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Accelerating the therapeutic effects of non-invasive brain stimulation: A Neuroscience School of Advanced Studies (NSAS) challenge workshop

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A B S T R A C T

Background: Noninvasive brain stimulation is typically delivered once daily, but accelerated protocols delivering multiple daily treatments have re-emerged to shorten time to clinical improvement.

Methods: At the Neuroscience School of Advanced Studies Non-Invasive Brain Stimulation Challenge Workshop (Crans-Montana, Switzerland, October 21-24, 2025), we reviewed the literature on accelerated protocols across noninvasive brain stimulation modalities such as electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), transcranial electrical stimulation (tES), transcranial vagus nerve stimulation (tVNS), and transcranial focused ultrasound (tUS). Accelerated protocols were defined as multiple daily treatments (≥2/day).

Results: Accelerated ECT protocols date back to the 1960s, when multiple seizure inductions per day produced more rapid clinical improvement but greater cognitive adverse effects. Accelerated TMS protocols emerged in the mid-2000s and gained popularity in the late 2010s, when protocols delivering more than three treatments per day began to show faster antidepressant effects. Accelerated protocols with other modalities or for indications other than major depressive disorder are in early stages.

Discussion: Accelerated protocols may reduce response latency without diminishing response magnitude. However, the durability of accelerated protocols remains unclear, and systematic exploration of parameter space across modalities is needed.

1. Introduction

Noninvasive brain stimulation is commonly prescribed for individuals with acute, severe, or treatment-resistant neuropsychiatric illness [1]. Protocols vary by modality but typically involve one treatment per day, with clinical benefits emerging over weeks-to-months (Table 1). Interest has recently shifted toward *accelerated* protocols, which aim to compress treatment schedules to achieve comparable or greater benefit in less time.

We define accelerated protocols as those delivering two or more treatments per day (≥2/day) [2], though spacing, dosing, and tolerability vary across modalities. This definition focuses on treatment schedule rather than other parameters. Protocols that retain once daily treatment schedules but modify targeting [3,4], pulse timing [5], stimulus dosing [6], or augmentation strategies [7,8] are therefore not considered "accelerated" here; related strategies that increase total stimulation dose over shorter intervals are discussed for context.

Accelerated protocols offer both clinical and scientific advantages.

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Table 1
Conventional protocols for the treatment of MDD with noninvasive brain stimulation interventions.

Intervention	Conventional protocol	Marker for individual dosing
ECT	Once daily two to three times a week for 6-15 sessions[27, 164]	Seizure threshold (ST) 5-6x seizure threshold for right unilateral 1.5-2x seizure threshold for bilateral Seizure threshold is dynamic and increases over course of treatment
TMS	Once daily, 5 days a week for 36 sessions [161, 164]	Motor threshold (MT) 80-120% motor threshold depending on protocol
tES (tDCS, tACS)	Once daily, 5 days a week for ~30 sessions	Under investigation
tVNS	Under investigation	Under investigation (in infants there is change in heart rate)
tFUS for neuromodulation	Under investigation	Under investigation

ECT, electroconvulsive therapy; TMS, transcranial magnetic stimulation; tES, transcranial electrical stimulation; tDCS, transcranial direct current stimulation; tACS, transcranial alternating current stimulation; tVNS, transcutaneous vagus nerve stimulation; tFUS, transcranial focused ultrasound stimulation.

Clinically, rapid-acting treatment could reduce suffering, suicide risk, caregiver burden, and resource utilization. Accelerated protocols may also expand access to treatment in acute care or community settings. Scientifically, accelerated protocols allow cumulative dose and treatment spacing to be varied over short intervals. This framework is valuable for defining dose-response relationships, measuring parametric circuit alterations, and investigating plasticity-related effects.

In this narrative review, we summarize accelerated protocols for electroconvulsive therapy (ECT), TMS, and other neuromodulation modalities. The review emphasizes shared principles of accelerated stimulation across modalities and identifies opportunities for future research. This manuscript reflects an expert consensus that emerged from a targeted literature review and discussion at the Neuroscience School of Advanced Studies Non-Invasive Brain Stimulation Summit (Crans-Montana, Switzerland, October 21-24, 2025). It is dedicated to Summit co-director Nolan R. Williams, MD, who died on October 8, 2025 [9]. His work contributed to growing interest in accelerated protocols [10–12].

2. Electroconvulsive therapy

Electroconvulsive therapy (ECT) provides historical precedent for accelerated delivery, although its clinical application differs from contemporary practice.

Accelerated ECT dates back to the 1940s, when consecutive daily treatments were recommended for mania and catatonia [13,14]. These recommendations influenced "regressive ECT," a treatment for schizophrenia that involved multiple seizures within a single day. Some studies suggest that regressive ECT was more effective than single treatments administered two or three times per week [15–18]. This strategy was later formalized as multiple-monitored ECT (MMECT), which involved two to eight seizures during prolonged anesthesia or during repeated anesthetic inductions within a single day [19–21]. Seizure onset and offset were "monitored" with electroencephalography (EEG), an approach not yet routine for conventional ECT. Relative to conventional ECT, MMECT reduced length of stay and produced similar benefits on a shorter timescale [22–25]. However, it was discouraged because of greater acute cognitive impairment, progressively longer seizure durations, and rare reports of status epilepticus [22,25,26]. Some of these adverse events were likely worsened by treatment parameters now known to worsen cognitive effects, including bilateral electrode placement, sinewave stimulus, and non-individualized dosing [27]. MMECT has not been revisited using contemporary approaches such as right unilateral ultrabrief-pulse stimulation with individualized dosing [6,26,28,29].

Modern ECT is usually delivered once daily, so speed-tolerability tradeoffs are determined by weekly rather than daily frequency. Thrice-weekly treatment, common in the United States, produces faster improvement but more cognitive adverse events than the twice-weekly schedule used in Europe and elsewhere; once-weekly ECT is not recommended for acute treatment [28–33]. Higher stimulus intensity relative to seizure threshold is another strategy that has been explored as a way to accelerate response, with randomized trials showing faster improvement in MDD and schizophrenia [6,30–32].

Longitudinal changes in ECT practice should be interpreted in the context of shifts in patient population. ECT was introduced before modern psychopharmacology and was therefore administered earlier in the course of illness. Today, it is typically reserved for individuals with multiple treatment failures, including TMS and esketamine. As resistance to prior treatments has increased, acute courses have become longer and relapse rates after response have risen [33,34]. These trends strengthen the rationale for revisiting accelerated ECT using optimized dosing parameters.

3. Transcranial magnetic stimulation

Accelerated TMS has the most developed evidence base among noninvasive modalities, including randomized trials and regulatory clearance.

3.1. Major depressive disorder

Accelerated TMS (aTMS) is most extensively studied in MDD and has achieved regulatory clearance and clinical billing pathways [35,36]. Prior reviews have summarized the literature from 2007 to 2024 [2,37,38], encompassing early multi-session protocols and later trials such as the Stanford Neuromodulation Therapy (SNT) open-label [12] and randomized [11] trials that contributed to Food and Drug Administration (FDA) clearance of a TMS system [35] and Current Procedural Terminology (CPT) billing codes for connectivity-guided aTMS [36]. In these studies, SNT consisted of 10 hourly sessions of 1800-pulse intermittent theta burst stimulation (iTBS) delivered over five consecutive days (i.e. 50 sessions) using individualized connectivity-guided targeting, at 90% resting motor threshold adjusted for scalp-to-cortex distance. Here, we highlight notable developments in aTMS since 2024.

Two reports extend the SNT findings. In an abstract describing three-month SNT outcomes (n = 46), 37% and 32.6% of the intention-to-treat sample met response and remission criteria, respectively. Among acute responders, 43.2% maintained response and 46.9% maintained remission [39]. This modest durability suggests that retreatment strategies or protocol refinements may be necessary [40]. A separate clinical trial from the same group (n = 48) demonstrated antidepressant efficacy (50% remission with active vs 20.8% with sham) while identifying left anterior cingulate cortex beta power as a candidate pretreatment biomarker of response [41].

