Introduction

Background
Parkinson's disease (PD) is a neurodegenerative neurological disorder resulting from progressive cell death of dopamine neurons in the basal ganglia. Damages to neurons in the basal ganglia can negatively affect voluntary movements in different parts of the human body. When these movement disorders affect the voice control system, the patients start to develop voice disorders. The effect of PD on voice has primarily been associated with reduced loudness (hypoaesthesia) and reduced vocal pitch range, which appear to have a sensory contribution. Recent studies have suggested that PD can impair voice motor control and adaptation mechanisms [1-3]. Deep brain stimulation (DBS) is a common treatment of general motor impairment in PD, although its effect on voice has been reported to be highly variable [4-9].

Objective
The present study was a systematic investigation toward understanding the effect of DBS on voice production and motor control mechanisms. Our goal was to use objective measures of voice production and motor to address the following questions:
1. How does DBS affect voice production and motor control?
2. What are the neurophysiological correlates of DBS effect on voice?

Deep Brain Stimulation (DBS)
DBS is a neurological procedure involving the implantation of a neurostimulator (brain pacemaker) through electrodes, to specific brain areas for the treatment of movement and affective disorders. DBS has been used for treatment of Parkinson's disease, essential tremor, dystonia, chronic pain, major depression and obsessive-compulsive disorder (OCD).

Experimental Task and Results

Experimental task:
10 patients with Parkinson's disease with STN-DBS implantation repeated steady vocalizations of the vowel sound /a/. During vocalizations, a randomized (up or down) pitch-shift stimulus perturbed voice auditory feedback at 100 cents. Patients were tested in two blocks of DBS ON and OFF.

EKG Data Analysis:
EKG data was recorded from 64 channels. Results of the analysis indicated a significant suppression of Beta (13-30 Hz) and Gamma band power (30-50 Hz) for DBS ON vs. OFF. The suppression of Beta band power was significantly correlated with enhanced magnitude of voice motor control response to auditory feedback perturbation.

Effects of DBS on Voice Motor Control:
All subjects controlled their voice by producing compensatory responses that changed their vocal pitch in the opposite direction to auditory feedback perturbation. DBS ON did not modulate the magnitude of vocal compensation in response upward pitch-shift stimulus compared with DBS OFF condition (Figure 3a).

DBS ON resulted in significantly larger (p<0.05) vocal compensations in response downward pitch-shift stimulus compared with DBS OFF condition (Figure 3b).

DBS significantly reduced variability in pitch frequency (p<0.05), as indexed by lower jitter during DBS ON compared with DBS OFF condition (Figure 4).

DBS did not have an effect on voice pitch, intensity, harmonic-to-noise ratio (HNR) and shimmer (intensity variability).

Effects of DBS on Voice Motor Parameters:
Figure 5: Time-frequency plots of neural activity along with error bars indicating Beta band power power suppression in response to upward and downward pitch-shift stimuli in voice auditory feedback. C) Shows the correlation between modulation of Beta band power and magnitude of vocal responses to pitch perturbation in the auditory feedback.

Discussion
We propose that our findings support the following notions:

STN DBS has a positive impact on the mechanisms of voice motor control by helping individuals better control their vocal pitch during downward pitch-shift stimulus and in response to auditory feedback perturbation.

This notion is corroborated by our findings indicating that PD patients exhibited a significantly larger compensatory vocal pitch response to auditory feedback perturbation, and that general vocal pitch variability (jitter) was reduced for DBS ON vs. OFF condition.

DBS effect on voice control was significant only when patients increased laryngeal motor activity to raise pitch in response to downward pitch-shift stimuli.

We found a differential effects of DBS on vocal responses to upward and downward pitch perturbations in the auditory feedback, suggesting that the mechanisms that drive vocal folds muscle contraction (raising pitch) and relaxation (lowering pitch) are not equally facilitated by DBS.

The DBS-induced suppression of Beta band neural activity is a neurophysiological biomarker of improved voice motor control ability in patients with Parkinson's disease.

These findings are consistent with previous studies [10,11] and provide new insights into the neural mechanisms that incorporate auditory feedback for voice motor control.

Acknowledgement
This work was supported by the National Institute of Health, Grant Numbers: K23DC00589 and R01DC04290.

References