Ultrarapid Remission of Treatment-Resistant Depression in Parkinson Disease With Intermittent Theta Burst Transcranial Magnetic Stimulation

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Depression is a common comorbidity in patients with Parkinson disease (PD).[1] While first-line treatments such as antidepressants are effective for many, the issue remains of how to treat treatment-resistant patients while avoiding medications that may exacerbate Parkinson symptoms.[2] Repetitive transcranial magnetic stimulation (rTMS) targets the dorsolateral prefrontal cortex (DLPFC) and has shown mixed efficacy in this population.[3] Intermittent theta burst stimulation (iTBS), a novel rTMS protocol, delivers higher-frequency pulses and mimics brain theta rhythms associated with cognition.[4] To our knowledge, these are the first documented cases of ultrarapid remission using iTBS in PD patients with treatment-resistant depression.

Case 1

The patient was a 73-year-old woman with a history of severe recurrent depression dating back to 1973 and a diagnosis of PD in 2024. Her extensive pharmacologic history included escitalopram, citalopram, paroxetine, sertraline, venlafaxine, and bupropion, all of which were ineffective. She also underwent 2 years of cognitive-behavioral therapy (2022–2024) with no significant improvement. After a failed trial of duloxetine 120 mg, her depression was deemed treatment resistant. TMS was selected for its antidepressant efficacy and potential beneficial effects on PD symptoms.[5]

The patient received left-sided iTBS at 120% of the resting motor threshold, targeting the DLPFC. After 3 treatments, her 9-item Patient Health Questionnaire (PHQ-9)[6] score decreased by 50%, prompting a reduction of duloxetine from 120 mg to 60 mg. By treatment 5, her PHQ-9 was 0. Treatments continued through 36 sessions using sequential bilateral theta burst (iTBS and continuous TBS for the left and right DLPFC, respectively) for residual anxiety. The patient completed treatment in full remission.

Case 2

The patient was a 79-year-old woman with a history of major depressive disorder, posttraumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), generalized anxiety disorder, and PD. She presented with a PHQ-9 score of 17, indicating moderately severe depression. Previous trials included venlafaxine, escitalopram, and trazodone, with augmentation from buspirone. All of these medications were ineffective. Due to PD progression coinciding with worsening depression, she was selected for TMS therapy. Treatment began with left-sided iTBS at 120% motor threshold. After 3 sessions, her PHQ-9 score decreased to 8. By the seventh session, her score was 0. The patient reported improved motivation and reengagement in activities of daily living. No adverse effects were noted. She continued TMS through 36 sessions, achieving remission of depression with a significant reduction in anxiety symptoms. OCD and PTSD symptoms remained stable but were not the focus of treatment.

Discussion

These cases demonstrate the potential for iTBS to rapidly reverse treatment-resistant depression in patients with PD. iTBS delivers higher-frequency stimulation than traditional TMS and may more effectively engage cortical circuits relevant to both mood regulation and cognitive processing.[4] Both patients achieved PHQ-9 scores of 0 within 7 treatments. This was a significantly faster response than typically observed in TMS trials. Although we did not formally assess motor symptoms, both patients were concurrently treated with carbidopa-levodopa, and one received the dose 30 minutes prior to each TMS treatment. Emerging evidence suggests that dopaminergic agents may enhance TMS efficacy, and future research should explore these synergistic mechanisms.[7]

Primary care physicians often manage patients with PD and depression. These cases support the inclusion of TMS, particularly iTBS, as a consideration in refractory cases.

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