No independent group has yet validated the proprietary SNT targeting algorithm, which aims to stimulate the left dorsolateral prefrontal cortex region most anticorrelated to the subgenual cingulate cortex. However, multiple groups are replicating other protocol elements such as delivery schedule. Ongoing work is also examining the relative contribution of components, including daily session number [42] and connectivity-based targeting [43].

To examine dose-response relationships, we plotted sessions per day against total aTMS sessions, stratified by stimulation frequency and sample size (Fig. 1). No clear dose-response relationship emerged; a greater number of sessions did not consistently translate into better outcomes. This pattern suggests interaction with factors not captured in

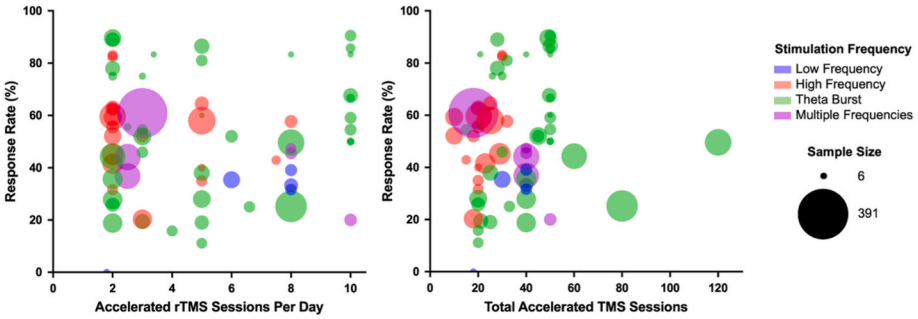

Fig. 1. Relationship between accelerated TMS parameters and treatment response.

these variables, such as individualized targeting. An open-label study leveraging scalp-based targeting reported a 50% response rate one month after treatment [44], lower than the corresponding rates in the original open-label SNT cohort (90% across timepoints, 70% at one month) [12]. Although no head-to-head trials of connectivity-versus scalp-based aTMS have been published, naturalistic data suggest improved outcomes with connectivity-based (78% versus 66% response rate, respectively) [45]. A double-blind randomized trial is needed.

Several aTMS trials have deviated from the SNT protocol. In a randomized trial (n = 100), active aTMS with a schedule of three 1200 pulse iTBS sessions per day for 15 weekdays (30-min spacing, 100% motor threshold, modified Beam F3 targeting) was superior to sham aTMS for MDD (Hamilton Depression Rating Scale 57.7% versus 31.87%, Cohen's d = 0.65) [46]. Separation between active and sham aTMS emerged late, consistent with prior aTMS trials in which clinical improvement continued after treatment ended [11].

A different line of work has introduced a one-day protocol (i.e., Optimized Neuroplastogen-Enhanced technique in Depression (ONE-D) combining off-label of d-cycloserine (125 mg) and lisdexamfetamine (20 mg) prior to 20 iTBS sessions (600-pulses each, 30-min spacing, 120% MT, modified scalp-based targeting approach) [47,48]. Preliminary open-label results suggest rapid antidepressant effects lasting at least 12 weeks, but these findings require cautious interpretation given the absence of control conditions, plasticity measures, and independent replication.

Finally, a BrainsWay-sponsored non-inferiority trial found that an accelerated H1 coil protocol (five sessions per day for six days within two weeks) produced faster clinical improvement but similar final outcomes compared to standard once-daily H1 coil treatment. The primary endpoint is currently available in preprint form [49], with secondary patient-reported outcomes reported in a peer-reviewed publication [50].

3.2. Is the "Lawfulness" of daily TMS for MDD preserved in aTMS?

Large patient registries of conventional once-daily TMS have identified several consistent observations that should be tested in accelerated protocols. First, longer treatment courses are associated with higher response and remission rates, with no clear plateau effect [51]. Evidence for a similar relationship in aTMS is limited and does not address parameters such as pulse dose, intersession interval, or coil orientation [2,52–54].

Second, the greatest symptom improvement during once-daily TMS typically occurs in the first ten sessions, with an average of 3% reduction per session [51]. Despite this trend, lack of early response does not ultimately predict non-response to conventional once-daily TMS [55]. Many individuals who do not initially improve will respond with further treatment. It is unclear why the degree of improvement per session is reduced after the first ten sessions, why there is a potential nadir effect, or whether it is possible to accurately estimate daily improvement with a questionnaire that has a 1-2 week recall window. In accelerated protocols, clinical effects may continue to emerge after treatment completion. Choice of assessment time points is therefore critical.

Fourth, scalp-based targeting with once daily TMS introduces spatial variability that may obscure symptom-specific changes that emerge when target location is considered [56,57]. Similar results would likely occur with aTMS guided by scalp-based targeting rather than by individual- or group-level, connectivity-based targeting.

Fifth, biological sex and age influence once-daily TMS outcomes, with greater average benefits observed in females and older adults [58]. Proposed explanations for the sex difference include shorter prefrontal scalp-to-cortex distance, greater prefrontal gray matter density and gyrification, and higher estradiol levels [59,60]. It is unclear if these biological sex and age trends will emerge from aTMS that alters dose, targeting, and other metrics.

3.3. Bipolar disorder

Two randomized trials (n = 24 and n = 13) using SNT-like protocols reported large antidepressant effects without treatment-emergent hypomania or mania in individuals with treatment-resistant bipolar depression [61,62]. In the larger trial, 5-day remission rates were 50% with active aTMS and 0% with sham aTMS (Cohen's d = −2.19 at 4-week follow-up). The study employed seedmap-guided targeting with e-field optimization, indicating that leveraging connectivity-based targeting can be used in this patient population.

3.4. Schizophrenia

aTMS has been explored for negative symptoms and auditory hallucinations in schizophrenia, although the evidence base remains limited and heterogeneous. Twice-daily iTBS to the left DLPFC or cerebellar vermis over 5-14 days (10-20 sessions total) has produced mixed effects on negative symptoms, with some studies reporting acute [63–66] and sustained [67] improvements and others reporting no active-sham differences [68,69]. Stimulation of the left temporoparietal junction or superior temporal sulcus (2 sessions per day for 2-5 days) has produced variable reductions in auditory hallucinations across case series [70–72], crossover designs [73,74], and sham-controlled trials [75–77].

Recent studies have increased treatment density or personalized circuit-based targeting. An open-label trial (n = 19) delivered 16 sessions over 4 days to the left DLPFC (8000 pulses/day; 32,000 total), producing a 68% response rate (≥20% improvement) and significant reductions in negative symptoms that persisted for at least 2 weeks (PANSS-N: 26.32 to 22.05, $p < 0.001$) [78]. A randomized trial (n = 80) delivered 40 sessions over 2 weeks to the left DLPFC region functionally connected to the ventral tegmental area, reducing negative symptoms at 4 weeks versus sham ($p < 0.001$, Cohen's d = 0.83) [79]. Individualized approaches are also under investigation, including a transdiagnostic protocol targeting a causally defined rostromedial prefrontal circuit [80,81] and a connectivity-guided 1Hz stimulation protocol that yielded a

number needed to treat of 3.5 in a preprint [82].

Taken together, these studies suggest that aTMS protocols were generally well tolerated by individuals with psychosis. Common adverse events included transient headache, neck discomfort, and local stimulation site pain. However, rare cases of mania or transient symptom exacerbation underscore the need for close monitoring. Larger controlled studies are needed to optimize stimulation parameters, confirm durability, explore symptom specificity, and define patient-selection criteria [83].

3.5. Obsessive compulsive disorder

A systematic review and meta-analysis of six randomized controlled trials found that active aTMS significantly reduced OCD (SMD 0.63) and depressive symptoms (SMD 0.52) and increased treatment response rates (OR 4.28) relative to sham aTMS. Adverse effects were more common with active aTMS (OR 5.16) but were reported as mild, and dropout rates were similar between groups (OR 0.74). However, only the antidepressant effects remained significant on longer-term follow-up [84].

3.6. Other indications and uses

Current studies are investigating aTMS for anorexia nervosa [85] and using aTMS as a causal probe of brain circuits underlying trans-diagnostic and diagnosis-specific behaviors [80].

4. Other modalities

For other modalities, evidence for accelerated protocols is limited and largely preliminary.

