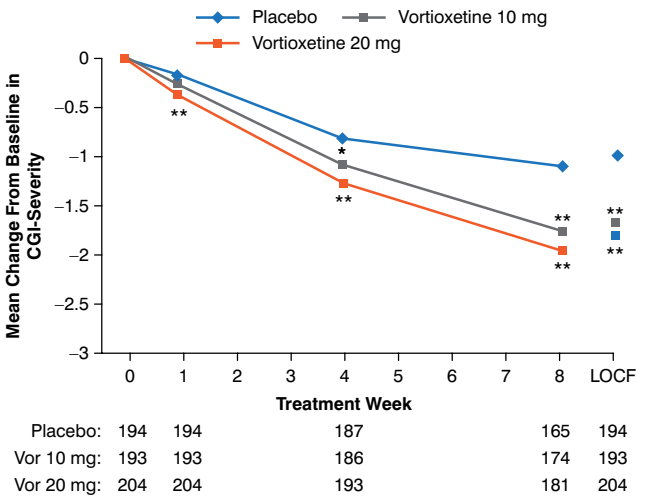
Figure 2. CGI-S Scores and LOCF



*p<0.01, **p<0.001 vs placebo.

CGI-S=Clinical Global Impression-Severity of Illness; LOCF=last observation carried forward.

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Vortioxetine 10 mg was distinguished from placebo on six of the 10 MADRS items at Week 4 and all 10 items at Week 8. Vortioxetine 20 mg was distinguished from placebo on 3 MADRS items at Week 1, 9 items at Week 4, and all 10 items at Week 8. The improvement in the rating of depression was manifest clinically, as indicated by improvement in CGI-S of –0.08 and –0.18 at Week 1 (p=0.077 and p<0.001, respectively); –0.27 and –0.43 at Week 4 (p=0.004 and p<0.001, respectively); and –0.65 and –0.85 at Week 8 (both p<0.001) for vortioxetine 10 and 20 mg versus placebo, respectively (Figure 2).

Vortioxetine was well tolerated. Most frequent adverse effects for the placebo, vortioxetine 10-mg, and vortioxetine 20-mg arms were nausea (4.1%, 16.4%, and 20.8%, respectively) and headache (7.1%, 8.2%, and 12.6%, respectively).

The secondary analyses establish the efficacy of the two vortioxetine doses on lessening depression in patients with MDD.

TMS Improves Anxiety Symptoms in Depression

Written by Nicola Parry

Gretchen J. Diefenbach, PhD, Institute of Living at Hartford Hospital, Hartford, Connecticut, USA, presented data from a meta-analysis of randomized controlled trials (RCTs) in transcranial magnetic stimulation (TMS) among depressed patients. The results showed that TMS appears effective in treating anxiety symptoms in patients with depression.

Although studies have increasingly shown evidence for the efficacy of TMS among patients with depression [Slotema CW et al. *J Clin Psychiatry* 2010; Schutter DJ. *Psychol Med* 2009], its anxiolytic effect is poorly documented. However, based on the comorbidity of anxiety and depression, this is an important area to investigate. Additionally, among patients with depression who also have anxiety, its symptoms tend to be more severe and also may be more treatment resistant.

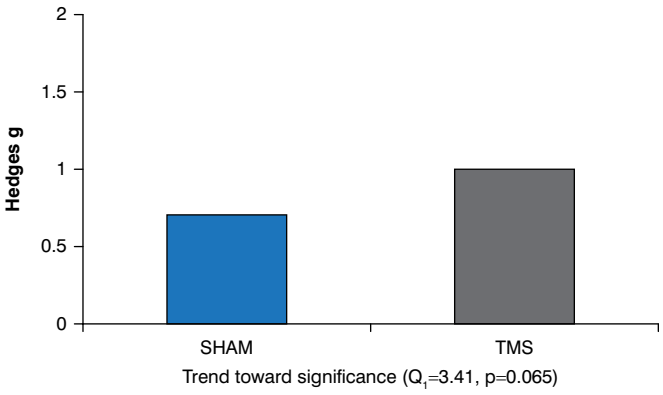
To further investigate this, Dr. Diefenbach and colleagues conducted a meta-analysis of data from RCTs to establish the pooled anxiolytic treatment effect of TMS among depressed patients. They used the Hamilton Depression Rating Scale as an outcome measure to assess anxiety symptom change, specifically using the anxiety/somatization subscale, which comprises 6 items: anxiety (psychic), anxiety (somatic), somatic symptoms (gastrointestinal), somatic symptoms (general), hypochondriasis, and insight.

