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Transcranial Magnetic Stimulation for Posttraumatic Stress Disorder: Prevention in the Context of New Trauma

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Abstract

Posttraumatic stress disorder (PTSD) is a disabling psychiatric disorder that can result from experiencing a traumatic event. While a single index trauma can result in PTSD, patients often have additional traumatic events over the course of their lives. Despite this, little research to date has focused on prevention of PTSD recurrence following a novel traumatic experience. We present three cases of individuals with chronic PTSD who experienced an additional traumatic experience during treatment with transcranial magnetic stimulation (TMS) at VA Providence. Despite expectations to the contrary, TMS appeared to prevent a recurrence or worsening of their PTSD symptoms. We discuss possible neurobiological explanations for these outcomes and implications for possible use of TMS to prevent PTSD following trauma.

Keywords

Transcranial Magnetic Stimulation; Post Traumatic Stress Disorder; Prevention

Background:

Post-traumatic stress disorder (PTSD) is a common consequence of experiencing a traumatic event, with lifetime prevalence in the general population around 7%.[1] Research has further demonstrated a dose-response effect, where experiencing additional traumatic events further increases risk for, and severity of, PTSD.[2,3] Rates of both trauma exposure and lifetime rates of PTSD are higher among Veterans,[2,4] making this population a high priority target for intervention.

Transcranial Magnetic Stimulation (TMS) is a form of noninvasive brain stimulation that uses pulsed magnetic fields to induce electrical changes in targeted areas of the brain.[5] TMS, used for the treatment of pharmacoresistant depression since 2008,[6] has demonstrated clinical efficacy for other comorbid disorders, including PTSD.[7,8] TMS has also recently shown promise as a maintenance therapy to prevent depression relapse in those who

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responded to a prior course of TMS.[9] However, research to date has not explored TMS to prevent relapse of PTSD symptoms.

We present three cases of Veterans with PTSD who experienced an additional traumatic life experience during TMS therapy at VA Providence. Treatment parameters were generally standard, on-label device settings (Magstim, UK; 10Hz to left dorsolateral prefrontal cortex, 120% of motor threshold, 3000 pulses per day). All patients completed the PTSD Checklist for DSM-5 (PCL-5)[10] and the Patient Health Questionnaire (PHQ-9)[11] at start of treatment and every 5th treatment to assess symptoms of PTSD and depression respectively (**See** Table 1). A 5-point change on the PHQ-9 and a 10-point change in the PCL-5 are considered clinically significant.

Case Presentations:

Case 1:

A man in his 50s with a history of chronic PTSD, Major Depressive Disorder (MDD), and generalized anxiety disorder presented for a standard course of TMS. Patient's trauma history included childhood physical abuse and combat exposure during deployment 15 years earlier. Prior to starting TMS, the patient's PHQ-9 score was 15, indicating moderate depression, and their PCL-5 was a 50, indicating moderate to severe PTSD. During TMS, this individual was involved in a serious motor vehicle accident that required surgery. This patient completed 40 sessions of TMS. At end of treatment, he completed the PHQ-9 and PCL-5, scoring an 11 and 40 respectively. Patient experienced a clinically significant response in PTSD symptoms, and reduction in depressive symptoms. After treatment, patient reported improvements in sleep, mood, and decreased vigilance. In addition, he reported ability to manage life stressors appropriately that, prior to treatment, would have left him incapacitated. At 6 months post treatment, Veteran continued to experience PTSD and depression symptoms, yet maintained functioning, reporting a PHQ-9 of 9 (PCL-5 not completed).

Case 2:

A woman in her 60s with chronic PTSD and MDD presented for TMS treatment. Patient had a past medical history of alcohol use and substance use disorders, as well as four inpatient hospitalizations for suicidal ideation and overdoses in the context of life stressors between two and five years before treatment. Patient was sober for two years prior to treatment, with relapses in the context of stressful events one year prior. Past traumatic experiences for this individual include sexual violence and unexpected death of siblings between childhood and her 40s. Prior to TMS treatment, this individual scored a 12 on the PHQ-9 and a 44 on the PCL-5, indicating moderate symptoms of depression and PTSD. Between treatment 10 and 15, the patient experienced a house fire with complete loss of her home and property. She was in the house, but unharmed. Patient completed 30 treatments, ending with a PHQ-9 of 6 indicating mild depression symptoms, and a PCL-5 of 25, consistent with PTSD symptoms that would no longer meet threshold criteria for PTSD diagnosis. At end of treatment, patient reported improvement in quality of life, as well as the ability to better handle this stressful event which otherwise would have increased her depression. Patient experienced

worsening symptoms (low mood, poor sleep, increased stress) in the 3 months following TMS treatment due to increasing stressors related to relocating housing. Following this 3-month period, however, as stressors subsided, symptoms improved. In the 6-month period following TMS, she did not have any relapses or any new inpatient hospitalizations.