4.1. Transcranial electrical stimulation

Transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) are forms of transcranial electrical stimulation (tES) that deliver electric current through scalp electrodes [86–88]. These modalities are safe, portable, and relatively inexpensive [89–92], and may be well suited for repeated or home-based delivery.

Among tES modalities, tDCS is the most extensively studied. The FDA recently cleared a home-based tDCS system for MDD using a conventional once-daily dosing schedule (2 mA, 36 sessions over 10 weeks) [93]. Notwithstanding this regulatory milestone, the clinical effects of 2 mA daily tDCS remain modest relative to the clinical effects of TMS and ECT. The largest and most recent patient-level meta-analysis ($k = 18$, $N = 1246$) found small but statistically significant antidepressant effects (Hedges' $g = 0.24$, 95% CI 0.11–0.35) and response rate (odds ratio 1.33, 95% CI = 1.04-1.72) for active versus sham tDCS [94]. Effect estimates were slightly larger in an earlier patient-level meta-analysis with fewer studies and greater uncertainty [95].

Several features of tDCS complicate the development of accelerated protocols. First, there is no immediate physiological marker analogous to the TMS motor threshold or the ECT seizure threshold with which to guide individualized dosing or enable iterative dose adjustments across sessions. This limitation may be particularly relevant in accelerated protocols, where closely spaced sessions may benefit from real-time adjustment of stimulation parameters. MRI-based current-flow modeling has been used to personalize dosing, but it is resource-intensive and uncommon. Second, deviations from standard protocols may increase the risk of skin irritation or burns [96,97].

Clinical neurophysiology studies suggest that the temporal spacing of tDCS treatments is critical for accelerated protocols. In healthy adults, the effects of two tDCS sessions depend on the inter-session interval, with approximately 20-min spacing associated with longer lasting excitability changes compared to shorter or longer intervals [96,97]. Data of multiple (e.g. 3 or more) tDCS sessions a day on neurophysiological metrics or imaging metrics is limited.

Clinical feasibility of these accelerated or "spaced" tDCS has been tested in small trials. In an open-label study, five daily sessions (2 mA, 20 min each, spaced 20 min apart) over two weeks (50 sessions total) was well tolerated, with mild contact dermatitis that resolved by follow-up [98]. Depression symptoms improved over time, although randomized trials are needed to determine clinical efficacy and assess blinding. Ongoing work is exploring alternative strategies to increase dose (e.g., 4-6 mA) and refine targeting (e.g., high-definition arrays) [99–103], although these approaches are distinct from acceleration per se.

Relative to tDCS, accelerated tACS has been less extensively studied. Most studies are small and open label, although there are two sham-controlled trials in schizophrenia [104,105] and one large sham controlled trial for MDD [106]. The largest study to date is a triple-blind, fully remote, randomized controlled trial comparing active versus sham accelerated tACS in adults with MDD ($n = 225$). Active treatment produced a small but statistically significant advantage at 1 week, and higher response rates at 4 weeks [107].

4.2. Vagus nerve stimulation

Vagus nerve stimulation (VNS) was initially developed as an invasive intervention requiring surgical implantation of a pulse generator with electrodes placed on the cervical vagus nerve. Recently, non-invasive approaches enabled stimulation at the auricular and cervical branches, as well as at peripheral targets near end organs. Accelerated protocols have rarely been studied with these noninvasive paradigms, but two proof-of-concept studies warrant discussion.

The open label iWAVE study delivered accelerated transcutaneous auricular VNS (taVNS) without pairing stimulation to a specific behavioral task [108]. Ten inpatient adults with depression or anxiety were assigned to either three 30-min sessions per day for three consecutive days or nine sessions within a single day. Both schedules were safe, feasible, and effective at reducing depression and anxiety in this small sample.

The second study leveraged an FDA-cleared rehabilitation strategy in which VNS is paired with a behavior to promote activity-dependent plasticity [109]. In an open-label pilot trial, taVNS was administered during bottle feeding in infants with feeding difficulty [110]. This study advanced prior work demonstrating that once daily taVNS facilitates oromotor learning in infants with oral feeding dysfunction associated with prematurity or brain injury [111,112]. Infants ($n = 21$) receiving stimulation during two daily feeding sessions for 2-3 weeks showed increased feeding volumes relative to the pre-intervention period. More than half achieved full oral feeds in a shorter time than a historical cohort treated with once daily taVNS (median 7 versus 12.5 days, $p < 0.05$), indicating that higher session density may accelerate response time [110].

4.3. Transcranial focused ultrasound

Transcranial Ultrasound Stimulation (tUS) is an emerging technique with substantial promise for noninvasive modulation of deep brain structures. Unlike high-intensity focused ultrasound (HIFU), which produces thermal ablation for therapeutic purposes, tUS uses lower ultrasound intensities to modulate ongoing neural activity reversibly. The mechanisms underpinning tUS modulatory effects remain under investigation and likely involve activation of mechanosensitive ion channels [113,114].

Multiple proof-of-principle, single-session studies in healthy participants demonstrate that tUS can alter regional neural activity, functional connectivity [115–119], and behavior across several domains [120,121]. These effects depend on stimulation site, brain state, acoustic parameters [113], and rigorous control of potential confounds [122]. However, the absence of a simple physiological marker - analogous to

seizure threshold in ECT or motor threshold in TMS – complicates dose selection and outcome interpretation.

Clinical applications are at an early stage, with no established protocols beyond single session feasibility studies [121,123]. The development of validated treatment frameworks is required before testing accelerated protocols [124]. A small, open-label study targeting bilateral nucleus accumbens reported acute craving reductions in individuals with severe opioid and other co-occurring substance use disorders that persisted for 90 days [125]. The same group reported similar findings for methamphetamine use disorder [126].

In an ongoing randomized trial for opioid craving, one individual developed a prolonged state of altered consciousness along with imaging-confirmed structural lesions [127–131]. This serious adverse event underscores the need for careful evaluation of device parameters, real-time monitoring, and strict adherence to emerging safety guidelines as the field considers accelerated protocols [132].

5. Recommendations across modalities

Several recommendations for advancing accelerated protocols across noninvasive brain stimulation modalities emerged from NSAS workshop discussions and targeted literature review. (Text Box 1). First, establish a marker for individual dosing. The motor threshold for TMS and the seizure threshold for ECT are imperfect, but they played a central role in setting individualized dosing. The development of an easily observable and measurable physiological response marker to tDCS, tACS, tVNS, tFUS could help the field optimize and accelerate protocols. Ideally, the marker would also reflect relevant physiological adaptations occurring over the course of treatment that impact dosing. For example, the ECT seizure threshold increases over the treatment course and has implications for optimal dosing [133].

Second, leverage neuroimaging and modelling to inform acceleration efforts. Neuroimaging can reveal anatomical features that have relevance for dosing and targeting, e.g. skull thickness and skull-to-cortex distance impacts ECT [134]. Similar variables have also been explored in TMS [60], which has an additional variable of coil orientation relative to underlying cortical anatomy [54]. Functional neuroimaging may also be used to personalize targeting, but more data are needed [43,135,136].

Third, use, develop, and validate scales to measure rapid symptom change. Most symptom scales were validated on recall windows of at least a week or more (e.g. the Hamilton Rating Scale for Depression, Montgomery-Asberg Depression Rating Scale, etc.). There are existing scales with shorter recall windows (e.g., Clinically Useful Depression Outcome Scale, Clinically Useful Anxiety Outcome Scale, etc.) [137,138], but additional scales might help capture which symptoms change on which time course. There is also value in developing and collecting clinician- and patient-reported scales in parallel, as they sometimes show important differences [139].Ecological momentary assessments and wearable physiological monitoring devices may also provide useful data on shorter timescales [140,141].

Fourth, explore adjunctive or combination interventions for synergistic effects on speed and magnitude of improvement. These possibilities include state-dependent effects, including potential interactions with homeostatic metaplasticity and circadian rhythms, as well as augmentation with pharmacology or psychotherapy [142,143]. Interactions between augmentation and accelerated delivery may be nonlinear, and combining these approaches may not be straightforward. Importantly, brain stimulation may be the primary treatment being augmented or the augmenting agent for a primary treatment [144–146].

