non-essential.

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

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

836

837 **7.2 Pediatric Research:** For over the last decade, neuromodulation has been safely integrated
838 in pediatrics with myriad diagnoses and disorders and promising outcomes [39, 40].
839 Protocols have integrated TMS, rTMS, tDCS and theta-burst in varying age ranges from
840 infancy through young adulthood. Although commenced in adult populations, pediatric tele-
841 neuromodulation protocols have not yet been established. In response to COVID-19, the
842 Pediatric Neuromodulation Laboratory in the Medical School at the University of Minnesota,
843 in conjunction with physicians from Gillette Children's Specialty Healthcare, and Mayo-
844 Rochester, have developed an online survey investigating the impact of COVID-19 and the
845 stay-at-home mandate on family/child access to rehabilitation care for children with cerebral

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

856

857 **7.3 Patients with Chronic Neurological Conditions:** Neuromodulation is an appealing option
858 for symptom management and rehabilitation for those living with chronic neurological conditions
859 such as multiple sclerosis, Parkinson's disease (PD) and other disorders with cognitive or
860 movement dysfunctions, with many positive signals from the literature and large controlled trials
861 underway. Specific considerations with these patients include potential cognitive impairments,
862 which may reduce the ability to understand and complete the required study procedures, as well
863 as sufficient motor functioning to operate any study equipment from a remote (home) location.
864 However, in our work to date, we have found that the majority of those living with MS, ages 18
865 to 80 years and with varying disability levels including wheelchair dependency and impaired
866 upper limb motor functions, can complete our remotely supervised protocol with guidance from
867 a tDCS technician and can also include caregiver training for support. It is important to include
868 these patients with more advanced disease for full representation of the disease spectrum
869 because they often have fewer treatment and rehabilitative options. Continuity of care for
870 patients in research or clinical protocols is important, and ongoing communications serve as a
871 connection to the clinic for those patients with stable disease who otherwise would not be in
872 contact with their treatment teams during the current time period.

873

874 **7.4 Addiction:** The secondary effects of the COVID-19 pandemic (e.g. periods of lockdowns,
875 closures of routine clinical services and forced self-isolation deriving) have uniquely
876 challenged the health and welfare of people vulnerable to drug and alcohol addiction as well
877 as those with behavioral addictions (gambling, gaming, compulsive eating, Internet and new
878 technologies). Inpatient or residential treatments have been interrupted since the substantial
879 risk of coronavirus spread with congregation of individuals in a limited space. Alcohol and

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

896

897 **7.5 Older Adults:** It has become clear that older adults have the highest rates of morbidity and
898 mortality associated with COVID-19. Consequently, older adults represent a vulnerable
899 population and careful consideration should be made when bringing them into a research or
900 clinical environment wherein they may be exposed to others that are infectious. Special
901 consideration should be given in regard to lab/clinic activities with older adults that have
902 comorbidities that further increase risk for poor COVID-19 outcomes, such as chronic
903 obstructive pulmonary disease. While standard PPE, sanitization and minimization of
904 person-to-person contact should be adhered to in all participants, it may be necessary to
905 discontinue ongoing in-person research activities for those at the highest risk for infection
906 and poor outcomes. In-home neuromodulation or treatment options in the daily care units for
907 older people may be a particularly good option for these individuals. Regardless of
908 comorbidities, labs/clinics working with older adults should adhere to the highest standard of
909 safety for minimizing COVID-19 transmission when continuing in-person research activities.

910

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

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

917

918

919 **8 Examples of Best Practices in Brain Stimulation Labs/Clinics across the World**

920 **8.1 Example 1, NYU Remotely Supervised or RS-tDCS:** In the Department of Neurology at
921 NYU Langone Health in midtown Manhattan, a protocol for remotely supervised tDCS (RS-
922 tDCS) [43-45] has been systematically developed and validated over the past five years with the
923 goal of increasing access to treatments for larger sample sizes and to extend the number of
924 treatment sessions. To date, using this protocol, >5,100 remotely supervised at-home sessions
925 have been delivered to patients with MS [46, 47] and other neurological conditions such as PD
926 [48] and cerebellar ataxia [49] and following ECT [50], targeting behavioral outcomes such as
927 cognitive and motor functions and fatigue. While reducing patient time and costs was the
928 original goal of the RS-tDCS protocol [51], the COVID-19 clinical research pause demonstrated
929 the broad utility of remotely supervised at-home treatment for clinical trials. To date, there are
930 two ongoing RCTs in MS participants, one pairing tDCS with cognitive training for 30 daily
931 sessions over 6 weeks (National MS Society), and the other pairing tDCS with upper extremity
932 motor exercises (US DoD) for 20 daily sessions.

933

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

947

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

962

963 **8.2 Example 2, University of Minnesota, Pediatric Transcranial Direct Current Stimulation:**

