

This bibliography provides citations for key studies associated with NeuroStar Advanced Therapy. Neuronetics, Inc. does not have the copyright to provide the actual hard copies of these studies.

Foundational Studies for FDA Clearance – Major Depressive Disorder (MDD):

1. *O'Reardon JP, Solvason HB, Janicak PG, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. *Biol Psychiatry*. 2007;62(11):1208-1216. doi:10.1016/j.biopsych.2007.01.018
O'Reardon et al 2007 - PubMed (nih.gov)
2. *Avery DH, Isenberg KE, Sampson SM, et al. Transcranial magnetic stimulation in the acute treatment of major depressive disorder: clinical response in an open-label extension trial. *J Clin Psychiatry*. 2008;69(3):441-451. doi:10.4088/jcp.v69n0315
Avery et al 2008 - PubMed (nih.gov)
3. *Janicak PG, Nahas Z, Lisanby SH, et al. Durability of clinical benefit with transcranial magnetic stimulation (TMS) in the treatment of pharmacoresistant major depression: assessment of relapse during a 6-month, multisite, open-label study. *Brain Stimul*. 2010;3(4):187-199. doi:10.1016/j.brs.2010.07.003
Janicak et al 2010 - PubMed (nih.gov)
4. *Janicak PG, O'Reardon JP, Sampson SM, et al. Transcranial magnetic stimulation in the treatment of major depressive disorder: a comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction treatment. *J Clin Psychiatry*. 2008;69(2):222-232. doi:10.4088/jcp.v69n0208
Janicak et al 2008 - PubMed (nih.gov)
5. Janicak PG, Dunner DL, Aaronson ST, et al. Transcranial magnetic stimulation (TMS) for major depression: a multisite, naturalistic, observational study of quality of life outcome measures in clinical practice. *CNS Spectr*. 2013;18(6):322-332. doi:10.1017/S1092852913000357
Janicak et al 2013 - PubMed (nih.gov)

Non-Industry NIMH Sponsored MDD Study – Validated the NNI Foundation Studies:

6. George MS, Lisanby SH, Avery D, et al. Daily left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: a sham-controlled randomized trial. *Arch Gen Psychiatry*. 2010;67(5):507-516. doi:10.1001/archgenpsychiatry.2010.46
George et al 2010 - PubMed (nih.gov)

NNI Long-Term Durability Data:

7. *Carpenter LL, Janicak PG, Aaronson ST, Boyadjis T, Brock DG, Cook IA, Dunner DL, Lanocha K, Solvason HB, Demitrack MA. Transcranial magnetic stimulation (TMS) for major depression: a multisite, naturalistic, observational study of acute treatment



outcomes in clinical practice. *Depress Anxiety*. 2012 Jul;29(7):587-96. doi: 10.1002/da.21969. Epub 2012 Jun 11. PMID: 22689344.

[Carpenter et al 2012 - PubMed \(nih.gov\)](#)

8. *Dunner DL, Aaronson ST, Sackeim HA, et al. A multisite, naturalistic, observational study of transcranial magnetic stimulation for patients with pharmacoresistant major depressive disorder: durability of benefit over a 1-year follow-up period. *J Clin Psychiatry*. 2014;75(12):1394-1401. doi:10.4088/JCP.13m08977 | **Free Article**
[Dunner et al 2014 - PubMed \(nih.gov\)](#)

NNI Outcomes Registry Data:

9. Sackeim HA, Aaronson ST, Carpenter LL, 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. doi:10.1016/j.jad.2020.08.005 | **Free Article**
[Sackeim et al 2020 - PubMed \(nih.gov\)](#)
10. Aaronson ST, Carpenter LL, Hutton TM, et al. Comparison of clinical outcomes with left unilateral and sequential bilateral Transcranial Magnetic Stimulation (TMS) treatment of major depressive disorder in a large patient registry. *Brain Stimul*. 2022;15(2):326-336. doi:10.1016/j.brs.2022.01.006 | **Free Article**
[Aaronson et al 2022 - PubMed \(nih.gov\)](#)
11. Hutton TM, Aaronson ST, Carpenter LL, Pages K, Krantz D, Lucas L, Chen B, Sackeim HA. Dosing transcranial magnetic stimulation in major depressive disorder: Relations between number of treatment sessions and effectiveness in a large patient registry. *Brain Stimul*. 2023 Sep-Oct;16(5):1510-1521. doi: 10.1016/j.brs.2023.10.001. Epub 2023 Oct 11. PMID: 37827360. | **Free Article**
[Hutton et al 2023a - PubMed \(nih.gov\)](#)

* Indicates that article includes key Safety Information

NNI Additional Indication Studies:

Dash vs Standard

12. Carpenter L, Aaronson S, Hutton TM, et al. Comparison of clinical outcomes with two Transcranial Magnetic Stimulation treatment protocols for major depressive disorder. *Brain Stimul*. 2021;14(1):173-180. doi:10.1016/j.brs.2020.12.003
[Carpenter et al 2021 - PubMed \(nih.gov\)](#)

Anxious Depression:

13. Hutton TM, Aaronson ST, Carpenter LL, et al. The Anxiolytic and Antidepressant Effects of Transcranial Magnetic Stimulation in Patients With Anxious Depression. *J Clin*



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Psychiatry. 2023;84(1):22m14571. Published 2023 Jan 11. doi:10.4088/JCP.22m14571 |
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Hutton et al 2023b - PubMed (nih.gov)

Obsessive Compulsive Disorder (OCD):

Neuronetics received clearance for the treatment of OCD through a 510(k) using a predicate device. The initial study that was used to obtain clearance for the predicate device was:

14. Carmi L, Tendler A, Bystritsky A, et al. Efficacy and Safety of Deep Transcranial Magnetic Stimulation for Obsessive-Compulsive Disorder: A Prospective Multicenter Randomized Double-Blind Placebo-Controlled Trial. *Am J Psychiatry*. 2019;176(11):931-938. doi:10.1176/appi.ajp.2019.18101180
Carmi et al 2019 - PubMed (nih.gov)

Theta Burst:

Neuronetics received clearance for the Theta Burst protocol through a 510(k) using a predicate device. The initial study that was used to obtain clearance for the predicate device was:

15. Blumberger DM, Vila-Rodriguez F, Thorpe KE, et al. Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial [published correction appears in Lancet. 2018 Jun 23;391(10139):e24]. *Lancet*. 2018;391(10131):1683-1692. doi:10.1016/S0140-6736(18)30295-2
Blumberger et al 2018 - PubMed (nih.gov)



Major Depressive Disorder

Efficacy



- ◆ **Clinical outcomes in a large registry of patients with major depressive disorder treated with Transcranial Magnetic Stimulation (Sackeim et. al 2020)**

- 83% Response, 62% Remission
- 5010 patients in real-world registry



- ◆ **Dosing transcranial magnetic stimulation in major depressive disorder: Relations between number of treatment sessions and effectiveness in a large patient registry (Hutton et. al 2023)**

- strong relations between the number of TMS sessions in a course and the magnitude of symptom reduction
- courses less than 30 sessions are associated with diminished benefit
- meaningful benefit accrues with treatment beyond 36 sessions

Durability



- ◆ **A Multisite, Naturalistic, Observational Study of Transcranial Magnetic Stimulation for Patients With Pharmacoresistant Major Depressive Disorder: Durability of Benefit Over a 1-Year Follow-Up Period (Dunner et. al 2014)**

- 2 out of 3 patients maintained treatment benefit over the following 12 months

Safety



- ◆ **Seizure risk with repetitive TMS: Survey results from over a half-million treatment sessions (Taylor et. al 2021)**

- NeuroStar Seizure Rate
 - 0.03 seizures per 10,000 sessions (0.0003%)
 - 0.06 seizures per 1000 patients (0.006%)



- ◆ **Transcranial Magnetic Stimulation in the treatment of major depression: A comprehensive summary of safety experience from acute exposure, extended exposure, and during reintroduction treatment (Janicak et. al 2008)**

- The most common adverse event was localized pain or discomfort at or near the treatment site.
 - This was considered mild to moderate and diminished greatly after the first week of treatment.

Standard vs. Dash Protocol



- ◆ **Comparison of clinical outcomes with two Transcranial Magnetic Stimulation treatment protocols for major depressive disorder (Carpenter et. al 2021)**
 - Both protocols are equally effective
 - Reducing interval from 26sec to 11sec has no impact on efficacy

Unilateral (L only) vs. Bilateral (L + R) Stimulation



- ◆ **Comparison of clinical outcomes with left unilateral and sequential-bilateral Transcranial Magnetic Stimulation (TMS) treatment of major depressive disorder in a large patient registry (Aaronson et. al 2022)**
 - Left unilateral TMS consistently had superior outcomes to L+R bilateral TMS

Theta Burst



- ◆ **Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial (Blumberger et. al 2018)**
 - Theta-burst was noninferior to 10 Hz rTMS in efficacy

Anxious Depression



- ◆ **The Anxiolytic and Antidepressant Effects of Transcranial Magnetic Stimulation in Patients With Anxious Depression (Hutton et. al 2023)**
 - MDD patients experienced an average of >50% reduction in GAD-7 scores
 - Change in depression & anxiety scores highly correlated

Obsessive-Compulsive Disorder



- ◆ **Efficacy and Safety of Deep Transcranial Magnetic Stimulation for Obsessive-Compulsive Disorder: A Prospective Multicenter Randomized Double-Blind Placebo-Controlled Trial (Carmi et. al 2019)**
 - 38% response rate

Original Clinical Trial Publications



- ◆ **Efficacy and safety of Transcranial Magnetic Stimulation in the acute treatment of major depression: A multisite randomized controlled trial. (O'Reardon et. al 2007)**
- ◆ **Daily Left Prefrontal Transcranial magnetic Stimulation Therapy for Major Depressive Disorder: A Sham-Controlled Randomized Trial. (George et. al 2010)**
- ◆ **Transcranial Magnetic Stimulation (TMS) for Major Depression: A Multisite, Naturalistic, Observational Study of Acute Treatment Outcomes in Clinical Practice. (Carpenter et. al 2012)**