Treatment of Depersonalization Disorder With Repetitive Transcranial Magnetic Stimulation

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High frequency repetitive transcranial magnetic stimulation (rTMS) was approved by the US Food and Drug Administration in 2008 to treat major depressive disorder in those who did not respond to at least 1 antidepressant trial. Previous studies have shown that both high frequency rTMS to the left dorsolateral prefrontal cortex (DLPFC) and low frequency rTMS to the right DLPFC have antidepressant efficacy in treatment-resistant depression. Although rTMS has been widely used in the treatment of depression, very few studies of rTMS in patients with depersonalization disorder (DPD) have been published so far. DPD involves persistent or recurrent experiences of unreality and feelings of detachment causing distress or functional impairment while insight remains intact. The prevalence of DPD is approximately 1% to 2%. Studies of the pharmacological treatment of DPD are limited, and medications have proven to be of limited benefit. We present the case of a 30-year-old man with major depressive disorder and DPD who did not respond to pharmacotherapy. After the patient was treated with low frequency rTMS to the right DLPFC followed by high frequency rTMS to the left DLPFC, there was a significant reduction in his depersonalization symptoms. Given its effectiveness in our patient, the use of both low frequency rTMS to the right DLPFC and high frequency rTMS to the left DLPFC for treatment of DPD should be further explored. (*Journal of Psychiatric Practice 2017;23;141–144*)

KEY WORDS: transcranial magnetic stimulation (TMS), depersonalization disorder (DPD), high frequency, low frequency, dorsolateral prefrontal cortex (DLPFC), Cambridge Depersonalization Scale (CDS)

We present the case of a 30-year-old man with major depressive disorder (MDD) and depersonalization disorder (DPD) who did not respond to pharmacotherapy. After the patient was treated with low frequency repetitive transcranial magnetic stimulation (rTMS) to the right dorsolateral prefrontal cortex (DLPFC) followed by high frequency rTMS to the left DLPFC, there was a significant reduction in his depersonalization symptoms.

CASE DESCRIPTION

The patient, a 30-year-old single Chinese American man in the US Navy, was referred for rTMS for the treatment of MDD and DPD. The patient had no history of medical problems or illicit drug use. He was raised in an intact family and described himself as being shy and introverted in childhood. His developmental history was normal and he had no history of abuse or traumatic experiences in childhood. He had experienced 2 episodes of depersonalization symptoms at age 13 and age 17 that were short lived and spontaneously resolved. He did not identify any stressors contributing to these previous episodes of depersonalization symptoms.

His current symptoms started during his deployment to Afghanistan, and he was later diagnosed with MDD and DPD. He described feelings of unreality and being in a "dream-like state." His symptoms of DPD also included emotional numbing, feelings of disconnection and detachment, diminished sense of agency (feeling robotic, lacking control of his own movements), and feeling that his mind was empty of thoughts and memories. He did

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not meet criteria for any anxiety disorder. Treatment with bupropion was started, which reduced the patient's depressive symptoms. However, he continued to have depersonalization symptoms and was referred for treatment with rTMS. Bupropion treatment (300 mg/d extended release) was continued during his treatment with rTMS.