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

970

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

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

993
994 Our past studies have integrated repetitive transcranial magnetic stimulation (rTMS) and tDCS
995 with intensive rehabilitation in the pediatric population with perinatal stroke and resultant
996 cerebral palsy. Now with our latest study, ‘Single -Session tDCS in Cerebral Palsy’, [58] we are
997 investigating the neurophysiology and behavioral outcomes surrounding tDCS in children with
998 varying forms of circuitry. We had safely and feasibly completed sessions in 19 children with
999 stroke by the time COVID-19 put our study on hold. However, from the commencement of this
1000 study, this study garnered local, national and international interest from families of children with
1001 stroke, many traveling great distances and incurring staggering related costs of travel to
1002 participate. The COVID-19 challenge has now encouraged us to consider how to potentially
1003 integrate tele-neuromodulation for children at home and could allow a broader catchment area
1004 of families previously unable to travel and enroll. Integrating accessibility and compliance in
1005 these unique teams of parents/children with cerebral palsy, our remote training and education
1006 laboratory ‘tDCS supervisors’ will incorporate training the ‘lay assistant’ (parent) as to tDCS
1007 delivery, and the ‘tDCS user’ (child). For ease of tDCS electrode placement, integration of a pre-
1008 marked skull cap with 10-20 electroencephalogram system electrode coordinates, indicating the
1009 C3 C4 locations to approximate the primary motor cortex will facilitate anode/cathode
1010 positioning based on the indicated montage. Assessments of reliability of set-up, and electrode
1011 placement, and prior to commencing the stimulation sessions and monitoring tolerance and
1012 impedance will be paramount, along with establishing a consistent and reliable method of
1013 remote communication (e.g. Zoom) during the set-up, stimulation session, and pre/post
1014 assessment trials.

1015 Integrating a COVID-19 response to continue neuromodulation in the pediatric population with
1016 perinatal stroke and resultant cerebral palsy, as well as lack of access recruitment feedback
1017 garnered from our previous work with families nationally and internationally, this remote
1018 investigation will inform future larger externally-funded studies to remotely integrate children
1019 with mobility, financial, and access challenges (e.g. rural communities).

1020

1021 **8.3 Example 3 NIBS at the University of Magdeburg, Germany:** Most of the tDCS-tACS
1022 clinical trials were stopped in middle of March, 2020, there is one trial running with NeuroConn
1023 Mobile devices. The aim of this phase II study is to collect information about the efficacy of 10
1024 Hz tACS in the treatment of glaucoma [59], using a domiciliary tACS. The number of possible
1025 stimulation sessions is fixed (34 during 14 weeks) which cannot be changed remotely –and at
1026 this stage will not be changed due to safety reasons. To the best of our knowledge, this is the
1027 longest stimulation duration that was ever applied in this patient group. Furthermore, none of the
1028 stimulation parameters can be changed during treatment, only by shipping a new stimulation
1029 module to the patients. Patients are required to document adverse events and side effects in a
1030 diary and the stimulation module is saving the parameters of each session, which t can be
1031 downloaded in the study center. Unfortunately, several patients were not able to visit the center
1032 at the end of the stimulation session, therefore the objective measurements (e.g. perimetry) are
1033 still missing. The state of the patients are followed by regular phone calls, two of them indicated
1034 to terminate the participation in the trial, due to high levels of personal stress.

1035

1036 **8.4 Example 4, Example from a Multisite Definitive Phase III tDCS Trial at University of**
1037 **Florida and University of Arizona - Augmenting Cognitive Training in Older Adults: the**
1038 **ACT Trial:** The ACT trial is a multisite definitive Phase III clinical trial that investigates the
1039 benefits of pairing tDCS with cognitive training in older adults to remediate age-related cognitive
1040 decline and potentially prevent onset of mild cognitive impairment and dementia [60]. ACT
1041 involves a 3-month cognitive training intervention paired with 20 in lab/clinic sessions of either
1042 active or sham tDCS. Participants undergo cognitive training and tDCS 5 days/week for the first
1043 two weeks, then complete cognitive training at home on a study supplied laptop 4 days per
1044 week with 1 day per week in lab/clinic for stimulation. At present, the ACT trial has randomized
1045 307 of 360 older adults targeted for randomization in the trial. As this trial works with a
1046 population at high risk for poor COVID-19 outcomes, in-person study activities were stopped on
1047 March 13, 2020. At this time, 22 participants were actively in the intervention phase of the trial.
1048 As ACT is a definitive Phase III trial near its completion, a late phase change to at-home tDCS

1049 procedures would significantly undermine trial integrity for evaluation of definitive benefits from
1050 tDCS paired with cognitive training, as only a small subset of participants would receive the
1051 alternative intervention approach. Even were the current COVID-19 outbreak to occur earlier in
1052 the trial, a significant change in intervention procedures would likely not be feasible for a Phase
1053 III trial. In addition, the primary outcome measure in the ACT trial is currently not available
1054 through telemedicine, further preventing continuation of trial activities through a fully remote
1055 process. In ACT, 22 participants whose interventions were interrupted will need to be replaced.
1056 In addition, approximately 40 participants will miss the timing of their final 1 year follow-up
1057 assessment and MRI visits as of the current date. Careful consideration with the trials data
1058 safety monitoring board and funding agency program office will need to be given regarding
1059 whether these 40 participants will need to be replaced in the trial as well. Pre-COVID-19, ACT
1060 was within 14 months of completion. With the loss of 22 participants, the study will likely not be
1061 completed for 24-26 months. Should the 40 participants missing their 1 year time point need to
1062 be replaced, trial completion could be delayed to 36 months or more. While the extent of delay
1063 is still to be determined, this serves as a poignant example of how COVID-19 is directly
1064 impacting the speed of progress in medical science. This example also further highlights the
1065 critical importance of advancing remotely supervised methods of neuromodulation
1066 administration. In ACT, participants complete cognitive training at home for a large portion of the
1067 trial. Were this initially paired with remote tDCS, the overall impact on ACT would be
1068 significantly reduced. However, lack of availability of primary outcome measures for remote
1069 online or tele-administration would have still led the ACT trial to pause activities. Thus, it is also
1070 important to note that there is a strong need for overarching work attempting to facilitate remote
1071 assessment activities for clinical trials.

