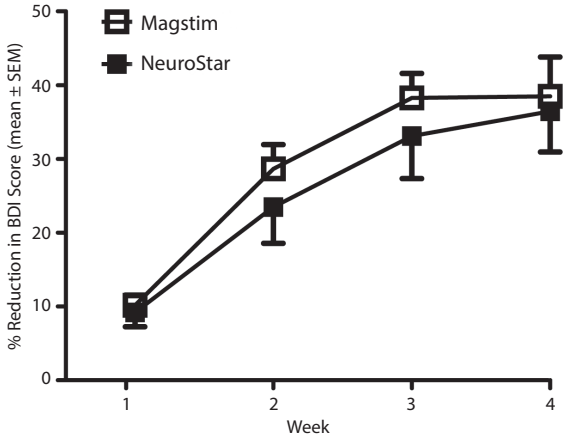
Comparative Efficacy of Repetitive Transcranial Magnetic Stimulation for Treatment of Depression Using 2 Different Stimulation Devices: A Retrospective Open-Label Study

To the Editor: Major depressive disorder (MDD) is a common disorder in which resistance to treatment is a significant problem.[1] In patients with medication-resistant depression, repetitive transcranial magnetic stimulation (rTMS), applied at 10–20 Hz to the left dorsolateral prefrontal cortex (DLPFC) or 1 Hz to the right DLPFC, is an adequate treatment alternative.[2–4] The US Food and Drug Administration (FDA) cleared the NeuroStar TMS Therapy and Brainsway Deep TMS systems[5] for this purpose. As of July 2015, 2 additional devices, the Magstim Rapid[2] and MagVita TMS Therapy Systems, have been cleared by the FDA, on the basis of substantial equivalence to the NeuroStar system. In fact, the Magstim, MagVita, and NeuroStar systems use figure-8 coils that induce similar electrical field distributions on the brain surface.[6] However, there is scarce published experimental or clinical trial evidence supporting equivalent antidepressant effectiveness between these systems.

Methods. A retrospective study was conducted to compare antidepressant efficacy between Magstim and NeuroStar devices in patients suffering from medication-resistant MDD episodes (*DSM-IV* criteria) who were treated at the Berenson-Allen Center (Boston, Massachusetts) from 2004 to 2013. The local institutional review board granted approval for this study. Depression severity was assessed using the 17-item Hamilton Depression Rating Scale (HDRS)[7] and the Beck Depression Inventory-II (BDI-II)[8] scales. Continuous measurements, presented as mean ± SEM, were normally distributed according to analysis of kurtosis, skewness, and comparison of mean and median and were compared using unpaired *t* tests. Binary data, presented as fractions, were compared using Fisher exact tests. A longitudinal mixed-effects model was used to test group differences (Magstim vs NeuroStar) in posttreatment reduction of depression severity score across weeks 1 to 4 of treatment. Best fit was tested using data transformations, polynomial models and interaction terms, model assumptions tested using analyses of residuals, and influence diagnostics conducted using Cook's distance. Analyses were performed using SAS (version 9.3, SAS Institute, Cary, North Carolina).

Results. We identified 154 patients treated for up to 6 weeks with 20 Hz stimulation of the left DLPFC (1,600 pulses delivered in 40 stimulation trains with 2-second duration and 28-second intertrain intervals) or 1 Hz stimulation of the right DLPFC (1,600 pulses). In both cases, intensity was set at 110% of resting motor threshold at the site 5 cm anterior to the motor "hotspot" for the contralateral hand muscles. Such treatment protocols were delivered using either a Magstim device with a commercially available 70-mm figure-8 coil, which was used in 113 patients, or a NeuroStar system, which was used in 41 patients, reflecting the fact that the latter was not available prior to 2009. Patients in the 2 groups did not differ regarding demographic, clinical, or treatment-related characteristics, including diagnosis, comorbidities, psychopharmacologic treatments, use of high-frequency left DLPFC stimulation, or the total number of rTMS treatments (Supplementary eTable 1). Magstim- and NeuroStar-treated patients also did not differ regarding posttreatment reduction of depression severity, measured using BDI-II (43.4 ± 3.2% vs 37.1 ± 5.8%, $t_{144} = 1$, $P = .3$, Figure 1) and HDRS (44.6 ± 3.9% vs 54.3 ± 8.0%, $t_{61} = -1.2$, $P = .3$). The proportion of responders (ie, patients with 50% or greater reduction of depression severity) was also similar according to both BDI-II (51/108 vs 17/38, $P = .9$) and HDRS (22/49 vs 8/14; $P = .5$). To control for potential biases, we restricted analyses to patients diagnosed with MDD receiving only high-frequency left DLPFC stimulation (n = 100) and again found no differences between Magstim and NeuroStar regarding reduction of depression severity (BDI-II: 44.5 ± 3.9% vs 38.6 ± 6.2%, $t_{96} = 0.8$, $P = .4$; HDRS: 46.5 ± 4.7% vs 49.8 ± 8.3%, $t_{39} = -0.3$, $P = .7$) and proportion of responders (BDI-II: 35/72 vs 11/26, $P = .7$; HDRS: 15/32 vs 4/9, $P = 1$). In further analyses conducted with all patients receiving only left-side rTMS (n = 128) and with patients treated since 2009 (n = 83), that is, excluding those treated when NeuroStar was not an option, we also found no statistically significant differences between outcomes in Magstim- and NeuroStar-treated patients (data not shown).

