

January 19, 2007

Re: Meeting on January 26th Concerning Transcranial Magnetic Stimulation

Dear Ms. Scudiero:

I would like to give my opinion concerning transcranial magnetic stimulation (TMS) which is being considered at your January 26th meeting. This email replaces the email that I sent yesterday that contains typos.

I am a psychiatrist who has been Director of a busy 61-bed psychiatric inpatient service at Harborview Medical Center in Seattle for 25 years. Major depression is the most common diagnosis of our patients. Major depression is the psychiatric disorder that is most commonly associated with suicide: it also results in increased morbidity and mortality from non-suicidal causes (1).

We find that psychotherapy and antidepressant medications are often inadequate in bringing patients out of their depression and often recommend electroconvulsive therapy (ECT). ECT is the most effective treatment of major depression (1-4). When compared with antidepressant medication in hospitalized depressed patients, ECT results in a greater percentage of response, a greater degree of response, and a faster response compared with medication. Unfortunately, ECT is associated with significant side effects: a 1 in 10,000 risk of death, post-ictal confusion, memory disturbance and headache. I have been Director of our ECT service for 27 years and have treated about 30 patients per year with ECT. There is a clear need for a less intrusive treatment for patients who are not responding well to psychotherapy and medication. The recent STAR*D study has shown low response and remission rates in patients after they have failed adequate trials of antidepressant medication. Currently, patients who are medication-resistant face a very difficult dilemma: either trying yet another antidepressant that is likely to be ineffective or cause side effects or trying ECT and experiencing its side effects. TMS offers an excellent alternative for these patients.

Over the past 31 years, my clinical research has focused on treatment of depression. (See my CV that is attached.) In my early years, I researched ECT and tested the efficacy of antidepressant medications. Subsequently, I obtained NIMH funding to assess the efficacy of light therapies in the treatment of seasonal affective disorder. Over the last 10 years I have assessed TMS as a treatment for major depression including two NIMH grants. I also participated in the Neuronetics multi-site study.

The results of our first NIMH grant are summarized in a paper published last year (5). In this paper, we found that in medication-resistant patients with major depression, TMS has a 31% response rate and a 20% remission rate, significantly higher than with sham stimulation (6% and 3%). Comparing the TMS-sham differences of 25% for response rate and 17% for remission rate, we find these differences at least as good as for the antidepressant-placebo differences. I believe that antidepressant medication effects are clinically significant and that TMS effects are also clinically significant. Although the absolute response and remission rates seen with TMS are lower than with most antidepressant studies, almost all TMS studies are with medication-resistant samples, while antidepressant studies are almost always with non-resistant samples.

The Neuronetics trial was very well-designed and rigorously implemented. Their results also show a clear antidepressant signal. These results are consistent with the meta-analyses of controlled trials of TMS in depression.

Our experience has been that the TMS is very well tolerated. We and other investigators have looked for neurocognitive disturbances from the TMS and have found no decrements in function.

Overall, TMS provides a treatment alternative that is clearly needed. TMS is effective in medication-resistant patients and is very well-tolerated. I envision TMS as being very useful for medication-resistant patients with major depression who are not yet willing to risk the side effects of ECT.

Sincerely,

David H. Avery, M.D.
Professor, Psychiatry and Behavioral Sciences
University of Washington School of Medicine
Seattle, Washington

1. Avery, D.H. and Winokur, G.: Mortality in depressed patients treated with electroconvulsive therapy and antidepressants. *Arch. Gen. Psych.* 33:1029-37, 1976.
2. Avery, D.H. and Winokur, G.: The efficacy of electroconvulsive therapy and antidepressants in depression. *Biol. Psychiatry* 12(4):507-21, 1977.
3. Avery, D.H. and Winokur, G.: Suicide, attempted suicide, and relapse rates in depression following ECT and antidepressant therapy. *Arch. Gen. Psych.* 35:749-753, 1978.
4. Avery, D.H. and Lubrano, A.: Depression treated with imipramine and ECT: The de Carolis study reconsidered. *Am. J. Psych.* 136(4B):559-562, 1979.
5. Avery DH, Holtzheimer PE, Fawaz W, Russo J, Neumaier J, Dunner DL, Haynor DR, Claypoole KH, Wajdik C, Roy-Byrne P. A controlled study of repetitive transcranial magnetic stimulation in medication-resistant major depression. *Biological Psychiatry* 59:187-194, 2006