1072

1073 **9. NIBS New Opportunities**

1074 This section focuses on not simply accommodating the pandemic situation but using this period
1075 to update or enhance existing NIBS practices using techniques that have already been
1076 validated. We specifically consider telemedicine approaches using tDCS (9.1), accelerating in-
1077 clinic TMS procedures (9.2), and introducing new NIBS protocols to address existing and
1078 emerging COVID-19 morbidities (9.3).

1079

1080 **9.1 Tele-neuromodulation (in home)**

1081 Considering past remote neuromodulation studies and current COVID-19 related challenges,
1082 'Tele-neuromodulation' holds one of the greatest opportunities for innovation and growth in the

1083 NIBS field right now [61]. Moreover, it is generally the case that administration of remote
1084 neuromodulation would allow those with limited accessibility (e.g. mobility issues, geographic
1085 location, financial barriers, limited access to communication technologies) to interventions not
1086 previously realized. Rapidly expanding investigations of tDCS in the home setting in adult
1087 populations have been well-tolerated and shown high compliance, and low drop-out rates in
1088 diagnoses such as depression [62], stroke [57], MS [44, 46, 47] PD [48], and amyotrophic lateral
1089 sclerosis [63], as well as in seriously ill multi-symptomatic palliative-care patients . Considering
1090 the acute challenges in neuromodulation access for all, an additional consideration is the
1091 expanding field of pediatric telemedicine, with implications for safe and feasible
1092 neuromodulation applications in the home setting [54, 64, 65].

1093
1094 As outlined in case examples (Sections 8.1, 8.2), for those centers already engaged in remote
1095 supervised tDCS, strategic and incremental protocols changes allow continuation (and even
1096 expansion) of protocols. For those centers exploring transition of in-center tDCS to remotely
1097 supervised tDCS, there are well established principles under the Remote Supervised rubric that
1098 allow home-based tDCS with compromising reproducibility [46] and detailed supporting
1099 documentation [45, 56, 65, 66].

1100
1101 For those protocols providing NIBS treatments that inherently require in-center application,
1102 notably TMS and ECT, and where COVID-19 related streamlining of in-center protocols is not
1103 practical (for specific patients), transition to home-based tDCS may be considered as a valid
1104 alternative option. There is evidence that tDCS can extend the benefit of TMS or ECT
1105 treatments [50, 67]. When ECT and TMS services are not available the operant decision is not
1106 the comparative efficacy of various NIBS techniques [68] but the risk/benefit ratio of trialing
1107 tDCS. The risk of tDCS is considered non-significant and safe, including across clinical
1108 populations [69-71] - indeed tDCS is broadly applied to healthy subjects (e.g. college students;
1109 [72]). Specifically for major depressive disorder, controlled trials [73-75], meta-analysis [68, 76,
1110 77] and expert consensus [78] suggest tDCS is comparably effective with significantly less
1111 adverse events than drug therapy. Consideration for deploying remote-tDCS treatment should
1112 be based on the latest clinical trial data [56].

1113

1114 **9.2 In-clinic Brain Stimulation**

1115 While the portability and cost of tES devices lend themselves to a relatively easy shift toward in-
1116 home usage and training, most TMS studies are currently tied to a fixed clinical or laboratory

1117 location, which is often in a hospital environment. This is a challenge for researchers that are
1118 weighing the cost benefit ratio of restarting their therapeutic intervention trials in an environment
1119 wherein participants and staff members may be exposed to the COVID-19 virus. The balance is
1120 likely different for mechanistic TMS studies designed to characterize a disease or biology itself,
1121 without any anticipated therapeutic effect.

1122
1123 That said, there are several sites conducting therapeutic TMS clinical trials across the globe that
1124 have been allowed to remain open through the COVID-19 epidemic. Even more are resuming
1125 operations as universities, hospital systems, and countries at large begin to reopen clinical
1126 research operations (Section 2). In fact, while the majority of TMS research trials were put on
1127 pause during the COVID-19 period, clinical delivery of TMS continued in many U.S. states and a
1128 variety of countries for individuals with treatment' refractory major depression, often with
1129 modified clinical workflows to ensure safety related to COVID-19. Below we will outline topics
1130 that are common to many clinical services and trials that remained open (or are reopening) as
1131 well as some new areas for innovation and risk-reduction when performing TMS in the COVID-
1132 19 era.

1133
1134 **9.2.1. Converting Consent, Screening, and Follow-Up Visits to Electronic, Voice, or Video**
1135 **Format.** A common theme echoed in this manuscript is to shift any non-essential in-person visit
1136 to electronic/video format. For many research studies there is a Consent Visit, Screening Visit,
1137 and Follow-Up visits. One of the benefits of the COVID-19 crisis has been a widespread
1138 familiarity and increasing comfort with video conferencing software (e.g. Zoom, Webex, VSee).
1139 It is important to ensure the security of the videoconferencing platform when connecting with
1140 patients or study participants, however, with respect to institutional requirements for HIPAA
1141 compliant communications. Given that TMS studies often require at least one in-person
1142 intervention visit, transforming our protocols to embrace video techniques for all other visits
1143 would improve the risk benefit ratio for the staff and the participants. Additionally, research
1144 groups may want to consider adding "COVID-19-related illness" as an exclusionary criteria or as
1145 part of the risks for participating in a research study which relies on multiple in-person visits
1146 (should the institution deem this necessary).