Fifth, determine whether accelerated interventions trade durability for speed. For TMS, it has been suggested that rapid clinical benefits may be less durable [147]. Longitudinal data will be critical for testing this possibility and for assessing whether accelerated protocols alter the trajectory of psychiatric illness. In medicine, some rapid-acting interventions provide transient symptom relief and therefore must be used repeatedly as symptoms arise (e.g., triptans, bronchodilators, etc.) [146,148,149]. Others act quickly and modify the disease course, with time-limited treatment courses (e.g., antibiotics for bacterial infection). Psychiatric illnesses are not yet defined at the level of pathophysiology required to make this distinction directly, but longitudinal symptom trajectories and recurrence patterns may provide indirect evidence of durable, illness-modifying effects. Clarifying these temporal profiles also has practical implications for resource utilization, scalability, and access. Accelerated protocols shorten the overall treatment course but often lengthen individual treatment days. As a result, socioeconomic factors may influence which individuals are able to pursue which treatment schedules.

Finally, define the safety and regulatory pathways for accelerated protocols. Parameter changes intended to increase dose or alter treatment schedules may introduce risks that are not captured by existing evidence. Timely and transparent reporting of adverse events will be necessary to refine consensus safety guidelines and to inform regulatory evaluation of novel accelerated approaches [89,124,128,131,150–152]. These considerations will influence trial design, reporting standards, and the pace at which accelerated interventions can be implemented in clinical practice.

6. Conclusion

Untreated or inadequately treated brain disorders carry substantial burdens of morbidity, mortality, and societal costs, underscoring the need for faster and more effective treatments. Efforts to accelerate treatment response to noninvasive brain stimulation date back to at least the 1960s with multiple-monitored ECT [21]. More recent work, including the SNT protocol, has contributed to renewed interest in strategies to hasten treatment benefits [10–12].

This review synthesizes findings across modalities to identify shared principles and gaps for future study. The strength and consistency of evidence vary substantially across modalities, with the most robust data for TMS in MDD and more limited or heterogeneous evidence for other approaches. One emerging principle is that session density is a key determinant of accelerated response for ECT, TMS, and possibly tDCS, although the broader parameter space remains incompletely explored. Systematic exploration of additional parameters is needed to define optimal dosing strategies. Accelerated noninvasive brain stimulation

Text Box
Summary of suggestions across procedures

1. Establish a reliable physiological marker for individual dosing/target engagement
2. Consider using neuroimaging and modelling to inform efforts at acceleration
3. Use and develop validated measures that capture change in short time courses
4. Explore adjunctive/combination approaches to accelerate benefits (e.g., pharmacology, psychotherapy, state-dependence, etc.)
5. Determine whether accelerated interventions trade durability for speed.
6. Define the safety and regulatory pathways for accelerated protocols.

offers a platform not only for more rapid clinical benefit, but for refining dose-response models.

CRediT authorship contribution statement

Joseph J. Taylor: Writing – review & editing, Writing – original draft, Conceptualization. **Charlotte J. Stagg:** Writing – review & editing, Writing – original draft, Conceptualization. **Indrit Bègue:** Writing – review & editing, Writing – original draft, Conceptualization. **Marom Bikson:** Writing – review & editing, Writing – original draft, Conceptualization. **Andre R. Brunoni:** Writing – review & editing, Writing – original draft, Conceptualization. **Kevin A. Caulfield:** Writing – review & editing, Visualization, Conceptualization. **Enoch Ng:** Writing – review & editing, Writing – original draft, Conceptualization. **Jayce Doose:** Writing – review & editing, Visualization, Conceptualization. **Harold A. Sackeim:** Writing – review & editing, Writing – original draft, Conceptualization. **Mark S. George:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Marom Bikson: The City University of New York holds patents on brain stimulation with MB as inventor. MB has equity in Soterix Medical Inc. MB consults, provides expert witness support, received grants, assigned inventions, and/or served on the SAB of SafeToddles, Zabara Family Foundation, Boston Scientific, Axonics, SigmaStim, Lumenis, Halo Neuroscience, Wave Neuroscience, Neurolief, Allergan (Abbvie), Apple, Ybrain, Ceragem Clinical.

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Mark S. George: Dr. George serves as a consultant to Abbott, LivaNova and Neurolief. MUSC has research funds for clinical trials he runs from Abbott and LivaNova. He is a co-holder of a patent through MUSC on taVNS for infant feeding. He has no equity interest in any device company.

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References

[1] Williams NR, Taylor JJ, Kerns S, Short EB, Kantor EM, George MS. Interventional psychiatry: why now? J Clin Psychiatry 2014;75(8):895–7.
[2] Caulfield KA, Fleischmann HH, George MS, McTeague LM. A transdiagnostic review of safety, efficacy, and parameter space in accelerated transcranial magnetic stimulation. J Psychiatr Res 2022;152:384–96.
[3] Siddiqi SH, Khosravani S, Rolston JD, Fox MD. The future of brain circuit-targeted therapeutics. Neuropsychopharmacology 2023.
[4] Siddiqi SH, Taylor JJ, Horn A, Fox MD. Bringing human brain connectomics to clinical practice in psychiatry. Biol Psychiatry 2023;93(5):386–7.
[5] George MS, Huffman S, Doose J, Sun X, Dancy M, Faller J, et al. EEG synchronized left prefrontal transcranial magnetic stimulation (TMS) for treatment resistant depression is feasible and produces an entrainment dependent clinical response: a randomized controlled double blind clinical trial. Brain Stimul 2023;16(6):1753–63.
[6] Sackeim HA, Prudic J, Devanand DP, Kiersky JE, Fitzsimons L, Moody BJ, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. N Engl J Med 1993;328(12):839–46.
[7] Cole J, Sohn MN, Harris AD, Bray SL, Patten SB, McGirr A. Efficacy of adjunctive D-Cycloserine to intermittent theta-burst stimulation for major depressive disorder: a randomized clinical trial. JAMA Psychiatry 2022;79(12):1153–61.
[8] Brunoni AR, Valiengo L, Baccaro A, Zanao TA, de Oliveira JF, Goulart A, et al. The sertraline vs. electrical current therapy for treating depression clinical study: results from a factorial, randomized, controlled trial. JAMA Psychiatry 2013;70(4):383–91.
[9] George MS, Sackeim HA, , IN MEMORIAM, Nolan R, Williams MD. Neuropsychopharmacology 2026;51:534–5.
[10] Williams NR, Sudheimer KD, Bentzley BS, Pannu J, Stimpson KH, Duvio D, et al. High-dose spaced theta-burst TMS as a rapid-acting antidepressant in highly refractory depression. Brain 2018;141(3):e18.
[11] Cole EJ, Phillips AL, Bentzley BS, Stimpson KH, Nejad R, Barmak F, et al. Stanford Neuromodulation Therapy (SNT): a double-blind randomized controlled trial. Am J Psychiatry 2021. appiajp202120101429.
[12] Cole EJ, Stimpson KH, Bentzley BS, Gulser M, Cherian K, Tischler C, et al. Stanford accelerated intelligent neuromodulation therapy for treatment-resistant depression. Am J Psychiatry 2020;177(8):716–26.
[13] L K, PH H. Shock treatments and other somatic procedures in psychiatry. Grune & Straton; 1946.
[14] Fink M. Convulsive therapy: theory and practice. New York: Raven Press; 1979.
[15] Murillo LG, Exner Jr JE. The effect of regressive ECT with process schizophrenics. Am J Psychiatry 1973;130(3):269–73.
[16] Rothschild D, Van Gordon DJ, Varjabedian A. Regressive shock therapy in schizophrenia. Dis Nerv Syst 1951;12(5):147–50.
[17] Exner Jr JE, Murillo LG. Effectiveness of regressive ECT with process schizophrenia. Dis Nerv Syst 1973;34(1):44–8.
[18] Weil PL. 'Regressive' electroplexy in schizophrenia. J Ment Sci (96):514-520.
[19] Bridenbaugh RH, Drake FR, O'Regan TJ. Multiple monitored electroconvulsive treatment of schizophrenia. Compr Psychiatry 1972;13(1):9–17.
[20] Goldfarb C, Goldfarb S. Multiple monitored electroconvulsive treatment. Curr Psychiatr Ther 1977;17:275–81.
[21] White RK, Shea JJ, Jonas MA. Multiple monitored electroconvulsive treatment. Am J Psychiatry 1968;125(5):622–6.
[22] Roemer RA, Dubin WR, Jaffe R, Lipschutz L, Sharon D. An efficacy study of single- versus double-seizure induction with ECT in major depression. J Clin Psychiatry 1990;51(11):473–8.
[23] Yesavage JA, Berens ES. Multiple monitored electroconvulsive therapy in the elderly. J Am Geriatr Soc 1980;28(5):206–9.
[24] Berens ES, Yesavage JA, Leirer VO. A comparison of multiple and single electroconvulsive therapy. J Clin Psychiatry 1982;43(4):126–8.
[25] Maletzky BM. Conventional and multiple-monitored electroconvulsive therapy. A comparison in major depressive episodes. J Nerv Ment Dis 1986;174(5):257–64.
[26] Association AP. The practice of ECT: recommendations for treatment, training and privileging. third ed. Washington, D.C.: American Psychiatric Press; 2024.
[27] Sackeim HA. Modern electroconvulsive therapy: vastly improved yet greatly underused. JAMA Psychiatry 2017;74(8):779–80.