Before rTMS treatment, the patient had a score of 12 on the Montgomery-Asberg Depression Rating Scale (MADRS) (possible range of scores 0 to 60),[1] 4 on the Hamilton Anxiety Rating Scale (Ham-A) (possible range of scores 0 to 56),[2] and 149 (endorsing 20 of 29 items) on the Cambridge Depersonalization Scale (CDS).[3] The CDS is a valid and reliable 29-item scale (range of scores from 0 to 290) that measures the frequency and duration of depersonalization symptoms.[3] The patient began rTMS (with the NeuroStar device) to target depressive and depersonalization symptoms using low frequency (1 Hz) stimulation applied to the right DLPFC. Each treatment consisted of 1 Hz/s for a total of 1200 pulses delivered over 20 minutes at the standard setting of 110% of motor threshold (MT). MT, which was determined by visible twitch of the left abductor pollicis brevis in the "MT Hunt position" as per Neuronetics guidelines, was 1.28 which was higher than the published average (1.0) of the Neuronetics system. The coil was 6 cm anterior to the location where MT was determined. Coil angle was 0 degrees. The patient tolerated the procedure well and at session 7 noted a continued improvement in his mood, but his depersonalization symptoms persisted. At that time, the patient had a score of 8 on the MADRS, 2 on the Ham-A, and 132 on the CDS (endorsing 17/29 items). He continued right-sided rTMS for 24 sessions, with a gradual improvement in depressive and depersonalization symptoms—with a score of 4 on the MADRS, 2 on the Ham-A, and 83 on the CDS (endorsing 18/29 items). The patient requested that he be switched to high frequency (10 Hz) rTMS applied to the left DLPFC, with the goal of obtaining further improvement in his depersonalization symptoms. Each treatment consisted of 10 Hz over 4 seconds with a 26 second quiet interval, for a total of 3000 pulses delivered over 37.5 minutes. Coil angle was 0. The patient could not tolerate treatment at the standard setting of 120% of MT, due to pain experienced directly under the treatment coil. Instead, treatment was begun at 95% of MT and gradually titrated to 110% of MT. The patient noted obvious improvements in depersonalization symptoms after 6 high frequency sessions, with his score on the CDS decreasing to 57 (endorsing 15/29 items). He continued high frequency treatment, receiving a total of 32 sessions, and showed continued improvement in his depersonalization symptoms, with a score of 3 on the MADRS, 1 on the Ham-A, and 48 on the CDS (endorsing 14/29 items). He was scheduled for monthly maintenance treatment but was unable to receive his next treatment until 3 months later due to moving out of state. He has continued to remain stable with maintenance treatment. Figure 1 shows the patient's scores on the MADRS, Ham-A, and CDS over the course of treatment.

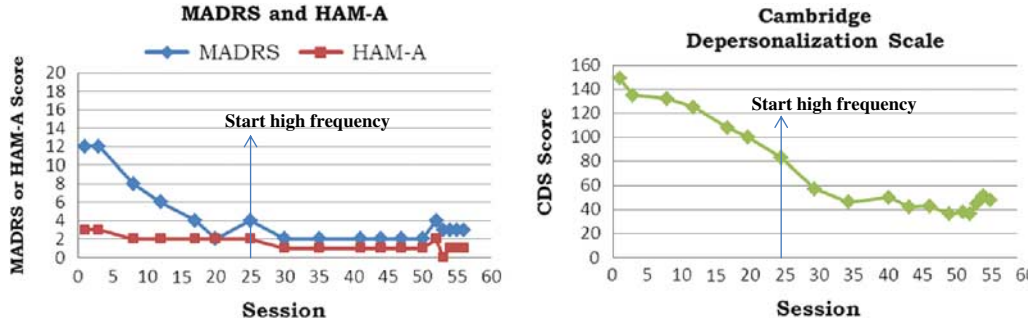
DISCUSSION

TMS is a noninvasive brain stimulation technique that uses electromagnetic fields to stimulate cortical neurons through an insulated coil placed over the scalp. The TMS coil creates brief magnetic pulses, similar to those generated by magnetic resonance imaging machines, which pass through the cranium and into areas of the brain implicated in mood regulation, such as the prefrontal cortex. Only cortical regions are stimulated directly, although TMS affects distal regions that are interconnected to the site of stimulation. Administering pulses in rapid succession is referred to as rTMS, and the pulses are given at either low or high frequency.

On the basis of results from a multisite, randomized, controlled clinical trial of high frequency rTMS over the left DLPFC,[4] rTMS was approved by the US Food and Drug Administration (FDA) in 2008 to treat major depressive disorder in those who did not respond to at least 1 antidepressant trial. Previous studies have shown that both high frequency rTMS to the left DLPFC[5,6] and low frequency rTMS to the right DLPFC[7] can have antidepressant efficacy in treatment-resistant depression. Although rTMS has been widely used in the treatment of depression, very few studies of rTMS in patients with DPD have been published so far.