1147
1148 **9.2.2. Utility of Theta Burst Stimulation.** Fixed frequency rTMS (e.g. 10 Hz) is the oldest and
1149 most established stimulation protocol and has been FDA-approved for use in treatment resistant
1150 major depressive disorder for many years. In recent years however, bursting frequency

1151 protocols (e.g. theta burst stimulation (TBS)) have emerged as highly potent and temporally
1152 efficient forms of brain stimulation; that is, 600 pulses of intermittent TBS (iTBS) delivered over
1153 45 seconds result in an elevation in cortical excitability comparable to 2000 pulses of 10 Hz
1154 TMS delivered over 15 minutes [79]. The effects of a single session last approximately 30
1155 minutes, but repeated sessions have similar durability and efficacy as 10Hz rTMS [80] 34 and
1156 were first described in the motor cortex. Several recent, clinical trials applying TBS to the
1157 dorsolateral prefrontal cortex have demonstrated treatment outcomes with iTBS are comparable
1158 to treatment outcomes with traditional 10 Hz rTMS in major depressive disorder. Furthermore,
1159 these protocols have similar side-effects, safety, and tolerability profiles. The advantages of
1160 elevated potency and efficiency are coupled with a rigorous biologic foundation as theta is an
1161 endogenous neural rhythm associated with learning and memory. By using TBS, the number of
1162 patients treated per day with current rTMS devices can be increased several times without
1163 compromising clinical effectiveness or safety. In this COVID-19 era, one way to minimize the
1164 length of the time that a participant or patient has to be present in the room with a staff member
1165 would certainly be for investigators to consider using bursting frequency rTMS protocols which
1166 appear to be more efficient pulse-to-pulse. The shorter duration of the stimulation session also
1167 provides more flexibility when considering changes in workflow and schedules to ensure that
1168 patients do not overlap and thorough infection control measures are applied after every session.

1169
1170 That said, there has been some concern that the response to theta burst stimulation is highly
1171 variable [80, 81]. Although there have been very few sham-controlled comparisons of fixed
1172 frequency versus theta burst frequency TMS, the largest study to directly compare these
1173 protocols (which was not sham controlled), did not find a difference in the variability or the
1174 durability of response to 20 sessions of iTBS compared to conventional 10 Hz TMS in patients
1175 with depression [80]. While the relative efficacy and durability of these protocols is an empirical
1176 question that remains unanswered, in the COVID-19 era it seems that greater investigation into
1177 the factors that increase theta burst efficacy are warranted.

1178
1179 **9.2.3. Accelerated TMS Delivery.** The development of novel, accelerated TMS dosing
1180 strategies is another opportunity for clinical researchers. Previous studies have demonstrated
1181 that delivering multiple TMS sessions per day has similar efficacy to a single TMS session per
1182 day when the total number of TMS administrations is equal [82-84]. Given that the total number
1183 of TMS sessions appears to be a critical factor in behavioral change, these concentrated dosing
1184 protocols would be attractive to both patients and providers. While these protocols are being

1185 explored in research laboratories however, there is still a gap in our knowledge regarding the
1186 parameters that optimally balance efficiency with long-term efficacy. In one of the most
1187 concentrated TMS protocols to date Williams and colleagues (2018) recently published a study
1188 of 6 individuals with highly refractory depression (5 days, 10 sessions/day, 1800 pulses of
1189 iTBS/session, 50 minute inter-session interval) which demonstrated that this rapid dosing
1190 schedule was feasible and was effective as a rapid antidepressant [85, 86]. Galletly and
1191 colleagues (2010), for example, elegantly demonstrated that TMS delivered 3 times/week
1192 achieved overall similar outcomes to 5 times/week as long as the overall number of
1193 administrations was the same (18-20 administrations) [87]. While most accelerated TMS studies
1194 are being done in Major Depressive Disorder, they are also being used in many currently
1195 recruiting drug and alcohol treatment research trials [88-93]. These protocols reflect dosing
1196 schedules that are likely more tenable for patients who likely have job and family responsibilities
1197 (often 3 days per week versus the standard 5 days per week). They are being used by
1198 researchers around the world. By decreasing the number of times a participant or patient needs
1199 to come to the laboratory/clinic, accelerated TMS schedules will also minimize the number of
1200 days that individual spends out of the house, the number of times they use public transportation,
1201 and the number of other person-encounters they have over the course of their treatment (as 30
1202 sessions of TMS could be given in as little as 3 or 6 days as has been tried at various
1203 institutions in the United States). On the other hand, although it reduces the total time of TMS
1204 treatment, patients need to stay longer in the TMS environment, from one or two hours
1205 mounting up to the entire day.

1206

1207 **9.2.4. Other Technologies, such as Portable TMS.** A few other techniques and opportunities
1208 for innovative TMS protocol adaptations include greater reliance on neuronavigation for reliable
1209 and fast TMS coil positioning (as described in previous sections of this manuscript) and the
1210 delivery of TMS in off-site community clinics wherein the participant may have less exposure to
1211 potential COVID-19 carriers in the hospital environment. Perhaps the most provocative (but still
1212 chimerical) opportunity is for increased investment and innovation in a portable means for TMS
1213 delivery. There are several patents currently for portable TMS devices (e.g. for the treatment of
1214 migraine attacks Starling et al. [94]) and several papers have recently been published
1215 describing personalized TMS helmet designs which stabilize the coil [95] and wearable TMS coil
1216 designs [96]. Currently, however, there are no devices being made for commercial use. The
1217 ability to distill the power of electromagnetic induction as a brain stimulation tool into a
1218 briefcase-sized device has the potential to revolutionize non-invasive neuromodulation as a

1219 field. To see this materialize from a fantasy to a reality on the tails of the COVID-19 crisis could,
1220 in fact, be one of the biggest achievements the neuromodulation field may gain from this
1221 experience. It will, however, take talent, time, and investment to make this happen. One should
1222 also balance the safety balance of reducing exposure to the coronavirus with the exposure to
1223 the yet unclear risks of patient self-application of home-based TMS.