[28] Sackeim HA, Prudic J, Nobler MS, Fitzsimons L, Lisanby SH, Payne N, et al. Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. Brain Stimul 2008;1(2):71–83.

[29] Weiss A, Hussain S, Ng B, Sarma S, Tiller J, Waite S, et al. Royal Australian and New Zealand college of psychiatrists professional practice guidelines for the administration of electroconvulsive therapy. Aust N Z J Psychiatr 2019;53(7):609–23.

[30] Sackeim HA, Prudic J, Devanand DP, Nobler MS, Lisanby SH, Peyser S, et al. A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. Arch Gen Psychiatry 2000;57(5):425–34.

[31] Robin A, De Tissera S. A double-blind controlled comparison of the therapeutic effects of low and high energy electroconvulsive therapies. Br J Psychiatry 1982;141:357–66.

[32] Chanpattana W, Chakrabhand ML, Buppanharun W, Sackeim HA. Effects of stimulus intensity on the efficacy of bilateral ECT in schizophrenia: a preliminary study. Biol Psychiatry 2000;48(3):222–8.

[33] Sackeim HA, Prudic J, Devanand DP, Nobler MS, Haskett RF, Mulsant BH, et al. The benefits and costs of changing treatment technique in electroconvulsive therapy due to insufficient improvement of a major depressive episode. Brain Stimul 2020;13(5):1284–95.

[34] Jelovac A, Kolshus E, McLoughlin DM. Relapse following successful electroconvulsive therapy for major depression: a meta-analysis. Neuropsychopharmacology 2013;38(12):2467–74.

[35] FDA. Magnus Neuromodulation System (MNS) with SAINT Technology. Model Number 1001K 2022.

[36] CMS. July 2024 update of the hospital Outpatient Prospective Payment System (OPPS). https://www.cms.gov/files/document/r12665cp.pdf; 2024.

[37] Chen L, Klooster DCW, Tik M, Thomas EHX, Downar J, Fitzgerald PB, et al. Accelerated repetitive transcranial magnetic stimulation to treat major depression: the past, present, and future. Harv Rev Psychiatr 2023;31(3):142–61.

[38] van Rooij SJH, Arulpragasam AR, McDonald WM, Philip NS. Accelerated TMS - moving quickly into the future of depression treatment. Neuropsychopharmacology 2024;49(1):128–37.

[39] Geoly AD, Stimpson KH, Espil FM, Bentzley BS, Williams NR. Durability of clinical benefit with Stanford Neuromodulation Therapy (SNT) in treatment-resistant depression. Brain Stimul 2025;18(3):875–81.

[40] Geoly AD, Kratter IH, Toosi P, Cole EJ, Sahlem GL, Williams NR. Sustained efficacy of Stanford Neuromodulation Therapy (SNT) in open-label repeated treatment. Am J Psychiatry 2024;181(1):71–3.

[41] Kratter IH, Austelle CW, Lissemore JI, Wada M, Geoly A, Chaiken A, et al. Stanford neuromodulation therapy for treatment-resistant depression: a randomized controlled trial confirming efficacy, and an EEG study providing insight into mechanism of action and a potentially predictive biomarker of efficacy. World Psychiatry 2026;25(1):105–16.

[42] McTeague LM. Establishing the dose-response curve for accelerated rTMS: how much stimulation is enough?. In: *6th international brain stimulation conference*. 18. Kobe, Japan: brain stimulation; 2025, P230.

[43] Taylor JJ. The AINT trial: imaging- versus scalp-targeted accelerated TMS for depression. In: *6th international brain sitmulation conference*. 18. Kobe, Japan: Brain Stimulation Journal; 2025. p. 245.

[44] Chen M, Bjorklund J, Chang KY, Burkhardt G, Bulubas L, Weller S, et al. High dosage accelerated intermittent theta burst stimulation without precision targeting and dosing in depression: an open-label pilot study. Eur Arch Psychiatr Clin Neurosci 2025.

[45] DeSouza D, Meng NF, DeGaetano NP, Nakano E, Hoang V, Nguyen T, et al. Naturalistic outcomes with fMRI-Guided and Non-fMRI-Guided accelerated TMS for depression. medRxiv 2025.

[46] Ramos MRF, Goerigk S, Aparecida da Silva V, Cavendish BA, Pinto BS, Papa CHG, et al. Accelerated theta-burst stimulation for treatment-resistant depression: a randomized clinical trial. JAMA Psychiatry 2025.

[47] Vaughn D, Marino B, Engelbertson A, Dojnov A, Stine M, Weiss N, et al. Single-day TMS regimens with pharmacological augmentation of plasticity: five cases, 4. Transcranial Magnetic Stimulation; 2025.

[48] Vaughn D, Marino B, Engelbertson A, Dojnov A, Weiss N, Vila-Rodriguez F, et al. Real-world effectiveness of a single-day regimen for transcranial magnetic stimulation using optimized, neuroplastogen-enhanced techniques in depression (ONE-D). Research Square 2025.

[49] Hanlon CA, Roth Y, Bermudes RA, Brink E, Davis M, DeBrocco D, et al. Accelerated deep TMS for depression: results from a multisite, randomized non-inferiority trial. SSRN Preprint 2026.

[50] Tendler A, Roth Y, Bates M, Brink E, Davis M, DeBrocco D, et al. Patient-reported outcomes following accelerated vs. standard TMS with the H1 coil for major depression: a multisite randomized trial. Brain Stimul 2026:103048.

[51] Hutton TM, Aaronson ST, Carpenter LL, Pages K, Krantz D, Lucas L, et al. Dosing transcranial magnetic stimulation in major depressive disorder: relations between number of treatment sessions and effectiveness in a large patient registry. Brain Stimul 2023;16(5):1510–21.

[52] Schulze L, Feffer K, Lozano C, Giacobbe P, Daskalakis ZJ, Blumberger DM, et al. Number of pulses or number of sessions? An open-label study of trajectories of improvement for once-vs. Twice-daily dorsomedial prefrontal rTMS in major depression. Brain Stimul 2018;11(2):327–36.

[53] Caulfield KA, Brown JC. The problem and potential of TMS' infinite parameter space: a targeted review and road map forward. Front Psychiatr 2022;13:867091.

[54] Cerins A, Thomas EHX, Barbour T, Taylor JJ, Siddiqi SH, Trapp N, et al. A new angle on transcranial magnetic stimulation coil orientation: a targeted narrative review. Biol Psychiatry Cogn Neurosci Neuroimaging 2024;9(8):744–53.

[55] Sackeim HA, Aaronson ST, Carpenter LL, Hutton TM, Pages K, Lucas L, et al. When to hold and when to fold: early prediction of nonresponse to transcranial magnetic stimulation in major depressive disorder. Brain Stimul 2024;17(2):272–82.

