

Acute and Maintenance Efficacy of Deep TMS in Depression with Mixed Features

Jean-Michel Azorin* MD, Christophe Gouraud RN, Léa Guintrand RN

Clinique l’Emeraude, Clinea, 34 Traverse de la Seigneurie, 13009 Marseille, France

***Corresponding Author:** Jean-Michel Azorin, Clinique l’Emeraude, Clinea, 34 Traverse de la Seigneurie, 13009 Marseille, France, E-mail: jazorin@ap-hm.fr

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Abstract

Background: There is evidence that repetitive transcranial magnetic stimulation (rTMS) is efficacious against depression in bipolar disorder but there are less data for mania. Similarly it has been suggested that rTMS may be effective against depressive symptoms in mixed states, with fewer evidence regarding manic symptoms. Deep TMS (dTMS) has been reported to be efficacious in bipolar depression, but there are no data concerning mixed states.

Procedure: We report the case of a bipolar II patient, in which dTMS displayed acute and maintenance efficacy against the depressive and hypomanic symptoms of a depressive episode with mixed features.

Conclusion: Randomized-controlled studies should be conducted to assess the acute and maintenance efficacy of dTMS in depression with mixed features.

Keywords: Depression; Mixed features; Bipolar disorder; Deep TMS

1. Introduction

Clinical trials of transcranial magnetic stimulation (TMS) indicate the potential of repetitive TMS (rTMS) for reducing depressive symptoms in bipolar disorder, while results are more controversial for mania [1]. Only one small open study has examined the efficacy of rTMS as maintenance treatment for bipolar disorder [2]. These studies have suggested that rTMS may be effective against depressive symptoms in mixed patients without inducing any manic/hypomanic switch [3-5], while another has reported efficacy in the treatment of both depressive and manic symptoms in mixed states [6]. Deep (H1 coil) TMS (dTMS) generates electrical fields that have greater penetration depth compared to standard rTMS [7]. It was shown to be an effective and well-tolerated add-on therapy in resistant bipolar depressed patients receiving adequate pharmacotherapy [8]. In addition, maintenance

dTMS sessions were found to be helpful in maintaining euthymia in a 12 month follow-up period, after recovery from acute depressive episode [9].

We report in this study the case of a bipolar II patient who was successfully treated with dTMS, administered both as acute and maintenance treatment for depression with mixed features.

2. Case Report

This 43-year-old male bipolar II patient was hospitalized in our clinic in March 2018 for a depressive episode with mixed features according to DSM5 criteria. The following symptoms were part of the depressive picture: loss of interest, hopelessness, hypersomnia, fatigue and feelings of worthlessness. Associated hypomanic features were racing thoughts, talkativeness and grandiosity. Symptoms such as irritability, impulsivity, affective lability or risky behaviours were not present. The patient experienced his first depressive episode in April 2008 and his first hypomanic episode in December 2008. During ten years, he had experienced a mean of 2.2 ± 1.3 episodes per year. Since April 2008, he was treated with lamotrigine (400 mg/d). Adherence to treatment was fair. His depressive relapses were usually successfully treated with the addition of quetiapine (300 mg/d) to his regimen. The same held true for his hypomanic episodes (quetiapine 400 mg/d). For the first time in March 2018, he experienced depression with mixed features and the combination of lamotrigine with quetiapine appeared to be no more successful, whatever the doses used. This condition even worsened when paroxetine (20 mg/d) was associated with lamotrigine and quetiapine. Because of the expertise in our clinic to treat refractory depressed patients with dTMS, we decided to administer this kind of therapy 1 week after having stopped quetiapine and paroxetine. The patient was maintained on lamotrigine (400 mg/d). The coil was positioned over the left dorsolateral prefrontal cortex, which was found 6 cm anteriority to the 'hot spot' (ie, the optimal location on the scalp to evoke a maximum TMS response with minimum stimulator intensity), per a ruler attached to the subject's cap. The motor threshold MT (the lowest stimulation intensity necessary to evoke a motor potential with at least 50 μ V amplitude in 50 % of attempts) was assessed before treatment and then every week. The simulation consisted of 55 18 Hz, 2 s trains at 120 % MT intensity, with a between-train interval of 20s. The patient was stimulated every day for 4 weeks (except weekends), three days per week for the following 3 months, and then one day per week. Today he is still stimulated once a week, and this since August 2018.

Before beginning the treatment with dTMS, the patient had a 17-item Hamilton Depression Rating Scale (HDRS) score of 25, and a Young Mania Rating Scale (YMRS) score of 11. After 1 month of treatment the HDRS score dropped to 6, the YMRS score to 1, and criteria for depression with mixed features were no more fulfilled. Since that time, the patient had never experienced any relapse. His HDRS score has remained between 0 and 6, and his YMRS score between 0 and 2. The only medication received since April 2018 and maintained during all that time was lamotrigine (400 mg/d). No adverse effects were observed during both the acute and maintenance treatment.

3. Discussion

This case may be remarkable for three reasons. First, it is the first case of depression with mixed features fulfilling DSM5 criteria, to have been successfully treated with TMS. Second, it is the first report on the efficacy of dTMS in mixed episodes. Third, it is the first study to suggest maintenance efficacy of TMS in bipolar disorder over a period of two years.

The beneficial effects observed in this report could be explained by the deeper stimulation exerted by dTMS on dorsolateral and ventrolateral prefrontal areas which also project into other brain areas that present impaired functioning in bipolar disorder [8].

This study is based on a single case and it is therefore difficult to draw any firm conclusion or to generalize to different situations. The patient had a bipolar II disorder, no comorbid condition (either psychiatric or organic) and a 'stable' mixed depressive episode occurring on the basis of a hyperthymic temperament [10]. Mixed depressive patients with other types of bipolar disorder or with unipolar disorder, patients with comorbid conditions or patients with 'unstable' mixed depression, may have exhibited different responses to dTMS.

4. Conclusion

Nonetheless, this case report suggests that it may be worth evaluating in randomized controlled trials (RCTs), TMS as an intervention for mixed depression, either as acute or maintenance treatment. RCTs of dTMS for maintenance treatment of affective disorders are still lacking.

Conflicts of Interest

The authors declare that they have no competing interests.

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