1224

1225 **9.2.5. Consideration of tDCS as Alternative or Adjunctive Treatment.** As discussed above
1226 (Section 9.1). tDCS can be deployed at home with no or minimal required in-person interactions.
1227 On a situation based, providing tDCS as an alternative to TMS or optimized the benefits of TMS
1228 (e.g. tDCS for maintenance of TMS therapy) can be considered [97, 98].

1229

1230 In conclusion many of the TMS treatment trials that were temporarily halted in March 2020
1231 around the world have begun to put strategies in place to return to enrollment and execution.
1232 These decisions should be made with sensitivity to many factors including the potential risk of
1233 COVID-19 exposure to the participants and staff for in-person visits and the potential benefit to
1234 participants & patients of the intervention. Those trials involved structural or functional imaging
1235 remains restricted based on the opening of imaging facilities. Similarly, any TMS trials involving
1236 parallel in-person protocols (e.g. rehabilitation) are considered in totality. While there will be
1237 many factors that influence this decision for each TMS study, there are some common themes
1238 that will minimize risk (electronic visits when possible, accelerated treatment courses, shorter
1239 pulse sequences like theta burst, use of technological methods such as neuronavigation and
1240 scalp modeling to improve rigor and decrease contact) that not only improve the risk benefit
1241 ratio but will likely lead to a reimagination of the future of TMS delivery- perhaps even launching
1242 a new industry that merges the portability and affordability of tDCS devices with the benefits of
1243 electromagnetic induction as a mechanism of inciting brain change.

1244

1245 **9.3 New Clinical Opportunities (Indications) with NIBS in the era of COVID-19**

1246 In response to the COVID-19 outbreak, initial psychological and emotional reactions such as
1247 elevated levels of anxiety, fear, stress or anger and behavioral responses like social/physical-
1248 distancing, stockpiling goods, PPE and disinfectants have been predicted based on previous
1249 experiences [99], and then reported during the COVID-19 outbreak [100-103]. However,
1250 precipitated psychological responses might progress into severe mental concerns which can
1251 easily outlast the pandemic. Sleep disturbances, somatization, stress-related illnesses, post-
1252 traumatic stress disorder (PTSD), anxiety disorders, depressive disorders and health risk

1253 behaviors such as social isolation, substance abuse or suicide attempts might also surge [2,
1254 102, 104]. Accordingly, depressive and post-traumatic symptoms have been constantly reported
1255 and found to persist even 2.5 years after epidemics [105]. Evidence that similar symptoms are
1256 present among health care professionals and the general population during the COVID-19
1257 outbreak is already emerging from China, the epicenter of the outbreak [103, 106-108], and
1258 from Europe as well [109].

1259

1260 The consequences of COVID-19 might be more immense in terms of the number of affected
1261 and maybe in terms of symptom severity than previous outbreaks, not to mention its economic
1262 and political impact and their effects on an individual level. Apart from new cases with mental
1263 health issues, those already facing mental health problems or belong to a vulnerable population
1264 might experience their symptoms worsening [110, 111]. Increased risk of COVID-19 infection or
1265 potentially deteriorating mental health during the outbreak has been articulated concerning
1266 patients with cancer [112], dementia [113], PD [114], chronic pain [115], MS [116] and drug
1267 users [2].

1268

1269 In light of the potential surge of demand for mental health care, effective therapeutic options are
1270 critical. NIBS is a promising and versatile tool to consider. The administration of magnetic fields
1271 (i.e. TMS) or weak electrical currents (i.e. tES) induces long-term neuronal effects through
1272 modulating neuroplasticity [117]. One of the first and most successful areas of NIBS application
1273 is the use of HF-TMS over the left dorsolateral prefrontal cortex to alleviate depressive
1274 symptoms that now has a level A evidence (i.e. definite efficacy) [4]. Interestingly, promising
1275 results are emerging regarding the beneficial effects of NIBS on several clinical populations
1276 suggesting transdiagnostic opportunities. Level B (probable efficacy) recommendation has been
1277 proposed for the use of TMS in fibromyalgia, PD, MS, PTSD and stroke [5]. Evidence is less
1278 conclusive on tES; however, level B evidence supports the utility of tDCS in depression, chronic
1279 pain and fibromyalgia [6]. Moreover, prosperous results suggest the potential efficacy of NIBS in
1280 several other disorders e.g. in anxiety disorders [118], dementia [119], obsessive-compulsive
1281 disorder [120, 121] and pediatric attention-deficit hyperactivity disorder [122].

1282 In an outbreak situation, adaptation skills and flexibility are essential to adjust behavior to the
1283 new regulations; thus, to mitigate the spread of the virus. Cognitive control is impaired in several
1284 conditions [114, 123]; however, NIBS has successfully ameliorated cognitive impairment in
1285 different patient groups [123-125]. Another important skill, emotion regulation has improved in
1286 patients with anxiety disorders with the effects being sustained for 3 months after TMS [126].