[56] Siddiqi SH, Taylor SF, Cooke D, Pascual-Leone A, George MS, Fox MD. Distinct symptom-specific treatment targets for circuit-based neuromodulation. Am J Psychiatry 2020;177(5):435–46.

[57] Taylor JJ, Lin C, Jones E, Frandsen S, Becker C, Drew W, et al. Symptom-specific brain circuit stimulation: a head-to-head randomized trial. Research Square 2025.

[58] Sackeim HA, Aaronson ST, Carpenter LL, Hutton TM, Mina M, Pages K, et al. Clinical outcomes in a large registry of patients with major depressive disorder treated with transcranial magnetic stimulation. J Affect Disord 2020;277:65–74.

[59] Hanlon CA, McCalley DM. Sex/gender as a factor that influences transcranial magnetic stimulation treatment outcome: three potential biological explanations. Front Psychiatr 2022;13:869070.

[60] McCalley DM, Cadicamo NJ, Weijerman F, Tenekedjieva LT, Alzheimer's Disease Neuroimaging I, Knutson B, et al. Females have shorter scalp-to-cortex distances and receive stronger TMS electrical fields: implications for clinical treatment. Neuropsychopharmacology 2025.

[61] Sheline YI, Makhoul W, Batzdorf AS, Nitchie FJ, Lynch KG, Cash R, et al. Accelerated intermittent theta-burst stimulation and treatment-refractory bipolar depression: a randomized clinical trial. JAMA Psychiatry 2024;81(9):936–41.

[62] Appelbaum LG, Daniels H, Lochhead L, Bacio B, Cash R, Weissman CR, et al. Accelerated intermittent theta-burst stimulation for treatment-resistant bipolar depression: a randomized clinical trial. JAMA Netw Open 2025;8(2):e2459361.

[63] Bor J, Brunelin J, Rivet A, d'Amato T, Poulet E, Saoud M, et al. Effects of theta burst stimulation on glutamate levels in a patient with negative symptoms of schizophrenia. Schizophr Res 2009;111(1–3):196–7.

[64] Brunelin J, Szekely D, Costes N, Mondino M, Bougerol T, Saoud M, et al. Theta burst stimulation in the negative symptoms of schizophrenia and striatal dopamine release. An iTBS-[11C]raclopride PET case study. Schizophr Res 2011;131(1–3):264–5.

[65] Demirtas-Tatlidede A, Freitas C, Cromer JR, Safar L, Ongur D, Stone WS, et al. Safety and proof of principle study of cerebellar vermal theta burst stimulation in refractory schizophrenia. Schizophr Res 2010;124(1–3):91–100.

[66] Brady Jr RO, Gonsalvez I, Lee I, Ongur D, Seidman LJ, Schmahmann JD, et al. Cerebellar-prefrontal network connectivity and negative symptoms in schizophrenia. Am J Psychiatry 2019;176(7):512–20.

[67] Bation R, Magnin C, Poulet E, Mondino M, Brunelin J. Intermittent theta burst stimulation for negative symptoms of schizophrenia-A double-blind, sham-controlled pilot study. npj Schizophr 2021;7(1):10.

[68] Basavaraju R, Ithal D, Thanki MV, Ramalingaiah AH, Thirthalli J, Reddy RP, et al. Intermittent theta burst stimulation of cerebellar vermis enhances fronto-cerebellar resting state functional connectivity in schizophrenia with predominant negative symptoms: a randomized controlled trial. Schizophr Res 2021;238:108–20.

[69] Chauhan P, Garg S, Tikka SK, Khattri S. Efficacy of intensive cerebellar intermittent theta burst stimulation (iCiTBS) in treatment-resistant schizophrenia: a randomized placebo-controlled study. Cerebellum 2021;20(1):116–23.

[70] Poulet E, Brunelin J, Kallel L, D'Amato T, Saoud M. Maintenance treatment with transcranial magnetic stimulation in a patient with late-onset schizophrenia. Am J Psychiatry 2008;165(4):537–8.

[71] Jardri R, Bubrovszky M, Demeulemeester M, Poulet E, Januel D, Cohen D, et al. Repetitive transcranial magnetic stimulation to treat early-onset auditory hallucinations. J Am Acad Child Adolesc Psychiatry 2012;51(9):947–9.

[72] Montagne-Larmurier A, Etard O, Razafimandimby A, Morello R, Dollfus S. Two-day treatment of auditory hallucinations by high frequency rTMS guided by cerebral imaging: a 6 month follow-up pilot study. Schizophr Res 2009;113(1):77–83.

[73] Dollfus S, Jaafari N, Guillin O, Trojak B, Plaze M, Saba G, et al. High-frequency neuronavigated rTMS in auditory verbal hallucinations: a pilot double-blind controlled study in patients with schizophrenia. Schizophr Bull 2018;44(3):505–14.

[74] Poulet E, Brunelin J, Bediou B, Bation R, Forgeard L, Dalery J, et al. Slow transcranial magnetic stimulation can rapidly reduce resistant auditory hallucinations in schizophrenia. Biol Psychiatry 2005;57(2):188–91.

[75] Kim EJ, Yeo S, Hwang I, Park JI, Cui Y, Jin HM, et al. Bilateral repetitive transcranial magnetic stimulation for auditory hallucinations in patients with schizophrenia: a randomized controlled, cross-over study. Clin Psychopharmacol Neurosci 2014;12(3):222–8.

[76] Kimura H, Kanahara N, Takase M, Yoshida T, Watanabe H, Iyo M. A randomized, sham-controlled study of high frequency rTMS for auditory hallucination in schizophrenia. Psychiatry Res 2016;241:190–4.

[77] Koops S, van Dellen E, Schutte MJ, Nieuwdorp W, Neggers SF, Sommer IE. Theta burst transcranial magnetic stimulation for auditory verbal hallucinations: negative findings from a double-blind-randomized trial. Schizophr Bull 2016;42(1):250–7.

[78] Sverak T, Mayerova M, Obdrzalkova M, Ustohal L. Accelerated repetitive transcranial magnetic stimulation in the treatment of negative symptoms of schizophrenia: an open-label study. J ECT 2022;38(2):e24–5.

[79] Han Y, Jin F, Lee J, Hou W, Yang X, Zhang Y, et al. Accelerated iTBS with a personalised targeting method to treat negative symptoms of schizophrenia: a randomized controlled trial. Brain Stimul 2025;18(3):710–9.

[80] Aquadro E, Bomer L, Webler R, Pines A, DeSouza DD, Carreon D, et al. Expedition for new symptom-specific TMS targets: protocol for the first randomized causal circuit mapping trial. Contemp Clin Trials 2025;155:107978.

[81] Pines AR, Frandsen SB, Drew W, Meyer GM, Howard C, Palm ST, et al. Mapping lesions that cause psychosis to a human brain circuit and proposed stimulation target. JAMA Psychiatry 2025;82(4):368–78.

[82] Renaud Jardri PY, Amor Zaineb, Plaze Marion, Amad Ali, Roman David, Szaffarczyk Sébastien, Lefebvre Stéphanie, Pins Delphine, Cuenca Macarena, Coudriet Guillaume, Cachia Arnaud, Labreuche Julien, Cailliau Emeline, Delmaire Christine, Outteryck Olivier, Lopes Renaud, Pruvo Jean-Pierre, Edjlali-Goujon Myriam, Oppenheim Catherine, Bubrovszky Maxime, Vaiva Guillaume, Thomas Pierre, , the MULTIMODHAL Study Group, Domenech Philippe, Leroy Arnaud. The MULTIMODHAL randomized controlled trial: fmri-based symptom capture for guiding rTMS treatment of drug-resistant hallucinations in patients with schizophrenia. medRxiv 2026.

[83] Sinanaj L, Pallis K, Dehkordi AF, Huguelet P, Kaiser S, Begue I. Mapping symptom-general and symptom-specific targets for transcranial magnetic stimulation in schizophrenia: an electric-field modeling meta-analysis. Mol Psychiatr 2025.

[84] Joseph JT, Vishwanath R, Praharaj SK. Efficacy and safety of accelerated transcranial magnetic stimulation for obsessive-compulsive disorder: a systematic review and meta-analysis. Asian J Psychiatry 2025;106:104420.

