Pallidal Deep Brain Stimulation Disrupts Phase Coherence Between Globus Pallidus and Primary Motor Cortex in Parkinson's Disease

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Introduction

Perturbations in synchronized oscillatory activity in brain networks are increasingly recognized as important features in movement disorders. In Parkinson's Disease (PD), dopamine replacement and DBS therapy reduce the resting state amplitude of beta band (13-30 Hz) oscillatory activity in the subthalamic nucleus (STN), and these reductions correlate with improvements in bradykinesia and rigidity (Brown et al., 2001).

The globus pallidus is a commonly used target for deep brain stimulation (DBS) in Parkinson's disease (PD). Consistent with the evolving theory of excessive beta oscillatory activity in PD, several studies have shown higher resting state beta band oscillatory activity in the GP of PD compared to non-parkinsonian conditions (Silberstein et al. 2003, Weinberger et al., 2012). However, the effects of pallidal DBS on basal ganglia and cortical oscillations are unknown.

Objectives

1) Evaluate pallidal and cortical oscillatory activity in akinetic-rigid PD and in a nonparkinsonian disorder, isolated dystonia.

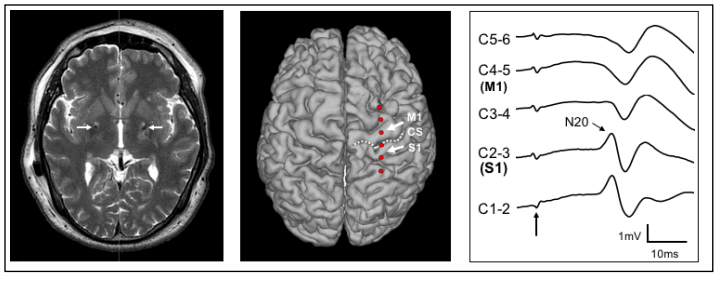
2) Find disease-specific pallidal and pallido-cortical oscillatory activities

3) Examine the effect of therapeutic pallidal stimulation on these oscillatory activities

Methods

Resting state pallidal local field potentials (LFP) were recorded intraoperatively from DBS electrodes in 20 akinetic-rigid PD and 14 primary isolated dystonia patients in the awake state.

Subdural ECoG strip was temporarily placed in the primary motor cortex (M1). Localization is confirmed anatomically and using reversal of the N20 wave from the somatosensory evoked potential (SSEP).



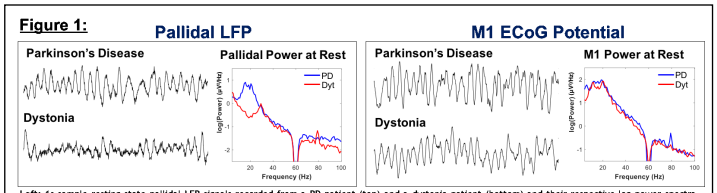
Data were processed and analyzed offline in MATLAB. Data were down sampled to 1 KHz.

Recordings were performed in two conditions. 1) During rest and 2) During the movement task, patients performed flexion-extension of the elbow or an iPad tapping task.

Power spectral density (PSD) and Coherence were calculated using Welch's periodogram method.

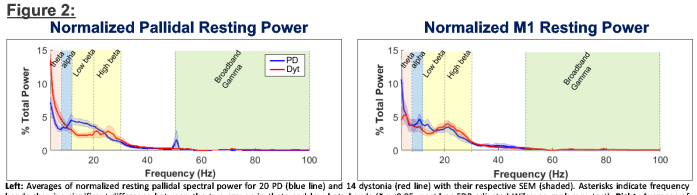
Results

Figure 1:



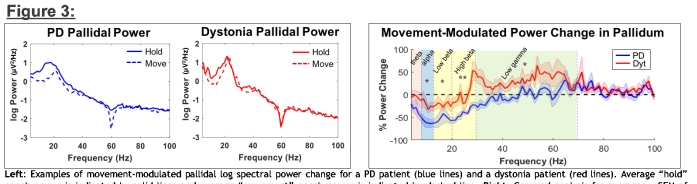
Left: 1s sample resting state pallidal LFP signals recorded from a PD patient (top) and a dystonia patient (bottom) and their respective log power spectra. Right: 1s resting state M1 ECoG potential recorded and log power spectral from a PD patient (top) and a dystonia patient (bottom).