1287 Depressive symptoms, anxiety and PTSD emerging or being accelerated by the COVID-19
1288 pandemic [102] might also be successfully mitigated with NIBS based on previous research [4,
1289 127, 128]. Furthermore, stress is also known to exacerbate disease-related symptoms such as
1290 the motor symptoms of patients with tic disorders or PD [114, 129, 130]. Preliminary evidence
1291 indicates the beneficial effects of TMS on motor performance as well [131, 132].

1292
1293 Recently, the possibility of COVID-19-associated nervous system diseases has also been
1294 clinically proven by detecting the ribonucleic acid (RNA) of the virus in the cerebrospinal fluid of
1295 a patient [133]. Neurological symptoms such as impaired consciousness, headache, dizziness
1296 and taste or smell impairment are not uncommon [134]. Therefore, the long-term follow-up and
1297 monitoring of severe cases of COVID-19 in terms of neurological symptoms is highly advised
1298 [135]. Through the enhancement of neural plasticity, some COVID-19-related neurological
1299 residual symptoms might be attenuated by NIBS. In a rat model, TMS has been found to reduce
1300 inflammation after focal brain injury [136] and to decrease the production of proinflammatory
1301 cytokines in patients with PD [137]. Moreover, patients with disorders of consciousness have
1302 shown neurobehavioral and electrophysiological gains after multiple sessions of NIBS [138-
1303 140]. Therefore, anti-inflammatory potential and neurological utilization of NIBS might also be
1304 investigated.

1305
1306 Finally, there may be opportunities to apply NIBS in the broader context of changing medical
1307 protocols. This could span changing methods and access to prescribed medications (e.g. ability
1308 to diagnose, monitor for adverse events) as well as any consideration of unexpected
1309 interactions between drugs (e.g. psychotropics) and antiviral medication. A general feature of
1310 NIBS is its non-drug non-systematic application nature, non-addictive nature, and ability to
1311 terminate or adjust dose (in clinic or remote for home-based treatment) and vice versa. Clearly,
1312 there is potential for NIBS as a unique treatment tool in the fight against the medical and
1313 psychological after-effects of the COVID-19 outbreak.

1314

1315 **10. Conclusion**

1316 The COVID-19 pandemic, just like all crises, has yielded challenges for researchers, clinicians,
1317 participants and patients, but also lessons to learn from and new opportunities to pursue. By
1318 synthesizing the experiences of experts from all over the world, this consensus paper
1319 establishes practical recommendations to follow in operationalizing NIBS during COVID-19
1320 pandemic, mitigating the risk of infections, and in preparing the NIBS community for any future

1321 epidemic/pandemic. Indeed, as we emerge from the current pandemic, the number of people
1322 who require innovative treatments such as NIBS due to direct and indirect effects of COVID-19
1323 onto the brain and mental health will significantly increase. This burden on the health care
1324 systems mandates broader investigation and adoption of therapeutic solutions such as the use
1325 of NIBS. For NIBS laboratories and clinics to contribute to the ease the burden of the pandemic,
1326 it is necessary to re-establish operation with prudent protocol modifications as soon as possible.

1327
1328 Maintaining ongoing and restarting operations at NIBS clinics and research institutions across
1329 the world requires accommodation to strict measures (namely social/physical distancing)
1330 introduced due to the COVID-19 outbreak. The suddenness and severity of initial restrictions
1331 resulted in significant disruptions to ongoing clinical treatment and trials (spanning suspension
1332 recruitment of participants, interruption of ongoing treatment, to complete suspension of in-
1333 person activities). The degree of interruption varied; for example, in-person non-clinical (non-
1334 essential) work was largely halted while remote-tDCS clinical activity continued. Interruption of
1335 ongoing trials is compounded by overall operational and programmatic uncertainties e.g. the
1336 situation of students and early career scientists, financial concerns. The overarching concern is
1337 when and how specific clinical and laboratory work can be resumed and what precautions are to
1338 be adopted. This document provides guidelines for maintaining and resuming NIBS operations.

1339
1340 We distinguish three phases of procedural responses (immediate COVID-19 impact, current
1341 practices, and future preparation), with current reactions of the NIBS community to the COVID-
1342 19 pandemic largely in early phases with reactions aiming to limit disruption to ongoing
1343 protocols. However, streamlining and expanding NIBS services is now ongoing.

1344
1345 Based on the analysis of international experts with domain relevant expertise covering NIBS
1346 technology, clinical services, and human trials, we formed recommendations to ensure the
1347 safety of participants, researchers and staff members during the re-establishment of access to
1348 NIBS clinical services and research operations. Apart from the obvious preparations (e.g.
1349 sanitization and social distancing protocols and remote data acquisition where possible),
1350 recommendations are also made regarding protocol optimization, methodological good
1351 practices, the support of all stakeholders including early career scientists. To foster this process,
1352 a checklist is also provided in the article. Mitigation plans to reduce the risk of infection for
1353 subjects/participants and research/clinical staff are preeminent but should be based on the
1354 applicable national and institutional guidance and scientific understanding to avoid being

1355 misdirected or unduly burdensome. Recommendation on precautions are also discussed
1356 considering pediatric research, older adults, patients with addiction, stroke, MS or other chronic
1357 neurodegenerative/inflammatory disorders.

