4 mA Adaptive Transcranial Direct Current Stimulation for Treatment-Resistant Depression: Early Demonstration of Feasibility with a 20-Session Course

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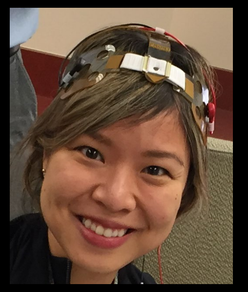

Introduction

Depression is a leading cause of disability worldwide, and 1/3 of patients suffering fail to respond to current treatment options [1-2].

Evidence supporting the use of transcranial direct current stimulation (tDCS) as a treatment for major depressive disorder (MDD) remains inconclusive [3]. One proposed reason is that commonly used treatment protocols fail to deliver enough current to adequately modulate the neural targets [4-5].

Few tDCS studies to date have investigated currents higher than 2.5 mA [6-9].

Methods

- **Design:** Single-blind (rater-blinded) study using 4 mA tDCS as an adjunct to treatment as usual
- **Subjects:** Moderate treatment-resistant MDD (failed 3-6 medications) recruited from the Washington University Treatment-Resistant Mood Disorders Center
- **Device:** tDCS 1x1 model 1300A (Ybrain, Republic of Korea) with adaptive software to briefly "RELAX" stimulation if needed
- **Stimulation:** Twenty sessions of 4 mA stimulation, 20 minutes/session, treatment 5 days/week, cathode target: right lateral prefrontal cortex, anode target: left lateral prefrontal cortex
- **Measures:** Depression rating scales (MADRS, HAMD-17, QIDS-SR), other cognitive & emotional scales (HAM-A, CGI, MOCA, NIH Toolbox, Q-LES-Q) and visual analog scale (VAS) pain ratings.

Results

Two subjects (n=2) enrolled thus far and have completed the full course of treatments. Both patients had MDD as confirmed by Mini-International Neuropsychiatric Interview (MINI). Demographics and outcome measures outlined in Table 1.

Demographics	Patient 1	Patient 2
Age	56	58
Gender	M	M
Failed Medication Trials	4	5
MADRS Change (Pre to Post, %)	↓100%	↓61%
Change in Q-LES-Q (Pre to Post)	↑59%	↑37%
Average Pain VAS	1.1	1.6
Max Pain VAS	3	3
Total Times Utilizing Adaptive Ramp-Down	0	0
NIH Toolbox Z-Score Change, Fluid Intelligence	↑1.1	↑0.8
NIH Toolbox Z-Score Change, Crystallized Intelligence	↑0.2	↔0
HAMD Change (Pre to Post, %)	↓100%	↓41%
QIDS-SR Change (Pre to Post, %)	↓100%	↓64%
HAM-A Change (Pre to Post, %)	↓100%	↓50%
CGI-S Baseline to Final Score	4 → 1	4 → 3

Table 1. Demographics & outcome measures. Changes are represented as a percent change from the baseline score to the immediate post-stimulation score. Green boxes = improvement in symptoms.

Tolerability: Patients noted scalp pain and tingling during stimulation. No headaches, scalp burns, dizziness, or other side effects were noted. Pain VAS scores never exceeded 3/10 and neither patient used the "RELAX" adaptive ramp-down feature (Table 1).

FIBSER scale of side effect burden was consistent with minimal to mild level of impairment from treatment.

Safety: Physical and neurologic exams conducted weekly demonstrated no changes. No serious adverse events occurred during the stimulation course.

Efficacy: Both patients demonstrated robust improvement in depression by the 10th stimulation session (2 weeks of treatment) that continued at the 20th session (4 weeks). 1 of 2 patients had partial relapse of symptoms by 2 weeks post-stimulation (Figure 1). Improvements were also noted in anxiety (HAM-A), quality of life (Q-LES-Q), and NIH Toolbox cognitive measures of fluid intelligence.

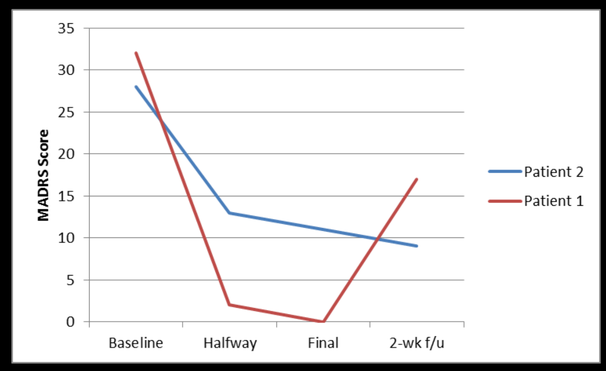

Figure 1. MADRS scores.

Discussion & Conclusion

- Use of 4 mA tDCS appears to be well-tolerated, safe, and potentially efficacious in the treatment of major depressive disorder
- Cognitive benefits most pronounced in working memory and processing speed testing were also noted in both subjects
- Randomized, double-blind, sham-controlled trials will be necessary to further investigate these findings
- Future studies should focus on achieving higher "doses" of tDCS to maximize benefits in patient populations

Disclosures

Dr. Marom Bikson is a stock/shareholder in Soterix Medical. There are no other relevant disclosures.

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