Successful Treatment of Refractory Organic Catatonic Disorder With Repetitive Transcranial Magnetic Stimulation (rTMS) Therapy

To the Editor: Catatonia can be the initial presentation in several organic diseases, with varying severity. Benzodiazepines are the first line of treatment, but atypical antipsycotics alone or in combination with lithium, carbamazepine, and memantine have also been found to be effective for catatonia. Nevertheless 15%–30% of patients do not respond satisfactorily.[1] Acute catatonic syndrome with autonomic instability and excitement have a fatal outcome in up to 31% of patients.[2] Refractory catatonia, that is, patients not responding to medical therapy, is generally treated with ECT. It has its own early, short-, and long-term adverse effects. Repetitive Transcranial Magnetic Stimulation (rTMS) is a noninvasive technique for indirect brain stimulation and is emerging as a treatment modality for several neuro-psychiatric conditions. rTMS has been little explored for catatonia, with only two cases hitherto reported.[3,4] Here, we are reporting a case of refractory organic catatonic disorder that responded to rTMS.

Case Reports

A 22-year-old woman presented with a 9-day history of intermittent fever and abnormal behavior. On the second day of her febrile illness, she developed fluctuating abnormal behavior characterized by apathy, nihilistic delusions, repetitive movements, and rapidly progressive rigidity of the whole body. She had no seizures. On admission, she was febrile (100°f), mute, and was avoiding eye contact. Saliva was pooled in the oral cavity and was drooling. There was axial and appendicular rigidity, fluctuating intermittently. There was intermittent prolonged posturing of limbs and opening of mouth. A differential diagnosis of viral encephalitis, acute psychosis, depressive stupor, and neuroleptic malignant syndrome (NMS) was entertained. She satisfied the criteria for DSM-IV-TR for "catatonia due to general-medical condition." Laboratory investigations showed neutrophilic leucocytosis and ESR 30 mm/Hr. EEG done on the 9th day of illness showed generalized background slowing (4–5Hz) and right frontal epileptiform discharge. A detailed MRI study of brain showed small areas of discrete hyperintense signals (nonenhancing) in subcortical white matter in the left frontal, right parietal, and right precentral sulcal region. Lumbar CSF on the tenth day was unremarkable. CSF was negative for HSV I, II PCR, and Japanese B Encephalitis virus IgM antibody. CPK level was 562u/liter on the 3rd day of illness, 322U/liter on the 4th day, and showed a downward trend thereafter. CSF examination, repeated on the 20th day of illness, showed 20 cells/mm^3 (100% lymphocytes), with other parameters being normal. By the 11th day of her illness, she had worsened, and the Bush Francis Catatonia rating score (BFCR) was 32. She was electively intubated and received intravenous lorazepam for a period of 20 days, along with sodium valproate (1,200 mg daily) and escitalopram (25 mg daily). After considering the possibility of Neuroleptic Malignant Syndrome, we administered bromocriptine 12 mg/day from the 13th to the 38th day of her illness. Clozapine 25 mg per day was added on Day 24th of illness, and the dose was gradually increased to 100 mg per day over 2 weeks. The relatives of the patient refused ECT therapy, so they were given option of experimental therapy with rTMS. The family accepted this treatment option and, after obtaining informed consent from her parents, rTMS was started Day 30th of her illness. We used Magstim Rapid[2] (The Magstim Company, Ltd., Whitland, Wales, UK) to provide the rTMS therapy.

A point of motor threshold (MT) for the Abductor pollicis brevis was determined for each hemisphere. A straight line 5 cm anterior and parasagittal from that point defined the dorso-lateral prefrontal cortex. The protocol consisted of 10 cycles of stimulation at 80% of the motor threshold, which was 62% of stimulator output for her, at 10 Hz, with 2-sec train, with intertrain interval of 58 sec for 10 cycles given to right and left hemisphere on Day 1. From the 2nd to the 10th day, the stimulation was increased to 20 cycles of 20 Hz. At the end of the rTMS therapy, her BFCR score decreased significantly to 9 from previous score of 32. She started to make good eye contact, to recognize and communicate verbally with relatives, and had minimal rigidity. EEG on discharge was normal. She was discharged on tab lorazepam 1.5 mg/day, tab duloxetine 40 mg/day, tab sodium valproate 1gm/day, and tab clozapine 75 mg in two divided doses. Three months after discharge she had

resumed her college studies and had no signs of catatonia. All the medications were gradually tapered and stopped. After 18 months, there were no further relapses.

Discussion

Nearly one-quarter of patients may go into a prolonged phase of catatonia, during which time medications tend to become ineffective. ECT is generally effective for resistant catatonia due to psychiatric conditions like schizophrenia and mood disorder; yet is effective in only 50% of cases with catatonia due to acute neurologic illness. Furthermore, its efficacy decreases in the prolonged phase of illness. This patient had dramatic improvement with rTMS therapy. The dorso-lateral prefrontal cortex is involved in "horizontal modulation" (cortico-cortical circuit) between prefrontal cortex and posterior parietal cortex and "top-down modulation" (cortico-subcortical circuit) between prefrontal cortex and basal ganglia.[5] Both circuits are involved in the initiation, execution, and termination of movement. The affective component of movement, the emotions and behavior associated with it, is governed by the horizontal modulatory circuit. In catatonia, there is dysfunction of these pathways due to deactivation of the prefrontal cortex and subsequent dysfunction of the posterior parietal cortex. The deficits in these regions are explained, although incompletely, on neuro-chemical basis, first, on the basis of response to lorazepam, a GABA-A receptor agonist, and, second, as suggested by functional imaging studies showing impaired modulation of the GABA-A receptor in the prefrontal and posterior parietal cortex. rTMS influences the GABA-ergic pathway through an unknown mechanism and hence is probably a more physiological treatment than ECT, which brings about a non specific excitation and may be harmful in few conditions. Further randomized, controlled trials will determine the role of rTMS in the treatment of catatonia.

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