1358

1359 As explicated through this document, appropriate safety protocols are crucial to provide NIBS
1360 for those who require mental health care regardless of, and also aggravated by, the outbreak.
1361 With well-coordinated and strategic responses, the NIBS community can play an expanding role
1362 in managing the burden related to the COVID-19 pandemic while continuing to generate clinical
1363 and scientific regarding the efficacy and underlying mechanisms of NIBS. As we have discussed
1364 above, expanding clinical trials with telemedicine-based NIBS are of high impact in the current
1365 situation and considering future outbreaks and longstanding need for vigilance. Since tES
1366 devices are more easily transportable and simple to use, the remote application of tES is more
1367 supported in contrast to TMS. Guidelines [46, 56] and empirical experience [140-142] regarding
1368 the at-home applications of tDCS are available. Experiences gained through this process as
1369 well as new perspectives gathered during the challenging era of COVID-19 might delineate new
1370 research and therapeutic goals and become invaluable when preparing for future outbreaks

1371

1372 The interest in telemedicine-based solutions has especially increased among the NIBS
1373 community [61] and the experiences gained from such studies conducted during the outbreak
1374 will be broadly valuable. Generally, remote NIBS solutions extend the availability of
1375 neuromodulation, and can reduce costs of increasing the trial sample sizes and treatment
1376 duration. The adaptation process of some in-clinic TMS solutions that sustained operation
1377 during the pandemic and protocols to reduce contact is addressed.

1378

1379 The NIBS community has faced varied degrees of disruption that has broadly challenged
1380 laboratories and clinics across the globe. By working around evolving restrictions and
1381 uncertainties, strategic (and not unduly burdensome) implementation of applicable safety
1382 procedures, and adaptation of protocol components to limit in-person activities, access to NIBS
1383 must be continued and re-established rapidly. In this article, approaches and practical
1384 recommendations have been provided. Indeed, if further outbreaks arise, the NIBS community
1385 will be better prepared for them.

1386

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1392

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1407

1408

1409

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Journal Pre-proof

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	<ul style="list-style-type: none"> • Inpatient and outpatient treatment services are still allowed • Assessments are done via telehealth 	<ul style="list-style-type: none"> • None mentioned 	<ul style="list-style-type: none"> • Implementation of teleconsultation 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • COVID-19 sub-wards • Non-urgent treatments and ambulatory consultation suspended • rTMS maintenance is allowed • ECT is allowed based on severity 	<ul style="list-style-type: none"> • Interruption of VNS and DBS implantation • Mental deteriorations in some patients • ECT capacity is reduced 	<ul style="list-style-type: none"> • Teleconference contacts, phone calls, or face to face contact (respecting the safety guidelines) 	<ul style="list-style-type: none"> • To be decided
India	Kasturba Medical College, Manipal Academy of Higher Education	March 23, 2020	Not specified	<ul style="list-style-type: none"> • Interruption of non-emergency services • Rotating schedules to provide essential services 	<ul style="list-style-type: none"> • Patients and staff under lockdown 	<ul style="list-style-type: none"> • Implementation of tele-consultation for the follow-up of old patients 	<ul style="list-style-type: none"> • Basic hygiene precautions*

Italy	Gallimberti & Partners (private addiction clinic)	March 9, 2020	May 18, 2020	<ul style="list-style-type: none"> • Interruption of clinical protocols • Only COVID-19 free patients are admitted 	<ul style="list-style-type: none"> • Data loss from ongoing studies • Increase of psychological distress in addicted patients 	<ul style="list-style-type: none"> • Implementation of teleconsultations (for psychological and medical support) 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of clinical protocols 	<ul style="list-style-type: none"> • Home-based protocols are not approved yet 		<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of all clinical activities 	<ul style="list-style-type: none"> • None mentioned 	<ul style="list-style-type: none"> • Teleconsultations for some patients 	<ul style="list-style-type: none"> • To be decided
United Kingdom	Institute of Cognitive Neuroscience, University College London	March 6, 2020	To be decided, maybe January 2021	<ul style="list-style-type: none"> • Interruption of care services for community-based aphasic stroke patients • Interruption of remote outpatient and treatment services 	<ul style="list-style-type: none"> • Redeployment of clinical staff to other units 	<ul style="list-style-type: none"> • Teleconsultation (mainly for advising families) 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of all inpatient and outpatient visits • No visitors allowed in the hospital 	<ul style="list-style-type: none"> • Interruption of research activities 	<ul style="list-style-type: none"> • Implementation of teleconsultation 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of all outpatient visits 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Continue treatments and enroll new patients to service remotely • Protocol for sanitation of equipment, including shipments (incoming and outgoing) of equipment to patients 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of ongoing preclinical studies • TMS studies suspended 	<ul style="list-style-type: none"> • Data loss from ongoing studies • Interruption of data collection • Re-organization of tDCS studies for remote administration • Follow-up of recruited participants 	<ul style="list-style-type: none"> • Implementation of teleworking • Data collection from remote studies 	<ul style="list-style-type: none"> • Basic hygiene precautions*
Austria	University of Graz	March 11, 2020	Mid-May	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Staff working in rotations 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing • Online follow-up of patients • Strengthening collaboration across centers 	<ul style="list-style-type: none"> • PPE • Sanitization protocols • Single-subject test sessions

