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Case Report

H-coil repetitive transcranial magnetic stimulation for treatment of temporal lobe epilepsy: A case report

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ABSTRACT

Low frequency repetitive TMS (rTMS) of a cortical seizure focus is emerging as an antiepileptic treatment. While conventional rTMS stimulators activate only superficial cortical areas, reaching deep epileptic foci, for example in temporal lobe epilepsy (TLE), is possible using specially designed H-coils. We report the results of rTMS in a young adult with pharmacoresistant bilateral TLE who underwent three courses (of 10, 15, and 30 daily sessions) of unilateral rTMS over the hemisphere from which seizures originated most often. Seizure frequency was assessed before and after each block of rTMS sessions, as was the tolerability of the procedure. Seizure frequency declined significantly, by 50 to 70% following each rTMS course. All sessions were well-tolerated.

1. Introduction

Transcranial magnetic stimulation (TMS) is a safe and well-tolerated method for noninvasive focal cortical stimulation where small intracranial electrical currents are generated by a rapidly fluctuating extracranial magnetic field [1,2]. Repetitive TMS (rTMS) stimulates the brain with a series of magnetic pulses and has an inhibitory effect on the neuronal activity when applied at a low (≤1 Hz) frequency [3]. Low frequency rTMS applied for 15–30 min can reduce regional cortical excitability, and when targeted to an epileptic focus, this can suppress seizures in patients with neocortical epilepsy [4,5] and interrupt ongoing seizures in status epilepticus [6,7]. However, in patients with temporal lobe epilepsy (TLE), rTMS has failed to achieve reliable therapeutic effects [8], presumably because of its inability to reach a deep-seated seizure focus.

Recently, a special H-coil version was developed to target deep areas of the temporal lobe. Deeper and larger volumes of stimulation can be induced by the unique shape of H-coils containing an array of elements which are contoured to the shape of the skull [9]. The H-coil has been successfully evaluated in terms of safety and efficacy of extratemporal cortical stimulation, is Food and Drug Administration (FDA)-approved for treatment of major depression [10–12], and is undergoing active evaluation in other disease states [13–16]. In the current study, we employed a system, previously tested in a saline phantom model, but not applied clinically, which we specifically adapted for mesotemporal lobe stimulation as an effort to test the safety and efficacy of 1-Hz rTMS in TLE.

Here, we describe a patient with pharmacologically intractable bilateral TLE whose seizures improved after H-coil rTMS. Case details are below.

2. Case report

A 25-year-old woman, cared for at Boston Children's Hospital, presented with initial seizure onset at age 14 years. Her most frequent seizure semiology was characterized by behavioral arrest and staring episodes, occurring initially approximately four times per week, with each seizure lasting 20–30 s. Each seizure was accompanied by a subjective sensation of lost time or confusion. While amnestic for content of individual seizures, the patient was aware that a seizure had occurred and maintained a careful seizure diary. Her ability to identify her own seizures after the fact was confirmed by her family members and periodic video-EEG monitoring during which these seizures were confirmed as epileptic. At the time of her visit, the frequency had since increased to multiple daily seizures. On EEG, she had bilateral independent seizure onsets from the left and right temporal regions. Her seizures persisted

Abbreviations: EEG, electroencephalogram; FDA, Food and Drug Administration; MMSE, Mini-mental State Exam; MRI, magnetic resonance imaging; MT, motor threshold; rMT, resting MT; TLE, temporal lobe epilepsy; TMS, transcranial magnetic stimulation; rTMS, repetitive TMS.

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despite adequate dosing of lamotrigine, levetiracetam, valproate, carbamazepine, and oxcarbazepine.

The patient's workup also included a normal physical exam, normal brain MRI, and EEG which showed interictal spikes in the bilateral temporal regions, and seizures originating as left or right temporal sharply contoured theta slowing progressing to spike and wave in the temporal region of origin before either termination or secondary generalization. Her past medical history was otherwise unremarkable with normal development from birth and normal IQ.

3. Materials and methods

3.1. Timeline

Written informed consent was obtained before recruitment into the trial at Boston Children's Hospital (Boston, MA). During the initial pretreatment phase (baseline, 28 days prior to initiation of rTMS) and following the treatment process (follow-up, 28 days following rTMS), the patient was asked to keep a seizure diary in which she was instructed to record each seizure she experienced. Following each treatment session, safety and tolerability questionnaires were completed by the participant, and the Mini-mental State Examination (MMSE) was administered.

The patient underwent three H-coil rTMS treatment courses between 2013 and 2015. The stimulating coil operates in either sham or verum mode, and for the first course of daily H-coil rTMS, the subject was blinded to the condition. Stimulation for the first course consisted of ten individual sessions. The patient was unblinded as to the condition for the second and third rTMS courses, where active stimulation was delivered for 15 and 30 sessions, respectively.

3.2. Treatment

As seizures arose more often from the right temporal lobe than from the left, the right side was chosen as the therapeutic focus. During each 30-minute daily session, 1800 pulses were applied at 1 Hz using the H12-coil (Brainsway Inc., Jerusalem, Israel; Fig. 1) which was specifically designed for this study with the focus of stimulation over the right temporal region (Fig. 1). The coil was embedded in a helmet that was positioned over the patient's scalp as previously described for the H-coil system [10,12]. While the precise anatomy of the stimulated region is not known, an approximation is that, at 120% of the patient's resting motor threshold (rMT), neural activation is induced mainly over the right temporal lobe, where the field intensity is maximal, and also in prefrontal and parietal regions. Stimulation of the extra-temporal regions is required to induce the broad and deep stimulation with an H-coil.

The patient's rMT, the lowest intensity of stimulation required to elicit a motor response of the finger flexors in 5 out of 10 consecutive trials, was determined by visual inspection of the hand during stimulation. For rMT measures, the coil was tilted such that the stimulating components were displaced rostrally from the temporal region toward the centroparietal area. Once rMT was obtained, the coil was tilted to the prime position with the active portion of the electromagnet over the right temporal region. rTMS was delivered at maximal-tolerated intensities (83%–110% rMT, see Results).

3.3. Patient assessment

At each rTMS session, the patient completed a side effects questionnaire. Specifically, presence and severity of headache, neck pain, and scalp pain/irritation were assessed before and after each rTMS session. In addition, after each rTMS session, the patient reported whether she had trouble hearing, thinking, or concentrating, or had changes in mood, or had any other subjective symptoms compared to before the start of the session.

Fig. 1. Schematic of right hemisphere H12 coil in prime position. Note the relatively broad distribution of the stimulating elements over the right hemisphere.

3.4. Data analysis

The subject maintained a seizure diary and recorded seizures digitally using Seizure Tracker online software (www.seizuretracker.com). All reported seizures were classified as either isolated seizures or seizure clusters. For purposes of analysis, a seizure cluster was defined by a group of seizures with no more than 15 min between each individual seizure. In these instances, the patient was aware that greater than one seizure had occurred but was amnestic for the precise number. Thus, we counted both the standalone seizures and seizure clusters. Results are presented as means ± SEM. Mann–Whitney U test was used to analyze changes in seizure frequency following each rTMS course and to analyze the relapse during follow-up.

4. Results

4.1. Tolerability

Given that the only other FDA-approved H-coil protocol – for prefrontal cortex stimulation – suggests stimulating at 120% rMT, we intended to gradually increase stimulation intensity to 120% of rMT in our patient. However, the stimulation intensity was less than 120% rMT. During the patient's first rTMS course, while rMT was 59% of machine output (MO), stimulation at intensity >49% MO (83% rMT) caused