



Transcranial Magnetic Stimulation for Major Depressive Disorder

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Definitions

1. **Transcranial magnetic stimulation (TMS)** — also referred to as repetitive transcranial magnetic stimulation (rTMS) when repeated — is an evolving non-invasive brain stimulation technique that utilizes briefly pulsed electromagnetic fields to induce electrical currents in the cerebral cortex. The treatment is currently being investigated for treatment-resistant depression in individuals diagnosed with major depressive disorder (MDD) of the non-psychotic type.
2. **Patient Health Questionnaire-9 (PHQ-9)** — a screening tool for depression; scoring is based on responses to the below problems, in combination with occurrence-frequency and the number of days:
 - a. Little interest or pleasure in doing things
 - b. Feeling down, depressed, or hopeless
 - c. Trouble falling or staying asleep, or sleeping too much
 - d. Feeling tired or having little energy
 - e. Poor appetite or overeating
 - f. Feeling bad about yourself — or that you are a failure or have let yourself or your family down
 - g. Trouble concentrating on things, such as reading the newspaper or watching television
 - h. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual
 - i. Thoughts that you would be better off dead or of hurting yourself in some way

PHQ-9 Depression Severity Scoring*

Score	Depression Severity	Proposed Treatment Actions
0 – 4	None-minimal	None
5 – 9	Mild	Watchful waiting; repeat PHQ-9 at follow-up
10 – 14	Moderate	Treatment plan, considering counseling, follow-up and/or pharmacotherapy
15 – 19	Moderately Severe	Active treatment with pharmacotherapy and/or psychotherapy
20 – 27	Severe	Immediate initiation of pharmacotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management

* PHQ-9 is adapted from PRIME_MD Today, developed by Spitzer, Williams, Kroenke and colleagues, Copyright 1999, by Pfizer, Inc. All rights reserved. Reproduction permitted for the purposes of clinical care and research only.

Guideline

Adult members diagnosed with MDD without psychoses are eligible for TMS as a treatment of last-resort when administered by a licensed psychiatrist, and when all of the following criteria are met during the same episode of illness:

1. Moderate–severe depression (PHQ-9 score > 15).
2. Failure of pharmacotherapy (concurrent with psychotherapy); both a and b must be met:*
 - a. Drug trials consisting of both:
 - i. ≥ 4 antidepressants
 - ii. ≥ 2 different classes
 - b. Psychotherapy; either modality tried:
 - i. Cognitive behavioral
 - ii. interpersonal

*For protocol guidance; see Appendix — [Modified Antidepressant Treatment History Form \(ATHF\)](#)

Treatment Course*

TMS (Left dorsolateral; ≥5Hz; ≥ 100% motor threshold; ≥ 1600 pulses per session)

1. < 10 Sessions
2. 10–14 Sessions
3. 15–19 Sessions
4. ≥20 Sessions

* An acute course may consist of 30–60 min sessions over a 5-day period. Treatment response defined as a ≥ 50% drop from baseline depression scores with remission occurring when the member achieves a PHQ-9 score of < 9.

Limitations/Exclusions

1. Alternate brain stimulation technologies such as vagus nerve stimulation; an invasive technology being investigated for depression, are not considered medically necessary for depression.

2. TMS is not considered medically necessary if the above criteria are not met or when any of the following are applicable:
 - a. Presence of degenerative neurologic conditions (e.g., dementia, multiple sclerosis, Parkinson’s disease, etc.).
 - b. Active current substance use.
 - c. Presence of cranial implants consisting of metallic materials, which may be sensitive to magnetics (e.g., aneurysm clips, bullet fragments, coil stents, cochlear implants, electrodes/stimulators, etc.).
 - d. Presence of severe cardiovascular disease.
 - e. Utilized as on-going maintenance therapy.

Applicable Procedure Codes

90867	Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; initial, including cortical mapping, motor threshold determination, delivery and management
90868	Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent delivery and management, per session
90869	Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment; subsequent motor threshold re-determination with delivery and management

Applicable ICD-10 Codes

F32.2	Major depressive disorder, single episode, severe without psychotic features
F33.2	Major depressive disorder, recurrent severe without psychotic features

References

- Advanced Interventions. Antidepressant Treatment History Form. 2018. <http://www.advancedinterventions.org.uk/index.php/tools/athf.html>. April 2009. Accessed **June 12, 2018**.
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- Specialty-matched clinical peer review.