Belgium	Université Libre de Bruxelles	March 15, 2020	To be decided	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing 	<ul style="list-style-type: none"> • To be decided
Belgium	Ghent University	March 17, 2020	May 4, 2020 (under strict safety conditions)	<ul style="list-style-type: none"> • Interruption of research activities (preclinical and clinical) 	<ul style="list-style-type: none"> • Interruption of data collection • Data loss from ongoing TMS studies 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing 	<ul style="list-style-type: none"> • Continuation of teleconferencing • Basic hygiene precautions*
Brazil	Federal University of Espírito Santo	March 18, 2020	To be decided	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection 	<ul style="list-style-type: none"> • Implementation of teleconferencing 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection 	<ul style="list-style-type: none"> • Data mining • Computational modelling • Remote patient follow-up • Implementation of teleconferencing • Development of a questionnaire to measure COVID-19-related anxiety 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of most clinical operations; continuation of urgent patients and acute care 	<ul style="list-style-type: none"> • Interruption of data collection • Early career scientists losing time and opportunities 	<ul style="list-style-type: none"> • Virtual clinics • Pooling data across labs for new analysis opportunities 	<ul style="list-style-type: none"> • Priority to young early career scientists • Structured screening system
China	Shanghai Mental Health Center	Jan 29, 2020	May, 2020	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing • Re-analyzing previously collected data 	
China	University of Science and Technology of China	February 1, 2020	May, 2020	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Regular meetings for Journal Clubs were stopped 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Delays in projects • Potential depletion of project funding 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing • Daily updates on COVID-19 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Delays in projects • Potential depletion of project funding 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing 	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Having to close a study without meeting the predefined sample size 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing 	<ul style="list-style-type: none"> • PPE • Testing of patients
Germany	University Medical Center Göttingen	March 20, 2020	May 15, 2020	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Pause of recently started studies • Lower statistical power for studies terminated earlier 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Non-urgency activity suspended 	<ul style="list-style-type: none"> • Interruption of data collection 	<ul style="list-style-type: none"> • Implementation of teleworking • Implementation of teleconferencing 	<ul style="list-style-type: none"> • Basic hygiene precautions*
Iran	National Brain Mapping Lab (NBML)	February 23, 2020	April 4, 2020	<ul style="list-style-type: none"> • Interruption of all preclinical experiments • Interruption of all in-person study activities 	<ul style="list-style-type: none"> • Interruption of data collection • Decreased number of sessions and incoming projects 	<ul style="list-style-type: none"> • Implementation of teleworking • Webinars 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Data loss from ongoing studies 	<ul style="list-style-type: none"> • Implementation of teleworking 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of ongoing research 	<ul style="list-style-type: none"> • Interruption of data collection • Home-based protocols are not yet approved 	<ul style="list-style-type: none"> • Implementation of teleworking 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • All ongoing studies and lab activities suspended 	<ul style="list-style-type: none"> • Financial burdens and uncertainties • Need to complete all preclinical research by the end of fiscal year after reopening 	<ul style="list-style-type: none"> • Computational experiments remotely • Implementation of teleworking • Communication with collaborators 	<ul style="list-style-type: none"> • Assessment of symptoms • Basic hygiene precautions* • Ventilation of the rooms

Portugal	University of Coimbra	March 9, 2020	Approximately mid-May 2020	<ul style="list-style-type: none"> • All ongoing studies suspended 		<ul style="list-style-type: none"> • Conduction of online experiments later implemented in the lab's work • Implementation of teleworking 	<ul style="list-style-type: none"> • PPE
Russia	National Medical Research Center for Psychiatry and Neurology, St.-Petersburg	March 26, 2020	Approximately mid-May 2020	<ul style="list-style-type: none"> • All ongoing studies suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Data loss from ongoing studies 	<ul style="list-style-type: none"> • Implementation of teleworking 	<ul style="list-style-type: none"> • To be decided
Switzerland	NCM lab, ETH Zürich	March 16, 2020	<p>June 8, 2020 for low risk volunteers</p> <p>Unclear for vulnerable populations</p>	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Data loss from ongoing studies • Psychological effects of COVID-19 might influence the data 	<ul style="list-style-type: none"> • Implementation of teleworking 	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • All ongoing studies suspended 	<ul style="list-style-type: none"> • Interruption of data collection • Decreased testing capacity due to safety precautions • Fewer healthy participants • Lower statistical power for studies terminated earlier 	<ul style="list-style-type: none"> • Implementation of teleworking • New lab routines to keep staff motivated • Analysis of data from nearly complete studies 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of ongoing research 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Implementation of teleworking • New lab routines to keep staff motivated • Collecting follow-up data remotely • Participation to online workshops 	<ul style="list-style-type: none"> • PPE • Home-based tDCS • Shift schedules for staff members • Social distancing measures
United Kingdom	University of Oxford	March 13, 2020	To be decided	<ul style="list-style-type: none"> • Interruption of ongoing research (clinical and preclinical) 	<ul style="list-style-type: none"> • Interruption of data collection 	<ul style="list-style-type: none"> • Implementation of teleworking • Conducting modelling and in silico studies 	<ul style="list-style-type: none"> • To be decided
FL, USA	University of Florida	March 13, 2020	TBD, tentatively June 1, 2020	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Implementation of teleworking 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • All ongoing studies and in-person activities suspended 	<ul style="list-style-type: none"> • Data loss from ongoing studies • Interruption of data collection 	<ul style="list-style-type: none"> • Implementation of teleworking 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Interruption of all outpatient visits outside of standard care or justified risk 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Continue tele-research program with home-based remotely supervised tDCS • Protocol for sanitation of equipment, including shipments (incoming and outgoing) of equipment to participants 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • All studies considered 'non-essential operations' on immediate hold, which placed infant and child stroke studies on hold 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • 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

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

Initial
<ul style="list-style-type: none"> • Cessation of non-essential in-person research activities <ul style="list-style-type: none"> ◦ 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 <ul style="list-style-type: none"> ◦ 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. <ul style="list-style-type: none"> ◦ 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
<ul style="list-style-type: none"> • 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
<ul style="list-style-type: none"> • 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)
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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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