Letter to the Editor

Resistant bipolar depressive disorder: case analysis of adjunctive transcranial magnetic stimulation efficiency in medical comorbid conditions

To the Editor:

There are controlled trials and meta-analyses (1) that provide support for repetitive transcranial magnetic stimulation (rTMS) having efficacy in the treatment of resistant depressive disorders. However, only one study has, to date, addressed this issue in patients with bipolar disorder without medical comorbidities (2) and the other recent studies do not mention comorbid status (3, 4). Yet, medical comorbidities are found in 59% of patients with bipolar disorder (5). Exploring the efficiency of rTMS in these patients is therefore of great importance, especially since comorbidities are known to complicate the clinical course of the illness, with evidence of increased rates of chronicity and non-recovery (6, 7). We report here a case of a patient with a history of multi-resistant bipolar depression and several medical comorbidities who responded to rTMS after unsuccessful trials of drug treatments.

Case report

A 58-year-old man was referred for admission to hospital because of acute bipolar depressive disorder which had started one year earlier. His previous depressive episodes had lasted between six and ten months, and were all characterized by fatigue, anxiety, sadness of mood with anhedonia, and negative thinking including suicidal ideas. He had no psychiatric or addictive comorbidities, but had many medical comorbidities, including metabolic syndrome, sleep apnea syndrome, mitral regurgitation, non-alcoholic liver steatosis, benign prostatic hyperplasia, and psoriasis. He also suffered from an asymptomatic multiple myeloma. There was no history of substance use or personality disorder, nor any family history of psychiatric diseases. Results relating to thyroid testing were within the normal range.

Because of several adverse side effects and/or lack of efficacy, the treatment protocols were changed several times (see Table 1) according to international recommendations (8). Combinations of mood stabilizers and antidepressant agents were not well tolerated, with severe side effects, and none was effective for depressive symptomatology. No mood stabilizer combinations were tested due to the problems with tolerance. The use of lamotrigine was a contraindication because of the patient’s psoriasis.

The most effective treatment was the combination of aripiprazole and clomipramine which led to partial remission for four weeks. However, clinical relapse occurred despite treatment and good tolerance. An increase to 225 mg of clomipramine for more than four weeks provided no clinical response, and electroconvulsive therapy was discouraged by the anesthesiologist because of his numerous medical comorbidities.

Magnetic stimulation was then performed using a Medtronic MagPro X100 stimulator and a figure eight-shaped water-cooled coil (Medtronic, Inc., Minneapolis, MN, USA). At the first rTMS session, the patient underwent a determination of his resting motor threshold (RMT) by an electromyogram. The coil was positioned 5 cm anteriorly and in a parasagittal plane. rTMS was delivered to the left dorsolateral prefrontal cortex (DLPFC) at a frequency of 10 Hz at 120% of right RMT. Each session consisted of 5-sec trains with a 25-sec intertrain interval (a total of 2,000 pulses/session). Forty treatment sessions were administered in an eight-week period (five sessions/week), totaling 80,000 pulses. After acute treatment, rTMS was tapered with the same stimulation parameters, over a
six-month period, before stopping treatment. The patient’s mood remained stable and he is now functioning well with a regimen of clomipramine 150 mg and aripiprazole 10 mg daily.

Discussion

Given that there was virtually no alternative, improvement following TMS is particularly heartening. This patient experienced a strong and sustained antidepressant response to adjunctive rTMS, without any adverse events or induced mania. He maintained improvement for a long time after stopping TMS with no major change in pharmacotherapy. Although the chronologic relationship between TMS and clinical improvement supports its efficiency in our case, we cannot exclude the possibility of spontaneous recovery.

This case highlights the difficulty in treating resistant bipolar depression with comorbid conditions (9). The evidentiary base that informs therapeutic decisions remains woefully inadequate and justifies the development of new recommendations with consideration of medical comorbidities (10, 11). Evidence-based guidelines are indeed derived from clinical studies involving highly selected patients who are not representative of ‘real world’ practices. Most patients with bipolar disorder have medical comorbidities which decrease the efficiency of treatments; i.e., patients are taking multiple medications, thus increasing the risk of poor tolerance and/or severe adverse side effects and poor efficacy of the treatment (12).

Our case suggests that rTMS could be prescribed more often and earlier in the management of bipolar depressive disorders with medical comorbidities. rTMS could be very useful to prevent the occurrence of disturbing drug side effects, to avoid worsening of medical comorbidities, and thus to increase the chances of recovery from resistant depressive states.

Further studies are needed to evaluate the risks and the efficacy and efficiency of this therapeutic strategy, particularly in patients with bipolar disorder with medical comorbidities.

Disclosures

The authors of this paper do not have any commercial associations that might pose a conflict of interest in connection with this manuscript.

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Depressive disorder, comorbidity, rTMS


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