They performed a literature search of the Scopus, Medline, and PsycINFO databases, using search terms including *transcranial magnetic stimulation* or *TMS* or *rTMS*; *controlled trial* or *sham* or *RCT*; and *depression* or *depressive disorder* or *MDD*, which identified 634 articles through June 2013. To be included in the meta-analysis, studies were required to be an RCT comparing TMS versus sham that treated depressive symptoms as the primary target, with TMS targeting the dorsolateral prefrontal cortex. They also had to comprise an adult sample with major depressive disorder, register the Hamilton Depression Rating Scale, and be published in English. Of these 634 articles, 64 met the inclusion criteria, but none of the publications contained all the relevant data, so authors were contacted directly. Complete data were subsequently acquired for 12 studies. Of the combined study participants (n=709), 395 received TMS and 314 received sham treatment.

There was no significant difference in mean pretreatment scores between the 2 groups. The statistics associated with the null result are as follows: rTMS group mean score, 7.56; sham group mean score, 7.48; $t(25)=0.15$; p=0.88. However, analysis of the in-group pooled treatment effect showed a moderate treatment effect for sham and a large treatment effect for TMS, with the difference between them trending toward statistical significance (p=0.065; Figure 1). There was also a moderate but significant difference (p<0.001) in posttreatment between-group effect sizes. Patients who received TMS reported lower anxiety somatization subscale scores than those who received sham. The large fail-safe number (n=102) suggests that these meta-analytic findings are robust.

The researchers did not pursue analyses of treatment moderators, since there was no significant difference (p=0.56) in between-study heterogeneity, which implied that the results were generally uniform across the different studies.

Figure 1. Posttreatment Between-Group Effect



TMS=transcranial magnetic stimulation.
Reproduced with permission from GJ Diefenbach, PhD.

The results of this meta-analysis indicate that TMS is superior to sham for treating anxiety symptoms in patients with depression, and Dr. Diefenbach concluded that it is important to consider expanding TMS treatment to anxiety disorders. She also indicated that it is important for investigators in future studies to include anxiety assessments in their TMS research, to evaluate changes in individual symptoms, response rates, and anxious depression status.

Electroconvulsive Therapy Improves Major Depression More Than Drugs Alone

Written by Nicola Parry

Lucas Primo de Carvalho Alves, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil, presented a poster with results of a study demonstrating that electroconvulsive therapy (ECT) improves the symptoms of major depression more than pharmacological therapy alone [APA 2014 (poster NR5-06)].

The primary indication for use of ECT is in patients with depressive disorders who relapse despite the use of prescription medications. Although meta-analytical studies have demonstrated the efficacy of ECT in treatment of depressive disorders, it is challenging to successfully translate study results into clinical practice, particularly in patients with medical and psychiatric comorbid disease.

With this in mind, Alves and colleagues designed a study to evaluate the outcomes of ECT in severely depressed individuals admitted to a psychiatric inpatient facility.

To be included in the study, patients were required to be older than 18 years with a diagnosis of depression according to Mini International Neuropsychiatry Interview criteria. In total, 147 patients were enrolled and divided into 2 groups: ECT-treated (n=43; mean Hamilton Rating Scale for Depression [HAM-D] score, 25.05) and non-ECT-treated (n=104; mean HAM-D score, 21.61).

Primary outcomes were improvement in depression based on the HAM-D score; response (HAM-D improvement ≥50%); remission (HAM-D score ≤7); and duration of hospitalization.

Based on mean HAM-D score from admission, symptoms of depression were significantly improved in the ECT-treated group (p=0.004; mean HAM-D score at discharge, 7.7) compared with the non-ECT-treated group (mean HAM-D score at discharge, 7.5).

The mean duration of hospitalization was significantly higher for patients in the ECT-treated group (p<0.001; 35.48 days), compared with those in the non-ECT-treated group (24.57 days).

Although patients in the ECT-treated group had significantly higher depression scores at the time of admission to the study than those who did not receive ECT, at the time for discharge, patients in both groups had similar scores. Alves stated that this increased response rate highlights the efficacy and effectiveness of ECT in severely depressed patients.

He concluded that the longer hospitalizations in ECT-treated patients emphasizes the need for advance knowledge of clinical predictors of the response to ECT, to reduce the time between admission and the first session for patients who will benefit from ECT.

First-Line Antidepressants Produce Similar Responses in Major Depressive Disorder

Written by Nicola Parry

Radu V. Saveanu, MD, Leonard M. Miller School of Medicine, University of Miami, Miami, Florida, USA, presented results from the first half of the randomized controlled International Study to Predict Optimized Treatment in Depression [iSPOT-D; NCT00693849]. The study demonstrated that, for patients with major depressive disorder (MDD), escitalopram, sertraline, and venlafaxine extended release (XR) produced similar treatment response rates, with mild and similar side effects.

Although antidepressant medications (ADMs) are effective, their benefit could be enhanced by identifying pretreatment clinical or neurobiological features that predict response versus nonresponse to treatment, as well as features or moderators that help identify which specific treatment is the best match for a particular patient.