DPD involves persistent or recurrent experiences of unreality and feelings of detachment causing distress or functional impairment while insight remains intact; the prevalence of DPD is approximately 1% to

FIGURE 1. Severity of symptoms.



Arrow indicates end of low frequency right-sided rTMS and start of high frequency left-sided rTMS at session 25. Montgomery-Asberg Depression Rating Scale (MADRS) consists of 10 items based on clinical interview (range of scores from 0 to 60). Hamilton Anxiety Rating Scale (Ham-A) consists of 14 self-report items (range of scores from 0 to 56). Cambridge Depersonalization Scale (CDS) consists of 29 self-report items (range of scores from 0 to 290) designed to measure depersonalization and derealization symptoms.

2%.[8] Symptoms include increased perceptual acuity, lack of affective response, and a feeling of a lack of control over one's actions, including speech.[3]

A study of 117 patients with DPD found 64% with comorbid anxiety disorders and 73% with a lifetime comorbid unipolar mood disorder.[9] The mean age of onset for DPD is between 16 and 23 years, with fewer than 20% having an onset after 20 years of age.[9,10] The onset of DPD can be de novo or can occur after illicit drug use or secondary to stress.[9,10]

Studies of the pharmacological treatment of DPD are limited. Results of a study of 32 patients with DPD suggested that combining lamotrigine with selective serotonin reuptake inhibitors may be beneficial.[11] In a study designed to test the hypothesis that the opioid system has a role in the pathogenesis of depersonalization, a single dose of intravenous naloxone was administered to 11 patients with DPD; 7 of the patients showed marked improvement and 3 had a total remission of symptoms.[12]

The authors of 2 case reports[13,14] and 2 publications describing clinical trials[15,16] have reported that rTMS was effective in reducing symptoms of DPD. The first case report involved a woman with comorbid DPD and MDD who responded to low frequency rTMS to the right DLPFC.[13] The day after treatment she reported a dramatic decrease in depersonalization symptoms, although her progress did not continue in the coming weeks. In this case, an improvement in depersonalization symptoms was achieved after a single session. The second case report involved a man with comorbid DPD and MDD who did not respond to pharmacotherapy. He was treated with high frequency (20 Hz) rTMS to the left DLPFC and had a 28% reduction in DPD symptoms after 6 sessions.[14] In our patient, both low frequency rTMS to the right DLPFC and high frequency rTMS to the left DLPFC were effective. In the first clinical trial of rTMS in DPD, 6 of 12 patients with DPD who were treated with low frequency rTMS to the right temporal-parietal junction for 3.5 weeks responded.[15] It has been suggested that impaired processing at the temporal-parietal junction may lead to out of body experiences, in which a person is awake and sees his or her body and the world from outside the physical body.[17] In the second clinical trial which included 17 patients with medication-resistant DPD, a single session of right-sided low frequency (1 Hz) rTMS to ventrolateral prefrontal cortex reduced depersonalization symptoms,[16] supporting the model of increased ventrolateral prefrontal cortex activity in DPD.

Our patient's depersonalization symptoms partially responded to low frequency rTMS to the right DLPFC. He was started on low frequency rTMS to reduce the risk of side effects, including the risk of seizure. At the patient's request, he was switched to high frequency rTMS to the left DLPFC with the hope of obtaining further improvement in his depersonalization symptoms. It is possible that, if low frequency rTMS had been continued longer, the patient may have experienced continued improvement in depersonalization

symptoms. It is also possible that the number of pulses per session contributed to the patient's continued response after changing protocols. Given the effectiveness of rTMS in our patient, the use of both low frequency rTMS to the right DLPFC and high frequency rTMS to the left DLPFC for treatment of DPD should be further explored.

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