Figure 1. Longitudinal Assessment of Antidepressant Response in Magstim- and NeuroStar-Treated Patients[a]



[a]Percent reduction of depression severity (Beck Depression Inventory-II score) relative to pretreatment levels (mean ± SEM) was assessed weekly after starting treatment and was found to increase significantly according to treatment week (β = 12.8 ± 1.1, $P < .0001$), but was not significantly different according to treatment equipment (NeuroStar vs Magstim, β = −0.3 ± 3, $P > .9$; longitudinal mixed-effects model).

These findings are suggestive of equivalent antidepressant efficacy between Magstim and NeuroStar systems and support the current patterns of use of the Magstim equipment for treatment of depression. However, interpretation of these data should be performed in the context of the study design, namely its retrospective and open-label nature, and in particular given that patients were not randomized between treatment systems. Definitive evidence of the equivalence between the 2 stimulation devices will thus require a randomized noninferiority trial, which is necessary to confirm the findings reported here.

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transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. *Biol Psychiatry*. 2007;62(11):1208–1216.
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Potential conflicts of interest: **Dr Pascual-Leone** serves on the scientific advisory boards for Nexstim, Neuronix, Starlab Neuroscience, Neuroelectrics, and Neosync and is listed as an inventor on several issued and pending patents on the real-time integration of transcranial magnetic stimulation with electroencephalography and magnetic resonance imaging. **Drs Oliveira-Maia**, **Garcia-Guarniz**, and **Press** and **Ms Sinanis** report no financial or other relationship relevant to the subject of this letter.

Funding/support: Work on this study was supported in part by grants from the Sidney R. Baer Jr Foundation and Harvard Catalyst | The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, UL1 RR025758). Dr Pascual-Leone is further supported by grants from the National Institutes of Health (R01HD069776, R01NS073601, R21 MH099196, R21 NS082870, R21 NS085491, R21 HD07616). Dr Oliveira-Maia is funded by Fundação para a Ciência e Tecnologia (Lisboa, Portugal) through a Junior Research and Career Development Award from the Harvard Medical Portugal Program (HMSP/ICJ/0020/2011).

Role of the sponsor: The sponsors had no role in the planning, conduct, or reporting of the study.

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Supplementary material: See accompanying pages.

J Clin Psychiatry 2016;77(6):e743–e744
dx.doi.org/10.4088/JCP.15l10275

Supplementary material follows this letter.

THE JOURNAL OF
CLINICAL PSYCHIATRY
THE OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF CLINICAL PSYCHOPHARMACOLOGY

Supplementary Material

LetterTitle: Comparative Efficacy of Repetitive Transcranial Magnetic Stimulation for Treatment of Depression Using 2 Different Stimulation Devices: A Retrospective Open-Label Study

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DOI Number: 10.4088/JCP.15l10275

List of Supplementary Material for the letter

1. eTable 1 Comparison Between Magstim- and NeuroStar-Treated Patients

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published letter. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary eTable 1. Comparison between Masgtim and Neurostar-treated patients

Variables	Magstim	NeuroStar	p
Age (years)[1]	46.7 ± 1.3	50.3 ± 2.3	0.2
Gender (% male)	44.2	34.1	0.3
BDI-II (score at baseline)[1]	34.3 ± 1	31.9 ± 1.5	0.2
HAM-D (score at baseline)[1]	19.4 ± 0.8	19.3 ± 0.8	0.9
Refractory depression (%)[2]	67.3	70	0.8
Bipolar disorder (%)	20.5	19.5	1
Anxiety disorder (%)	21.4	28.2	0.4
Personality disorder (%)	6.8	7.7	1
Antidepressants (%)	67.3	64.1	0.8
Anticonvulsants or benzodiazepines (%)	71	79.5	0.4
Lithium (%)	18.9	5.1	0.1
Antipsychotics (%)	46.2	43.6	0.9
Left DLPFC stimulation (%)	88.5	87.8	1
Total treatment sessions (n)[1]	17.3 ± 0.6	19.2 ± 1	0.1

[1]Data presented as mean ± standard error of the mean and analyzed using t-tests. All remaining data is presented as % and analyzed using Fisher's exact tests.

[2]Refractory cases were defined according to prior electroconvulsive therapy or prior psychiatric hospitalization[1]

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