Brain Stimulation 9 (2016) 960–961

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrnl.com

Letter to the Editor

Deep rTMS for Neuropsychiatric Symptoms of Huntington's Disease: Case Report

Huntington's disease (HD) is an autosomal dominant, progressive, neurodegenerative disorder characterized by abnormal movements, cognitive dysfunction, and prominent neuropsychiatric symptoms. The prevalence of psychiatric symptoms ranges from 33 to 76% causing significant functional impairment and decreased quality of life [1]. Emotional symptoms typically precede the onset of motor symptoms and they are frequently treatment resistant. Suicide continues to be the leading cause of death among individuals with HD, and the presence of depressed mood has shown to be associated with, and predictive of suicidality [2].

We report on the use of deep repetitive transcranial magnetic stimulation (dTMS) in a 77-year-old man with late onset HD and severe, treatment refractory depression (TRD) and generalized anxiety disorder (GAD). Prior to age 70, he was a high functioning attorney with no history of psychiatric symptoms. Over the course of seven years he became progressively overwhelmed at work, reporting worsening depression, anxiety, apathy and suicidal ideation. He failed therapeutic trials with various selective serotonin reuptake inhibitors (SSRIs), a Monoamine Oxidase Inhibitor (MAOI), augmentation with several second-generation antipsychotics, nefazodone, mirtazapine and 16 electroconvulsive therapy (ECT) treatments with no benefits. He was referred for a neurological evaluation of choreoathetoid movements, and was diagnosed with late onset HD, confirmed by genetic testing. Further attempts at pharmacologic treatment included benzodiazepines, SSRIs, antipsychotics, cannabis, and botulinum toxin in the glabellar region without benefit. Aripiprazole was introduced in 2014, which suppressed his abnormal movements with parkinsonian side effects.

An acute series of dTMS was introduced to target symptoms of depression and anxiety after the patient and his family described a significant increase in symptoms and severity over the past two weeks. The patient reported being dissatisfied with his life, stopping activities he was doing previously, having increased problems with memory, feeling worthless, empty, and hopeless. Symptoms of anxiety included persistent worry, rumination, and feeling overwhelmed about finances and other daily tasks. The patient and his family described increased difficulty performing daily tasks and getting in and out of a seated position, feeling exhausted, slow, and stiff upon awakening and throughout the day, and difficulty using his hands to eat.

The patient was administered dTMS using the Brainsway H1 coil over the right dorsolateral prefrontal cortex at 1 Hz and 120% of the motor threshold (54), for 1600 pulses per session. This dTMS treatment location and dosage were chosen due to concern about increasing his profound anxiety and increased seizure risk with high frequency dTMS (>1 Hz). The Geriatric Depression Scale (GDS) was utilized as an objective scale to measure symptoms of depression throughout his dTMS treatment series, and anxiety was measured through patient self-report and family observation report.

Upon completion of 49 daily sessions of dTMS, the patient's depression score fell 12 points from an initial value of 14/15 to 2/15. He reports feeling satisfied with life, regaining energy, increased interest in activities, and no longer feeling that his situation is hopeless, helpless, or feeling worthless. He remains in remission after eight months without maintenance treatments. Per self and family report, cognitive impairments, generalized anxiety and health anxiety improved significantly. Physical pain, headaches and stomach pain improved over the course of dTMS. Abnormal vocalizations and choreiform movements decreased, possibly from aripiprazole. Side effects from dTMS were mild including lacrimation in the right eye and scalp discomfort at the site of the treatment.

The pathological expansion of the cytosine–adenine–guanine repeats in HD results in polyglutamine stretches in Huntington protein causing GABAergic neuronal loss in the striatum [3]. Impaired cortical functioning and plasticity are seen in HD [4], and inhibitory transcranial magnetic stimulation to the supplementary motor area or M1 has demonstrated motor improvements [5,6]. The H coil stimulates a large volume of neurons in the prefrontal cortex with connections to reward circuitry and the basal ganglia [7]. A right sided inhibitory protocol was chosen because of his prominent anxiety. However a left sided high frequency stimulation protocol may have worked as well. Further investigation is warranted.

Acknowledgments

Rebecca C. Fischer, MD and Kathleen Ang-Lee, MD.

Molly Davis
Pacific Center for Neurostimulation, Seattle, WA, USA

Angela Phillips*
Pacific Center for Neurostimulation, Seattle, WA, USA

Department of Nursing, The University of Washington, Seattle, Seattle, WA, USA

Aron Tendler
Brainsway LTD., Jerusalem, Israel

Angela Oberdeck
Pacific Center for Neurostimulation, Seattle, WA, USA

No additional funding was received for this manuscript.

* Corresponding author. 10740 Meridian Ave N, Suite 205, Seattle, WA, USA. Fax: 206-356-1151
E-mail address: AngelaLeahPhillips@gmail.com (A. Phillips)

Received 17 August 2016
Available online 13 September 2016

http://dx.doi.org/10.1016/j.brs.2016.09.002

References

[1] van Duijin E, Kingma EM, van der Mast RC. Psychopathology in verified Huntington's disease gene carriers. J Neuropsychiatry Clin Neurosci 2007;19(4):441–8.
[2] Halpin M. Accounts of suicidality in the Huntington disease community. Omega (Westport) 2012;65:317–34.
[3] Macdonald M. A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. Cell 1993;72(6):971–83.
[4] Crupi D, Ghilardi MF, Mosiello C, Rocco AD, Quartarone A, Battaglia F. Cortical and brainstem LTP-like plasticity in Huntington's disease. Brain Res Bull 2008;75(1):107–14.
[5] Lorenzano C, Dinapoli L, Gilio F, Suppa A, Bagnato S, Currà A, et al. Motor cortical excitability studied with repetitive transcranial magnetic stimulation in patients with Huntington's disease. Clin Neurophysiol 2006;117(8):1677–81.
[6] Brusa L, Versace V, Koch G, Bernardi G, Iani C, Stanzione P, et al. Improvement of choreic movements by 1 Hz repetitive transcranial magnetic stimulation in Huntington's disease patients. Ann Neurol 2005;58(4):655–6.
[7] Roth Y, Zangen A. Reaching deep brain structures: the H-coils. In: Transcranial magnetic stimulation. 2014. p. 57–65.