Case 3:

A man in his 30s with chronic PTSD and MDD presented for TMS treatment. Prior trauma was related to combat exposure from deployment 12 years prior. Patient had a history of two suicide attempts two and four years before treatment without hospitalization, as well as one hospitalization for anxiety in the context of marital conflict. At start of treatment, patient scored a 24 on the PHQ-9 and a 68 on the PCL-5, consistent with severe depression and PTSD. Patient also had chronic suicidal ideation without intent or plan. Over the course of TMS, he experienced additional stressors related to divorce, including forced separation from children and housing instability requiring VA homeless services' housing relocation assistance. Following treatment, the patient scored a 16 on the PHQ-9 and a 49 on the PCL-5, indicating moderate symptoms, and a clinically significant response in both symptoms of PTSD and depression. The patient reported increased quality of life, improved sleep and decreased rumination. Of note, he experienced reductions in suicidal thoughts, with a 2-week period during treatment with no thoughts of suicide. Following treatment, in the context of further stressors, veteran reported occasional thoughts about death and anxiety, yet no suicidal ideation or attempts.

Discussion:

We present three cases of individuals with treatment resistant PTSD and MDD who experienced an additional serious traumatic experience during a standard course of TMS treatment. All patients experienced clinically significant reductions in PTSD symptoms, and 2 individuals reported clinically significant reductions in depressive symptoms. These individuals reported qualitative improvements aligning with these clinical gains, including improvements in mood, anxiety, vigilance and sleep. A common theme across all patients was they noted feeling more capable of handling ongoing stressors related to their trauma. This is reflected in symptoms remaining below pre-treatment levels, and lack of relapse to substance use and suicidal behavior as had been precipitated by stressful life experiences in the past.

These cases, taken together, indicate that being actively engaged in TMS treatment during a traumatic experience could have a preventative effect against the exacerbation of PTSD symptoms. Several pharmacological treatments for PTSD have been tested in a preventative capacity (reviewed in [12]), such as propranolol[13] with mixed results limited by small sample sizes and lack of a control group. We recognize similar limitations in this report preclude any definitive results about the efficacy of TMS in this context. Although not all individuals who experience a trauma will go on to develop PTSD, it is associated with a wide range of poor outcomes,[14] and those who develop chronic PTSD are less likely to reach remission.[15] Therefore, intervening before symptom onset after first trauma, or before symptom exacerbation in those known to have a history of PTSD, is particularly important.

TMS may pose a unique preventative mechanism against exacerbation of PTSD in relation to its targeting of specific brain regions implicated in PTSD, namely the Dorsolateral Prefrontal Cortex (DLPFC). The DLPFC is an important node of the Executive Control Network (ECN), which allows top-down regulation of executive control and emotional regulation. PTSD is associated with hypoactivity in the DLPFC.[16] Therefore, TMS that aims to increase activity in the DLPFC may facilitate a patient's ability to regulate emotions and process stressors. This is reflected in our cases by individuals reporting increased ability to respond to new traumatic events that previously would have affected their functioning.

This case series indicates TMS may prevent the exacerbation or onset of PTSD symptoms in patients experiencing traumatic events while engaged in treatment. Given the nature of TMS, neuroimaging could be used to guide TMS treatment course decisions in clinical settings for those who experience a novel traumatic event during treatment. While beyond the scope of this case series, future studies could investigate the potential to develop TMS as an initial intervention to prevent PTSD in those who have experienced a traumatic event, particularly for those who have previously responded well to TMS treatment.

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Table 1:

Patient PCL-5 and PHQ-9 Scores During Treatment

	Case 1		Case 2		Case 3	
Treatment #	**PHQ-9**	**PCL-5**	**PHQ-9**	**PCL-5**	**PHQ-9**	**PCL-5**
Baseline	15	50	12	44	24	68
Treatment 5	15	49	2	23	21	58
Treatment 10	11	42	3	24	14	46
Treatment 15	16	43	3^	22^	19	49
Treatment 20	11^	51^	2	32	18	45
Treatment 25	12	47	4	25	17	45
Treatment 30	11	38	6*	25*	17	47
Treatment 35	11	38	-	-	16*	49*
Treatment 40	11*	40*	-	-	-	-

* Denotes individual's endpoint treatment

^ Denotes first questionnaires after traumatic event. Not applicable to case 3 due to ongoing events.