Consensus Recommendations for rTMS in Depression: Not Entirely Correct!

To the Editor: The recently published consensus recommendations[1] on use of transcranial magnetic stimulation (TMS) for treating depression are very thorough and the most comprehensive recommendations published to date. However, there were several points that should not be accepted into guidelines.

First, there is no evidence that adding pharmacotherapy to TMS improves response and remission rates. A study of active TMS + placebo medication, active TMS + active medication, sham TMS + active medication, and sham TMS + placebo medication has not been done yet.

Second, the article states (in the section Evidence Basis for Antidepressant Efficacy) that 21% of subjects in the H1-coil multicenter trial[2] failed 3 or more medications in the current trial (second-stratum group). In fact, 41.5% of the patients failed 3 or more medications in the current episode.[2]

Third, in the same section, the article compares the H-coil second-stratum group to Sequenced Treatment Alternatives to Relieve Depression (STAR*D) steps/levels 3 and 4, while in fact only level 4 is comparable to the H1-coil second-stratum group (patients in both failed 3 or more medications in the current episode). Moreover, the 28.9% remission rate in the second-stratum group with the H1-coil occurred in the context of a double-blind antidepressant-free study, while the 13% remission rate for STAR*D step 4 was in an open-label study, a design in which patients typically have higher response and remission rates.[3]

Fourth, there is no evidence for any role of a physical examination component to evaluate the medical safety of rTMS. Every clinical trial for TMS included a physical examination component at baseline and endpoint, and none reported any significant findings. While our colleagues in primary care are eliminating more and more screening physical examination components that lack evidence, we should not add physical examinations to the treatment of depression patients.

Fifth, informed consent is a process and not a form, and the process should not differ between pharmacologic or TMS treatments. The potential for serious side effects from medications is much greater than from TMS, and there is no need for a consent form for medications or TMS separate from a general consent for treatment. Rather, there should be documentation of a risk-benefit conversation with the individual patient. There are advantages to an informed consent form, in that it simplifies the documentation, but there is no advantage to signing a consent form a second time for a second treatment course.

Sixth, confirmation or redetermination of the motor threshold (MT) in patients on medications should probably be done by the operators on a daily basis. The most likely cause of a TMS-induced seizure is a change in cortical excitability, measured as the resting MT. The most likely culprit for MT changes is medication (a change in intake, absorption, or metabolism).

Seventh, patients with implanted vagal nerve stimulation devices (or other conductive metal in the neck) can be treated with rTMS with no safety concerns.[4,5] Regardless of the coil, there is no magnetic field or induced electrical field that reaches the neck.[6,7]

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Dr McClintock and Colleagues Reply

To the Editor: We appreciate the interest of Drs Tendler and Gersner in our recent consensus recommendations for the clinical application of repetitive transcranial magnetic stimulation (rTMS) in the treatment of depression.[1] They raise 7 points about the consensus recommendations. Regarding their first point about combining rTMS with medication, we clarify that while published data suggest that the combination of rTMS and current pharmacotherapy is safe,[2] there is no randomized controlled evidence at present that the combination, relative to rTMS alone, would confer greater response and remission rates.

Regarding their second and third points about the antidepressant treatment resistance level that characterized the sample in the industry-sponsored H1-coil randomized controlled clinical trial,[3] we note that Table 1 in the published report by Levkovitz et al indicated that 21.8% and 20.7% of participants in the active deep-TMS and sham groups, respectively, failed 3 or more medications.[3] Drs Tendler and Gersner suggest that participants from the Levkovitz et al[3] study were comparable to patients treated in step 4 of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study.[4] While open-label and randomized controlled clinical trials may generate different clinical outcomes, we maintain that the Levkovitz et al[3] study sample may be comparable to STAR*D patients in either step 3 or step 4 since many patients in step 1 of the STAR*D study (n = 3,057) had received prior treatment for their current depressive episode before entering the study.[5]

Regarding the fourth point, Drs Tendler and Gersner object to the recommendation for physical examination in rTMS patient care. However, the American Psychiatric Association (APA) Practice Guideline for the Treatment of Patients With Major Depressive Disorder[6] indicated that pretreatment evaluation should include identification of medical disorders that may contribute to the patient's presentation or complicate care. Moreover, the APA Practice Guideline[6] further recommended coordination of care between the psychiatrist and other health professionals, such as a primary care provider, who may be performing physical examinations. Thus, we recommend that a targeted physical examination (either newly conducted or previously conducted and documented in the medical record) be a component of the pre-rTMS treatment evaluation to provide the prescribing clinician with, in addition to the medical history, sufficient knowledge to make informed medical decisions and ensure medical safety and necessity of rTMS.[7,8]

We agree with their fifth point that informed consent is a process and not a form, and we recommend that the informed consent process be documented, which includes the written informed consent form. Moreover, informed consent is part of standard clinical care,[9] and we clarify that reconsenting is necessary when there has been a change in treatment protocol, risks, or benefits related to rTMS antidepressant treatment.[10]

In their sixth point, Drs Tendler and Gersner note that the patient's motor threshold should be assessed on a daily basis. We disagree with daily checking of the motor threshold, as there is only 1 study of this[11] and otherwise little evidence to suggest that the motor threshold is unstable over a standard rTMS treatment course (eg, 4–6 weeks). Rather, we recommend that the motor threshold be established before starting rTMS and rechecked if there has been a clinical event or change in medication that could alter the seizure threshold.

To their seventh point, we disagree that "patients with implanted vagal nerve stimulation devices…can be treated with rTMS with no safety concerns." While it is generally safe to use rTMS in patients treated with VNS as long as the TMS coil is not activated near the implanted VNS device and leads,[12,13] we recommend caution given the limited safety data and coordination with clinicians experienced in the application of VNS therapy to review contraindications to rTMS and/or to monitor the functioning of the VNS device.

It has been almost a decade since the US Food and Drug Administration cleared rTMS for the treatment of depression in adults. Over that time period, the clinical use of rTMS has increased, and, as the letter by Drs Tendler and Gersner points out, the practice of rTMS is in clear need of consensus guidelines to standardize quality, evidence based, clinical care. We appreciate the comments by Drs Tendler and Gersner as they highlight a number of practical issues that clinicians may have with varying standards of care, and we hope our consensus recommendations will serve as a vehicle to advance and inform these discussions.

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