Figure 2:



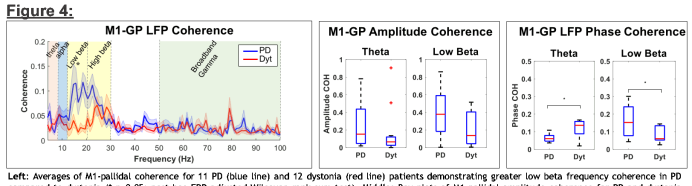
Left: Averages of normalized resting pallidal spectral power for 20 PD (blue line) and 14 dystonia (red line) with their respective SEM (shaded). Asterisks indicate frequency bands showing significant difference between the two groups in theta and low beta bands (* p<0.05; post-hoc FDR-adjusted Wilcoxon rank sum test). Right: Averages of normalized resting M1 spectral power for 11 PD (blue line) and 12 dystonia (red line) with their respective SEM (shaded) demonstrating no differences in spectral power.

Figure 3:



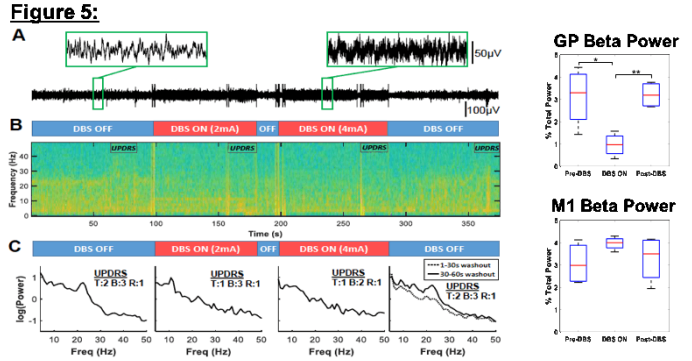
Left: Examples of movement-modulated pallidal log spectral power change for a PD patient (blue lines) and a dystonia patient (red lines). Average "hold" epoch power is indicated by solid lines and average "movement" epoch power is indicated by dashed line. Right: Grouped analysis for averages ± SEM of movement-modulated power changes in the pallidal LFP for 7 PD patients (blue line) and 10 dystonia patients (red line) who underwent an arm movement task (* p<0.05, **p<0.01; post-hoc FDR-adjusted Wilcoxon rank sum test).

Figure 4:



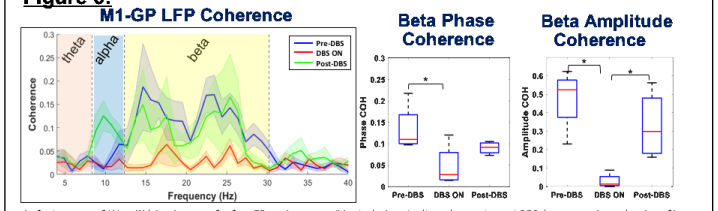
Left: Averages of M1-pallidal coherence for 11 PD (blue line) and 12 dystonia (red line) patients demonstrating greater low beta frequency coherence in PD compared to dystonia (* p<0.05; post-hoc FDR-adjusted Wilcoxon rank sum test). Middle: Box plots of M1-pallidal amplitude coherence for PD and dystonia patients showing no difference across theta or beta frequency bands. Right: Box plots of M1-pallidal phase coherence for PD and dystonia patients showing greater phase synchrony in theta frequency in dystonia and low beta frequency in PD (* p<0.05; post-hoc FDR-adjusted Wilcoxon rank sum test).

Figure 5:



A) Pallidal LFP pre, during, and post pallidal DBS stimulation. B) Time-frequency spectrogram showing power changes different stimulation conditions. UPDRS boxes indicated periods of clinical testing. C) Log power spectra of pallidal LFPs recorded during different conditions. T=tremor; B=bradykinesia; R=rigidity. D) Comparison of four PD patients during DBS OFF/ON recordings showed decreased total beta power in the DBS ON and compared to pre-DBS and post-DBS states (*p<0.05; repeated measure ANOVA). E) GPi DBS had no effect on M1 beta power.

Figure 6:



Left: Averages of M1-pallidal coherence for four PD patients pre- (blue), during- (red), and post- (green) DBS demonstrating reduction of beta coherence during GPi DBS. Box plots of averaged beta phase (middle) and amplitude (right) coherence pre-, during-, and post-DBS (*p<0.05; repeated measure ANOVA).

Conclusions

- **PD patients had elevated resting pallidal low beta band power compared to dystonia patients, whereas dystonia patients had elevated resting pallidal theta band power compared to PD.**
- **PD patients demonstrated relatively elevated phase coherence with the motor cortex in the beta band**
- **Dystonia patients had greater theta band phase coherence.**
- **Pallidal beta power and pallido-M1 beta coherence was reversible reduced by pallidal DBS in PD**

Our results support the hypothesis that specific motor phenomenology observed in movement disorders are associated with elevated network oscillations in specific frequency bands, and that DBS in movement disorders acts in general by disrupting elevated synchronization between basal ganglia output and motor cortex.

References

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