[85] Chen L, Thomas E, Jenkins L, Ho R, Francis V, Cerins A, et al. Functional connectivity-informed individualised transcranial magnetic stimulation therapy for anorexia nervosa – interim results from the FUNCTIAN pilot study. In: *6th international brain stimulation conference*. 18. Kobe, Japan: Brain Stimulation; 2025. p. 295.

[86] Woods AJ, Antal A, Bikson M, Boggio PS, Brunoni AR, Celnik P, et al. A technical guide to tDCS, and related non-invasive brain stimulation tools. Clin Neurophysiol 2016;127(2):1031–48.

[87] Truong DQ, Bikson M. Physics of transcranial direct current stimulation devices and their history. J ECT 2018;34(3):137–43.

[88] Cho H, Razza LB, Borrione L, Bikson M, Charvet L, Dennis-Tiwary TA, et al. Transcranial electrical stimulation for psychiatric disorders in adults: a primer. Focus 2022;20(1):19–31.

[89] Antal A, Bjekic J, Ganho-Avila A, Alekseichuk I, Assecondi S, Bergmann TO, et al. Low intensity transcranial electric stimulation: safety, ethical, legal regulatory and application guidelines (2017-2025: an update) - endorsed by the European Society for Brain Stimulation (ESBS) and by the International Federation for Clinical Neurophysiology (IFCN). Clin Neurophysiol 2025:2111436.

[90] Suhood AY, Summers S, Pascual-Leone A, Nitsche MA, Ziemann U, Bikson M, et al. Developing consolidated guidelines for reporting and evaluation of studies using transcranial electrical stimulation (CoRE-tES): protocol for an international Delphi study and expert consensus process. BMJ Open 2025;15(11):e108904.

[91] da Silva PHR, Vanderhasselt MA, Pilloni G, Charvet L, Padberg F, Bikson M, et al. Challenges and future directions of transcranial direct current stimulation for depression: insights from a systematic review and meta-analysis. Braz J Psychiatry 2025;47:e20243989.

[92] Brunoni AR, Ekhtiari H, Antal A, Auvichayapat P, Baeken C, Bensenor IM, et al. Digitalized transcranial electrical stimulation: a consensus statement. Clin Neurophysiol 2022;143:154–65.

[93] Bikson M, Brunoni AR, George MS. US FDA approves home-delivered tDCS for treating depression. Brain Stimul 2026;19(1):103021.

[94] Razza LB, Luethi MS, Moffa A, Aust S, Blumberger DM, Brunelin J, et al. Efficacy of transcranial direct current stimulation for depression: individual patient data meta-analysis. Br J Psychiatry 2026:1–10.

[95] Moffa AH, Martin D, Alonzo A, Bennabi D, Blumberger DM, Bensenor IM, et al. Efficacy and acceptability of transcranial direct current stimulation (tDCS) for major depressive disorder: an individual patient data meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry 2020;99:109836.

[96] Pilloni G, Woods AJ, Charvet L. No risk of skin lesion or burn with transcranial direct current stimulation (tDCS) using standardized protocols. Brain Stimul 2021;14(3):511–2.

[97] Hampstead BM, Ehmann M, Rahman-Filipiak A. Reliable use of silver chloride HD-tDCS electrodes. Brain Stimul 2020;13(4):1005–7.

[98] Monte-Silva K, Kuo MF, Hessenthaler S, Fresnoza S, Liebetanz D, Paulus W, et al. Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. Brain Stimul 2013;6(3):424–32.

[99] Khadka N, Borges H, Paneri B, Kaufman T, Nassis E, Zannou AL, et al. Adaptive current tDCS up to 4 mA. Brain Stimul 2020;13(1):69–79.

[100] Schlaug G, Cassarly C, Feld JA, Wolf SL, Rowe VT, Fritz S, et al. Safety and efficacy of transcranial direct current stimulation in addition to constraint-induced movement therapy for post-stroke motor recovery (TRANSPORT2): a phase 2, multicentre, randomised, sham-controlled triple-blind trial. Lancet Neurol 2025;24(5):400–12.

[101] Roncero C, Friedman M, Whittaker K, Popov A, Chertkow H. Administration of 4 mA tDCS to a person with progressive supranuclear palsy leads to improved walking speed. Brain Stimul 2021;14(6):1563–5.

[102] Workman CD, Fietsam AC, Rudroff T. Different effects of 2 mA and 4 mA transcranial direct current stimulation on muscle activity and torque in a maximal isokinetic fatigue task. Front Hum Neurosci 2020;14:240.

[103] Hsu G, Shereen AD, Cohen LG, Parra LC. Robust enhancement of motor sequence learning with 4 mA transcranial electric stimulation. Brain Stimul 2023;16(1):56–67.

[104] Mellin JM, Alagapan S, Lustenberger C, Lugo CE, Alexander ML, Gilmore JH, et al. Randomized trial of transcranial alternating current stimulation for treatment of auditory hallucinations in schizophrenia. Eur Psychiatry 2018;51:25–33.

[105] Ahn S, Mellin JM, Alagapan S, Alexander ML, Gilmore JH, Jarskog LF, et al. Targeting reduced neural oscillations in patients with schizophrenia by transcranial alternating current stimulation. Neuroimage 2019;186:126–36.

[106] Alexander ML, Alagapan S, Lugo CE, Mellin JM, Lustenberger C, Rubinow DR, et al. Double-blind, randomized pilot clinical trial targeting alpha oscillations with transcranial alternating current stimulation (tACS) for the treatment of major depressive disorder (MDD). Transl Psychiatry 2019;9(1):106.

[107] Gehrman PR, Bartky EJ, Travers C, Lapidus K. A fully remote randomized trial of transcranial alternating current stimulation for the acute treatment of major depressive disorder. J Clin Psychiatry 2024;85(2).

[108] Austelle CW, Cox SS, Connolly DJ, Baker Vogel B, Peng X, Wills K, et al. Accelerated transcutaneous auricular vagus nerve stimulation for inpatient depression and anxiety: the iWAVE open label pilot trial. Neuromodulation 2025;28(4):672–81.

[109] Dawson J, Liu CY, Francisco GE, Cramer SC, Wolf SL, Dixit A, et al. Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial. Lancet 2021;397(10284):1545–53.

[110] Jenkins DD, Moss HG, Adams LE, Hunt S, Dancy M, Huffman SM, et al. Higher dose noninvasive transcutaneous auricular vagus nerve stimulation increases feeding volumes and white matter microstructural complexity in open-label study of infants slated for gastrostomy tube. J Pediatr 2023;262:113563.

[111] Badran BW, Jenkins DD, DeVries WH, Dancy M, Summers PM, Mappin GM, et al. Transcutaneous auricular vagus nerve stimulation (taVNS) for improving oromotor function in newborns. Brain Stimul 2018;11(5):1198–200.

[112] Badran BW, Jenkins DD, Cook D, Thompson S, Dancy M, DeVries WH, et al. Transcutaneous auricular vagus nerve stimulation-paired rehabilitation for oromotor feeding problems in newborns: an open-label pilot study. Front Hum Neurosci 2020;14:77.

[113] Nandi T, Kop BR, Butts Pauly K, Stagg CJ, Verhagen L. The relationship between parameters and effects in transcranial ultrasonic stimulation. Brain Stimul 2024;17(6):1216–28.

[114] Yoo S, Mittelstein DR, Hurt RC, Lacroix J, Shapiro MG. Focused ultrasound excites cortical neurons via mechanosensitive calcium accumulation and ion channel amplification. Nat Commun 2022;13(1):493.

[115] Yaakub SN, White TA, Roberts J, Martin E, Verhagen L, Stagg CJ, et al. Transcranial focused ultrasound-mediated neurochemical and functional connectivity changes in deep cortical regions in humans. Nat Commun 2023;14(1):5318.

[116] Kim HC, Lee W, Weisholtz DS, Yoo SS. Transcranial focused ultrasound stimulation of cortical and thalamic somatosensory areas in human. PLoS One 2023;18(7):e0288654.