Appendix — Criteria for Rating Medication Trials for Antidepressant Failure

(Guidance available at <http://www.advancedinterventions.org.uk/index.php/tools/athf.html>)

1. TCA/Heterocyclics

A. Amitriptyline (Elavil, Endep), imipramine (Tofranil), desipramine (Norpramin, Pertofrane), trimipramine (Surmontil), clomipramine (Anafranil), maprotiline (Ludomil), doxepin (Sinequan, Adapin), nomifensine.

By dosage:

- a. Any drug < 4 wks or any drug <100 mg/day
- b. 4 wks or more and 100-199 mg/day
- c. 4 wks or more and 200-299 mg/day
- d. 4 wks or more and 300 mg/day or greater

By blood level: imipramine and desipramine only; levels take precedence

- a. 4 wks or more and DMI level 125 ng/ml
- b. 4 wks or more and IMI + DMI 225 ng/ml

B. Nortriptyline (Pamelor, Aventyl)

By blood level (blood levels take precedence):

- a. NT < 4 wks
- b. 4 wks or more and level < 50 ng/ml
- c. 4 wks or more and level 50-99 ng/ml
- d. 4 wks or more and level 100-150 ng/ml

By dosage:

- a. NT < 4 wks OR 4 wks or more dosage < 50 mg/day
- b. 4 wks or more and dosage 50-75 mg/day
- c. 4 wks or more and dosage 76-100 mg/day
- d. 4 wks or more and dosage >100

C. Protriptyline (Vivactil)

- a. drug < 4 wks or 4 wks or more and dosage < 30 mg/day
- b. 4 wks or more and dosage 31-40 mg/day
- c. 4 wks or more and dosage 41-60 mg/day
- d. 4 wks or more and dosage > 60 mg/day

NOTES:

For TCA-MAOI combinations: score each agent alone, as a separate trial.

For TCA-paroxetine/fluoxetine combination trials: after one week on 20 mg of paroxetine or fluoxetine the dosage equivalent of the TCA should be doubled to determine resistance rating.

II. Selective Serotonin Reuptake Inhibitors (SSRIs)

A. Fluoxetine (Prozac)

- a. drug < 4 wks or 4 wks or more and dosage 1-9 mg/day
- b. 4 wks or more and dosage 10-19 mg/day
- c. 4 wks or more and dosage 20-39 mg/day
- d. 4 wks or more and dosage 40 mg/day

B. Fluvoxamine (Luvox)

- a. drug < 4 wks or drug < 100 mg/day
- b. 4 wks or more and dosage 100-199 mg/day
- c. 4 wks or more and dosage 200-299 mg/day
- d. 4 wks or more and dosage 300 mg/day or greater

Please document both, but only one paroxetine trial (Paxil or Paxil CR) can count as an adequate therapy, not both.

C1. Paroxetine (Paxil/ Seroxat)

- a. drug < 4 wks or 4 wks or more and dosage <1-9 mg/day
- b. 4 wks or more and dosage 10-19 mg/day
- c. 4 wks or more and dosage 20-29 mg/day
- d. 4 wks or more and dosage 30 mg/day

C2. Paroxetine CR (Paxil CR)

- a. drug < 4 wks or 4 wks or more and dosage <12.5 mg/day
- b. 4 wks or more and dosage 12.5 mg/day
- c. 4 wks or more and dosage 25-50 mg/day
- d. 4 wks or more and dosage 62.5 mg/day

D. Sertraline (Zoloft)

- a. drug <4 wks or 4 wks or more and dosage < 50 mg/day
- b. 4 wks or more and dosage 50-99 mg/day
- c. 4 wks or more and dosage 100-199 mg/day
- d. 4 wks or more and dosage 200 mg/day

E. Citalopram (Celexa)

- a. drug < 4 wks or 4 wks or more and dosage 1-9 mg/day
- b. 4 wks or more and dosage 10-19 mg/day
- c. 4 wks or more and dosage 20-39 mg/day
- d. 4 wks or more and dosage 40 mg/day

