

Transcranial Magnetic Stimulation Therapy for the Treatment of Major Depressive Disorder

Daily left prefrontal repetitive transcranial magnetic stimulation (TMS) demonstrated therapeutic effects in patients with major depressive disorder (MDD), according to a recent study by George and colleagues. TMS is a brain intervention that alters activity within specific regions of the brain using electrical current. There has been some controversy regarding the reliability of previous sham studies that have investigated TMS, because some feel that sham TMS controls do not adequately mimic active TMS treatment. Thus, the concern was that controls were too obvious to investigators and study participants. The current study was designed with that potential flaw in mind, and the sham control was formatted to closely emulate the somatosensory experience of active treatment, including the sound of the device during administration and the pulsing sensation to the scalp.

This prospective, multicenter, randomized, active sham-controlled (1:1 randomization) trial included 190 patients with unipolar nonpsychotic MDD who were free of antidepressant, antipsychotic, and anticonvulsant medication for at least 2 weeks prior to baseline evaluation. Patients received active repetitive TMS (n=92) to the left prefrontal cortex (10-Hz pulses for 4 seconds with 26-second intervals between pulses for a total of 37.5 minutes per session; total of 3000 pulses per session) using a figure-eight solid-core coil or sham TMS (n=98), which consisted of a similar coil with a metal insert that blocked the magnetic field and scalp electrodes that simulated the active TMS sensation. Treatment was standardized at 120% magnetic field intensity relative to the individual patient’s resting motor threshold. Patients received 3 weeks of daily weekday treatment during the fixed-dose phase, followed by 3 additional weeks of blinded treatment for improvers. The two groups were well matched at baseline with regard to demographics and clinical characteristics. Of the 190 intent-to-treat patients, 154 completed and 120 were fully adherent.

The primary outcome was remission rate for the two treatment arms using logistical regression and controlling for age, treatment resistance, study site, and duration of the current depressive episode. Secondary outcomes included response rates, as determined by Hamilton Scale for Depression (HAM-D), Montgomery-Asberg Depression Rating Scale (MADRS), Clinical Global Impression Severity of Illness Scale (CGI-S), and Inventory of Depressive Symptoms-Self Report (IDS). Investigators also evaluated spontaneous adverse events that were related to repetitive TMS to assess for safety.

Patients who received active TMS treatment demonstrated a significant treatment effect compared with control (OR, 4.2; 95% CI, 1.32 to 13.24; p=0.02). Fourteen percent of patients in the TMS arm remitted versus 5% in the sham arm. The number that was needed to treat was 12. Patients who underwent TMS demonstrated significant improvement in MADRS (p=0.01), CGI-S (p=0.01), and IDS (p=0.001) scores compared with sham control (Table 1).

Table 1. Secondary Outcome Measures: Improvements from Baseline to End of Phase 1.

Scale/Treatment Group	Baseline – Mean (SD)	End of Phase 1 – Mean (SD)	p value
HAM-D/active	26.26 (4.95)	21.61 (9.26)	0.06
HAM-D/sham	26.51 (4.83)	23.38 (7.43)	
MADRS/active	29.48 (6.91)	24.59 (11.44)	0.01
MADRS/sham	29.81 (6.42)	27.75 (9.06)	
CGI-S/active	4.62 (0.70)	3.96 (1.14)	0.01
CGI-S/sham	4.63 (0.69)	4.30 (0.87)	
IDS/active	40.98 (9.27)	32.56 (15.40)	0.001
IDS/sham	40.07 (9.81)	36.70 (13.91)	

*Highlights from the
American Psychiatric
Association
163rd Annual Meeting*

It is important to note that site differences were found during the course of this study. In fact, most remitters (83%) and patients who were found to be less treatment-resistant (66.4%) originated at two of the four study sites. While site and resistance status did not appear to influence primary study results, interpretation of these variables did impact regression estimates.

There was no significant difference in spontaneous adverse events according to treatment arm. Five patients who were receiving TMS withdrew from study participation due to adverse events (one because of syncope after 14 treatments and four because of pain or headaches after initial treatment). No seizures or suicides were documented. The most common adverse events that were reported were headache, discomfort at stimulation site, and insomnia for both groups.

Overall, TMS was associated with more favorable outcomes compared with sham control. Daily left prefrontal TMS therapy was shown to have significantly greater antidepressant effects and was well tolerated in patients with unipolar depression. Safety profiles were similar between the two groups.

Citation:

George MS et al. *Arch Gen Psychiatry* 2010;67(5):507-516.

New Research Poster: Use of Tai Chi Can Improve Resilience, Quality of Life, Cognition in Depressed Older Adults

Use of Tai Chi, a mind-body exercise, in combination with antidepressants provides additional improvements in older adults with depression, according to new research being presented at the American Psychiatric Association's Annual Meeting.

Older adults with depression are at increased risk for decline in health functioning, morbidity and mortality, including suicide. Fewer than half of elderly depressed patients achieve remission and functional recovery in response to initial use of antidepressants alone.

Researchers Helen Lavretsky, MD, MS, and Michael Irwin, MD, University of California, Los Angeles, CA, studied a group of older adults with major depression and compared the use of an antidepressant combined with use of Tai-Chi-Chi (TCC, a brief standardized version of Tai Chi) to the use of an antidepressant combined

with a health education program. The older adults each participated in two hours per week of either Tai Chi or the health education program.

The Tai Chi (Figure 1) and health education participants demonstrated comparable improvement in the severity of depression. However, people in the Tai Chi group demonstrated significantly greater improvement in resilience, health-related quality of life, and cognitive function (memory, attention, and executive function).

Figure 1. Tai Chi Participants.



Tai-Chi intervention has an advantage in that it is easily translatable to the community and can be readily implemented among adults with physical limitations. Researchers concluded that “complementary mind-body interventions can improve partial response to antidepressants via stress-reduction, improved physical functioning, increased socialization, and reduced risks of polypharmacy.”