What is the role of autonomic activity in the treatment of depression with subcallosal cingulate deep brain stimulation?

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BACKGROUND

Major Depressive Disorder is associated with aberrant autonomic function as determined by cardiac vagal control and indexed by a reduction in resting state heart rate variability (HRV) (Bassett et al., 2016).

Mayberg et al. 2005 targeted the subcallosal cingulate (SCC) with deep brain stimulation (DBS) and produced clinical benefit in patients with treatment resistant depression as determined by a decrease in Hamilton Depression Rating Scale (HDRS-17).

The SCC is part of the central autonomic network, which is involved in vagal function and cardiac regulation (Lane et al., 2013; Riva-Posse & Mayberg 2014).

SCC DBS may impact autonomic function. We hypothesize an increase in HRV and a decrease in clinical symptoms with SCC DBS.

OBJECTIVES

• Does SCC DBS have an effect on cardiac vagal control (HRV) and depressive symptoms (HDRS-17) across treatment?

• Does the magnitude of change in HRV and depressive symptom severity correlate across treatment?

METHODS

Subjects: Nine subjects with treatment-resistant major depressive disorder received neurosurgical implantation of two leads in the subcallosal cingulate cortex; Clinical Trials ID: NCT01984710


b. Respiration and EKG recorded at a rate of 1000 samples per second during each time point.

c. HDRS-17 acquired at each timepoint.

d. Conditions (3-5 minutes each): i. DBS ON, DBS OFF

EKG Preprocessing and HR extraction: Low-pass filter (50Hz) applied to EKG. R-spikes identified and heartbeat interval (IBI) series extracted in QRSTool®. The root mean square of successive differences between adjacent r-spikes was calculated to reflect vagal influence on heart rate (RMSSD).

EKG

LEFT VENTRICLE

Figure 1: a. Change in Symptoms Over Time (HDRS-17) b. Change in RMSSD Over Time (RMSSD)

FIGURES

1a. Subjects exhibited a significant increase in HDRS-17 from Baseline to Week 24 of SCC DBS (df = 8, 48.27, As). Table 1a.

1b. Subjects (stimulation off) did not exhibit a statistically significant difference in HDRS from Baseline to Week 24 (df = 8, 48.27, p = 0.0421).

2a. Subject 5 exhibited the expected increase of vagal function (RMSSD) with treatment resistant depression (HDRS, As) significantly. Table 2a.

2b. Subject 5 exhibited a negative correlation between RMSSD and HDRS (r = -0.442).

3a. Subjects (stimulation on) did not exhibit a statistically significant difference in HRV from Baseline to Week 24 of SCC DBS (df = 8, 48.27, p = 0.0421).

3b. Subject 2 exhibited a negative correlation between HRV and HDRS (r = -0.6047, p = 0.5621).

4a. Change in Symptoms Over Time (HDRS-17) b. Change in RMSSD Over Time (RMSSD)

4b. Change in HRV did not predict change in HDRS (r = 0.064, p = 0.4530).

4c. Change in RMSSD did not predict change in HDRS (r = 0.126, p = 0.224).

5a. Subjects exhibited a significant increase in HDRS-17 from Baseline to Week 24 of SCC DBS (df = 8, 48.27, p = 0.0421).

5b. Subjects (stimulation off) did not exhibit a statistically significant difference in HRV from Baseline to Week 24 (df = 8, 48.27, p = 0.0421).

DEMOGRAPHICS

Table 1: a. Change in Symptoms Over Time (HDRS-17) b. Change in RMSSD Over Time (RMSSD)

FUTURE DIRECTIONS

Investigate long-term effects of SCC DBS on autonomic adaptability and mood in depressed individuals.

Record ambulatory cardiac activity in naturalistic settings with ecological momentary assessment.

Optimize stimulation treatment parameters with real-time heart rate variability biofeedback.