F. Escitalopram (Lexapro)

- a. drug < 4 wks or 4 wks or more and dosage 1-4 mg/day
- b. 4 wks or more and dosage 5-9 mg/day
- c. 4 wks or more and dosage 10-19 mg/day
- d. 4 wks or more and dosage 20 mg/day

III. Selective Serotonin and Norepinephrine Reuptake Inhibitors (SSNRI)

A. Duloxetine (Cymbalta)

- a. drug < 4 wks or 4 wks or more and dosage < 30 mg/day
- b. 4 wks or more and dosage 30-39 mg/day
- c. 4 wks or more and dosage 40-59 mg/day
- d. 4 wks or more and dosage 60 mg/day

B. Venlafaxine (Effexor and Effexor XL)

- a. drug < 4 wks or 4 wks or more and dosage < 75 mg/day
- b. 4 wks or more and dosage 75-224 mg/day
- c. 4 wks or more and dosage 225-374 mg/day
- d. 4 wks or more and dosage 375 mg/day

IV. Monoamine Oxidase Inhibitors (MAOIs)

A. Phenelzine (Nardil)

- a. drug < 4 wks or 4 wks or more and dosage < 30 mg/day
- b. 4 wks or more and dosage 31-60 mg/day
- c. 4 wks or more and dosage 61-90 mg/day
- d. 4 wks or more and dosage 91 mg/day

B. Moclobemide (Manerix)

- a. drug < 4 wks or 4 wks or more and dosage < 150 mg/day
- b. 4 wks or more and dosage 150-299 mg/day (100-200=30 Nardil)
- c. 4 wks or more and dosage 300-599 mg/day (300=60 Nardil)
- d. 4 wks or more and dosage 600 mg/day (600=90 Nardil)

C. Selegiline (Eldepryl)

- a. drug < 4 wks or 4 wks or more and dosage < 20 mg/day
- b. 4 wks or more and dosage 21-40 mg/day
- c. 4 wks or more and dosage 41-59 mg/day
- d. 4 wks or more and dosage 60 mg/day

D. Tranylcypromine (Parnate), Isocarboxazid (Marplan)

- a. drug < 4 wks or 4 wks or more and dosage < 20 mg/day
- b. 4 wks or more and dosage 21-40 mg/day
- c. 4 wks or more and dosage 41-60 mg/day

- d. 4 wks or more and dosage 61 mg/day

NOTES:

MAOI inhibition: 80 percent inhibition will rate 4.

For TCA-MAOI combinations: score each agent considered alone.

TCA/SSRI and any other combinations (e.g. , SSRI/bupropion) should be treated as TCA/MAOI combinations: rate each medication separately.

V. Other Antidepressants

A. Bupropion (Wellbutrin)

- a. drug < 4 wks or 4 wks or more and dosage < 150 mg/day
- b. 4 wks or more and dosage 150-299 mg/day
- c. 4 wks or more and dosage 300-449 mg/day
- d. 4 wks or more and dosage 450 mg/day

B. Mirtazapine (Zispin)

- a. drug < 4 wks or 4 wks or more and dosage < 15 mg/day
- b. 4 wks or more and dosage 15-29 mg/day
- c. 4 wks or more and dosage 30-44 mg/day
- d. 4 wks or more and dosage 45 mg/day

C. Nefazodone (Serzone)

- a. drug < 4 wks or 4 wks or more and dosage < 150 mg/day
- b. 4 wks or more and dosage 150-299 mg/day
- c. 4 wks or more and dosage 300-599 mg/day
- d. 4 wks or more and dosage 600 mg/day

D. Trazodone (Desyrel), Amoxapine (Asendin)

- a. drug < 4 wks or 4 wks or more and dosage < 200 mg/day
- b. 4 wks or more and dosage 200-399 mg/day
- c. 4 wks or more and dosage 400-599 mg/day
- d. 4 wks or more and dosage 600 mg/day

E. Reboxetine (Vestra)

- a. drug < 4 wks or 4 wks or more and dosage < 4 mg/day
- b. 4 wks or more and dosage 4-7 mg/day
- c. 4 wks or more and dosage 8 mg/day
- d. 4 wks or more and dosage 8 mg/day

VI. ECT

A. Unilateral or unknown ECT

- a. 1-3 ECT
- b. 4-6 ECT
- c. 7-9 ECT
- d. 10-12 ECT
- e. 13 or more ECT

B. Bilateral ECT

- a. 1-3 Bilateral ECT
- b. 4-6 Bilateral ECT
- c. 7-9 Bilateral ECT
- d. 10 or more Bilateral ECT

NOTES:

A point is added to an ECT trial if the patient has had 7 adequate bilateral treatments. The highest rating is a 5.