[117] Samuel N, Zeng K, Harmsen IE, Ding MYR, Darmani G, Sarica C, et al. Multi-modal investigation of transcranial ultrasound-induced neuroplasticity of the human motor cortex. Brain Stimul 2022;15(6):1337–47.

[118] Lee W, Kim H, Jung Y, Song IU, Chung YA, Yoo SS. Image-guided transcranial focused ultrasound stimulates human primary somatosensory cortex. Sci Rep 2015;5:8743.

[119] Martin E, Roberts M, Grigoras IF, Wright O, Nandi T, Rieger SW, et al. Ultrasound system for precise neuromodulation of human deep brain circuits. Nat Commun 2025;16(1):8024.

[120] Fine JM, Mysore AS, Fini ME, Tyler WJ, Santello M. Transcranial focused ultrasound to human rIFG improves response inhibition through modulation of the P300 onset latency. eLife 2023;12.

[121] Darmani G, Ramezanpour H, Sarica C, Annirood R, Grippe T, Nankoo JF, et al. Individualized non-invasive deep brain stimulation of the basal ganglia using transcranial ultrasound stimulation. Nat Commun 2025;16(1):2693.

[122] Kop BR, de Jong L, Kim BP, den Ouden HEM, Verhagen L. Parameter optimisation for mitigating somatosensory confounds during transcranial ultrasonic stimulation. Brain Stimul 2025;18(4):1224–36.

[123] Bancel T, Beranger B, Daniel M, Didier M, Santin M, Rachmilevitch I, et al. Sustained reduction of essential tremor with low-power non-thermal transcranial focused ultrasound stimulations in humans. Brain Stimul 2024;17(3):636–47.

[124] Davidson B, Xhima K, Cosgrove R, Hamani C, Eitan R, Rezai A, et al. A roadmap for focused ultrasound applications in psychiatry: proceedings of the 2024 symposium on focused ultrasound in psychiatry (FUS-PULSE). Brain Stimul 2025;18(5):1651–62.

[125] Rezai A, Thompson-Lake DGY, D'Haese PF, Meyer N, Ranjan M, Farmer D, et al. Focused ultrasound neuromodulation: exploring a novel treatment for severe opioid use disorder. Biol Psychiatry 2025;98(1):56–64.

[126] Mahoney JJ, Thompson-Lake DGY, Ranjan M, Marton JL, Carpenter JS, D'Haese PF, et al. A case report of focused ultrasound neuromodulation of the bilateral nucleus accumbens for methamphetamine use disorder. Exp Clin Psychopharmacol 2025.

[127] Zubair M Re, Rezai A, Ranjan M, Bhagwat A, et al. Brain injury during focused ultrasound neuromodulation for substance use disorder. Brain Stimul 2025;19(2):103030. Brain Stimul 2026.

[128] Rezai A, Ranjan M, Bhagwat A, Arsiwala T, Carpenter J, Schafer M, et al. Further clarification regarding brain injury during focused ultrasound neuromodulation for substance use disorder. Brain Stimul 2026;19(1):103014.
[129] Fouragnan E. Response to: brain injury during focused ultrasound neuromodulation for substance use disorder. Brain Stimul 2026;19(1):102989.
[130] Pauly KB. Letter to the editor in response to "Brain injury during focused ultrasound neuromodulation for substance use disorder". Brain Stimul 2025;18(6):2075–6.
[131] Rezai A, Ranjan M, Bhagwat A, Arsiwala T, Carpenter J, Schafer M, et al. Brain injury during focused ultrasound neuromodulation for substance use disorder. Brain Stimul 2025;18(6):2050–3.
[132] Aubry JF, Attali D, Schafer ME, Fouragnan E, Caskey CF, Chen R, et al. ITRUSST consensus on biophysical safety for transcranial ultrasound stimulation. ArXiv 2025.
[133] Francis-Taylor R, Ophel G, Martin D, Loo C. The ictal EEG in ECT: a systematic review of the relationships between ictal features, ECT technique, seizure threshold and outcomes. Brain Stimul 2020;13(6):1644–54.
[134] Peterchev AV, Rosa MA, Deng ZD, Prudic J, Lisanby SH. Electroconvulsive therapy stimulus parameters: rethinking dosage. J ECT 2010;26(3):159–74.
[135] Taylor JJ, Li J, Lin C, Jones E, Frandsen S, Becker C, et al. Symptom-specific brain circuit stimulation: a head-to-head randomized trial. PREPRINT (Version 1) available at Res Square 2024.
[136] Cash RFH, Zalesky A. Personalized and circuit-based transcranial magnetic stimulation: evidence, controversies, and opportunities. Biol Psychiatry 2024;95(6):510–22.
[137] Zimmerman M, Harris L, Martin J, McGonigal P. Reliability and validity of a self-report scale for daily assessments of the severity of depressive symptoms. Psychiatry Res 2018;270:581–6.
[138] Zimmerman M, Kiefer R, Kerr S, Balling C. Reliability and validity of a self-report scale for daily assessments of the severity of anxiety symptoms. Compr Psychiatry 2019;90:37–42.
[139] Rush AJ, Carmody TJ, Ibrahim HM, Trivedi MH, Biggs MM, Shores-Wilson K, et al. Comparison of self-report and clinician ratings on two inventories of depressive symptomatology. Psychiatr Serv 2006;57(6):829–37.
[140] Targum SD, Sauder C, Evans M, Saber JN, Harvey PD. Ecological momentary assessment as a measurement tool in depression trials. J Psychiatr Res 2021;136:256–64.
[141] Sequeira L, Perrotta S, LaGrassa J, Merikangas K, Kreindler D, Kundur D, et al. Mobile and wearable technology for monitoring depressive symptoms in children and adolescents: a scoping review. J Affect Disord 2020;265:314–24.
[142] Sack AT, Paneva J, Kuthe T, Dijkstra E, Zwienenberg L, Arns M, et al. Target engagement and brain state dependence of transcranial magnetic stimulation: implications for clinical practice. Biol Psychiatry 2024;95(6):536–44.
[143] Sohn MN, Brown JC, Sharma P, Ziemann U, McGirr A. Pharmacological adjuncts and transcranial magnetic stimulation-induced synaptic plasticity: a systematic review. J Psychiatry Neurosci 2024;49(1):E59–76.
[144] Hummel FC, Cohen LG. Non-invasive brain stimulation: a new strategy to improve neurorehabilitation after stroke? Lancet Neurol 2006;5(8):708–12.
[145] Elsner B, Kugler J, Mehrholz J. Transcranial direct current stimulation (tDCS) for improving aphasia after stroke: a systematic review with network meta-analysis of randomized controlled trials. J NeuroEng Rehabil 2020;17(1):88.
[146] Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT(1B/1D) agonists) in acute migraine treatment: a meta-analysis of 53 trials. Lancet 2001;358(9294):1668–75.
[147] Sackeim HA. Acute continuation and maintenance treatment of major depressive episodes with transcranial magnetic stimulation. Brain Stimul 2016;9(3):313–9.
[148] Goadsby PJ, Lipton RB, Ferrari MD. Migraine–current understanding and treatment. N Engl J Med 2002;346(4):257–70.
[149] Reddel HK, Bateman ED, Becker A, Boulet LP, Cruz AA, Drazen JM, et al. A summary of the new GINA strategy: a roadmap to asthma control. Eur Respir J 2015;46(3):622–39.
[150] Rossi S, Antal A, Bestmann S, Bikson M, Brewer C, Brockmoller J, et al. Safety and recommendations for TMS use in healthy subjects and patient pop- ulations, with updates on training, ethical and regulatory issues: Expert guidelines. Clinical neurophysiology. 2020.
[151] Trapp NT, Purgianto A, Taylor JJ, Singh MK, Oberman LM, Mickey BJ, et al. Consensus review and considerations on TMS to treat depression: a comprehensive update endorsed by the national network of depression centers, the clinical TMS society, and the international Federation of clinical neurophysiology. Clin Neurophysiol 2024;170:206–33.
[152] Blyth SH, Haq R, Menon S, King B, Torres Quesada G, Borodge D, et al. Evidence for safety and tolerability of transcranial magnetic stimulation for substance use disorders. Brain Stimul 2025;18(6):2043–9.