Subthalamic Local Field Potentials in Parkinson's Disease and Isolated Dystonia: An Evaluation of Potential Biomarkers

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Introduction

Subthalamic nucleus (STN) local field potentials (LFP) in PD patients show prominent beta (13-30 Hz) oscillatory activity, whose amplitude is suppressed by levodopa and by STN deep brain stimulation (DBS) in a manner that correlates with symptom improvement. This has led to the hypothesis that STN beta band oscillations may contain biomarkers diagnostic of the parkinsonian state, and that these features could be used for potential control signals for closed-loop DBS (Little et al., 2013).

Specific features of the STN LFP that have been proposed as potential diagnostic parkinsonian biomarkers include beta band power (Little et al., 2013) and coupling of beta phase to the amplitude of high frequency oscillations (HFOs, 250–350 Hz). However, STN LFP characteristics in non-parkinsonian conditions have rarely been studied and never compared directly to those of PD patients.

Objectives

Resting state STN LFPs in PD and isolated dystonia will be distinguished by one or more of the following:

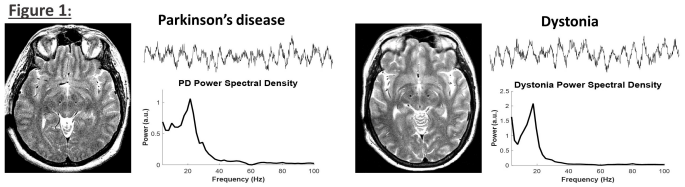
- ***Difference in spectral power in a physiologically relevant band – alpha, low beta, high beta, broadband gamma***
- ***Cross frequency interactions such as phase amplitude coupling***

Methods

To compare resting state LFP features in PD and isolated dystonia and evaluate disease-specific biomarkers, we recorded subthalamic LFPs from 28 akinetic-rigid PD and 12 isolated dystonia patients during awake DBS implantation. Spectral power and phase-amplitude coupling characteristics were analyzed.

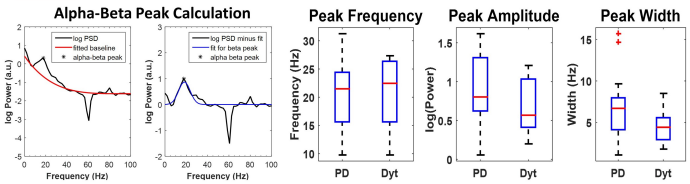
Results

Figure 1:



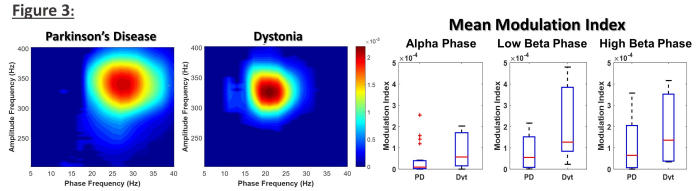
Left: Axial T2 weighted MRI showing bilateral DBS lead locations for a patient with PD (left) and dystonia (right). **Top:** one second sample resting state raw LFP signal. **Bottom:** Corresponding power spectra of a 30 second resting state LFP recording from top.

Figure 2:



Left: The log spectral power (excluding the alpha-beta range) is fitted using a polynomial function to find the power baseline (red line). The resulting alpha beta peak is then fitted using Gaussian function (blue line). The power peak is indicated by *. **Right:** Boxplots (median and 25-75th quartiles) showing characteristics of the alpha-beta peak frequency, amplitude, and width. There was no statically significant difference between PD and dystonia (PD vs. dystonia: frequency: p=0.7552; amplitude: p=0.0954; width: p=0.1077; Wilcoxon rank sum test.)

Figure 3:



Left: Comodulograms calculated by finding the modulation indices between phase of the low frequency (5-40 Hz) and amplitude of high gamma (200-400 Hz) frequency. Warmest colors represent the strongest coupling. **Right:** Boxplots of mean modulation indices in subjects who had detectable PAC (19/28 PD patients, 6/12 dystonia patients). There was no significant difference between groups (PD vs. dystonia: alpha: p= 0.4011; low beta, p=0.2035; high beta p=0.3547; Wilcoxon rank sum test).

	PD	Dystonia
N	28	12
Age (mean ± SD)	59 ± 10 yr	53 ± 15 yr
Gender	23 M, 5 F	7M, 5F
Disease duration (mean ± SD)	11 ± 4 yr	15 ± 11 yr
Target side	12 Left; 16 Right	6 Left; 6 Right
Preop Motor Score	44 ± 19[a]	16 ± 7[1] 14 ± 5[2]

Conclusions

- Direct comparison of STN LFPs in PD and isolated dystonia showed that in 26/28 PD and 11/12 isolated dystonia patients, the LFP power spectrum had a peak in the beta frequency range, with similar amplitudes between groups.
- Cross frequency interactions between beta phase and high frequency oscillations revealed significant interactions in 19/28 PD and 6/12 dystonia recordings without significant differences in maximal coupling.
- These features of beta oscillations recorded in the STN LFP may be important in the pathophysiology of basal ganglia disorders, but are not specific diagnostic biomarkers for the parkinsonian state.

Acknowledgement

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