If ECT and antidepressant medications are given simultaneously, this does not constitute a combination/augmentation trial. Each should be rated separately.

VIII. Augmentation Therapies

A. Lithium alone for MDD (For bipolar patients: levels take precedence over dosage)

By blood level:

- a. drug <4 wks or 4 wks or more and level < 0.4 mEq/L

- b. 4 wks or more and level 0.41-0.6 mEq/L
- c. 4 wks or more and level > 0.6 mEq/L

By dosage:

- a. drug <4 wks or 4 wks or more and dosage < 600 mg/day
- b. 4 wks or more and dosage 600-899 mg/day
- c. 4 wks or more and dosage 900 mg/day

Unipolar patients can receive a maximum rating of 2 for Li alone

B. Lithium as an augmenting agent

- d. antidepressant drugs I - IX rated level 3 and Li for at least 2 wks or CBZ rated level 3 and Li for at least 2 wks
- e. antidepressant drugs I-IX rated level 4 and Li for at least 2 wks

C. Carbamazepine (Tegretol) (For bipolar patients: levels take precedence over dosage)

By blood level:

- a. drug < 4 wks or 4 wks or more and level < 6
- b. 4 wks or more and level 6-7.9
- c. 4 wks or more and level 8 or more

By dosage:

- a. drug < 4 wks or 4 wks or more dosage < 400 mg/day
- b. 4 wks or more and dosage 400 – 999 mg/day
- c. 4 wks or more and dosage 1000 mg/day

Unipolar patients can receive a maximum rating of 2 for CBZ alone.

B. Lamotrigine (Lamictal)

For bipolar patients:

- a. drug < 4 wks or 4 wks or more dosage < 150 mg/day
- b. 4 wks or more and dosage 150 – 299 mg/day
- c. 4 wks or more and dosage 300 mg/day

C. Thyroid Hormone

- a. drug < 4 wks
- b. drug > 4 wks and dosage <25 mcg/day
- c. drug > 4 wks and dosage 25-49 mcg/day
- d. drug > 4 wks and dosage ≥50 mcg/day

IX. Benzodiazepines

A. Alprazolam (Xanax)

- a. alprazolam < 4 wks or 4 wks or more and dosage < 6 mg/day
- b. 4 wks or more and dosage 6 mg/day or greater

B. Other benzodiazepines (These drugs are not considered augmenting agents)

- a. any dosage for any duration

X. Miscellaneous

A. Stimulants, e.g., D-amphetamine (Dexedrine), methylphenidate (Ritalin), pemoline (Cylert) (These drugs are not considered augmenting agents)

- a. any dosage for any duration

B. Antipsychotics (These drugs are not considered augmenting agents)

- a. any dosage for any duration

C. Antipsychotics

- a. when used in nonpsychotic patients, should be rated together into one continuous trial, no matter how many different neuroleptics were given.

D. Clonidine (Catapres), L-tryptophan, thyroid hormones (Cytomel, Synthroid, etc.) estrogen, fenfluramine (These drugs are not considered augmenting agents)

- 0 any dosage for any duration

E. Sedatives (buspirone, zolpidem, lorazepam, clonazepam, and Benadryl). If the patient uses different sedatives, with the exception of alprazolam, they should be rated as one continuous trial.

- a. any dosage for any duration when used as a psychotropic

F. Phototherapy

- a. In any form

XI. Psychotherapy

A. Cognitive Behavioural Therapy (CBT)

- a. 1 < 4 visits
- b. 2 4-11 visits
- c. 3 12-15 visits
- d. 4 16 or more visits

B. Interpersonal Therapy (IPT)

- a. 1 < 4 visits
- b. 2 4-11 visits
- c. 3 12-15 visits
- d. 4 16 or more visits

C. Behavioural Activation Therapy

- a. 1 < 4 visits
- b. 2 4-11 visits
- c. 3 12-15 visits
- d. 4 16 or more visits