Comparison of GPi Local Field Potential Characteristics in Patients with Parkinson's Disease, Craniocervical Dystonia, and Generalized Dystonia

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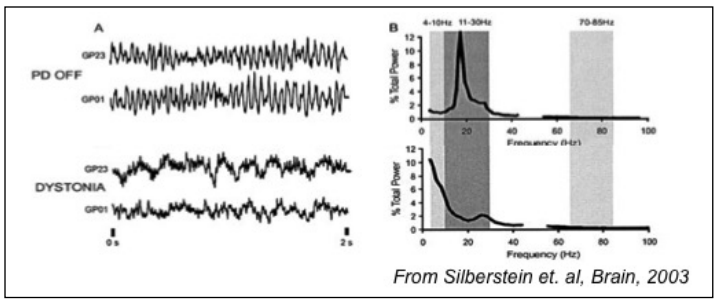
Introduction

Excessive beta (11-30Hz) synchronization has been observed in Parkinson's disease (PD) in the subthalamic nucleaus (STN) and globus pallidus internus (GPi), and is theorized to be a major component in the pathophysiology of movement disorders, as it limits the space available for information coding through spatial selectivity and temporal patterning. One study suggests that this excessive synchronization in the beta band is a distinct marker for the Parkinsonian state, as dystonia patients show greater power in the alpha frequency (4-10Hz), and less power in the beta band (Silberstein et. al, 2003).



From Silberstein et. al, Brain, 2003

In addition, cross frequency interactions between beta phase and high frequency gamma amplitude in basal ganglia LFPs have been proposed as a biomarker of the Parkinsonian state (Lopez-Azcarate et al., 2010; Connolly et al., 2015). Characterizing the differences in abnormal synchronization will give us further insight into network pathophysiology among different disease states.

Methods

Resting state GPi LFPs were recorded intraoperatively from DBS electrodes in 14 PD patients, 7 patients with craniocervical dystonia, and 4 patients with generalized dystonia in the awake state. Power spectral density (PSD) for each recording was computed using a fast Fourier transform (Welch method). Alpha-beta power characteristics were calculated by subtracting a fitted baseline from the log of the power spectrum, followed by fitting the difference using a Gaussian function. Calculated phase-amplitude interactions (PAC) between the amplitude of high frequency activity and alpha-beta phase as previously described (Lopez-Azcarate et al., 2010).

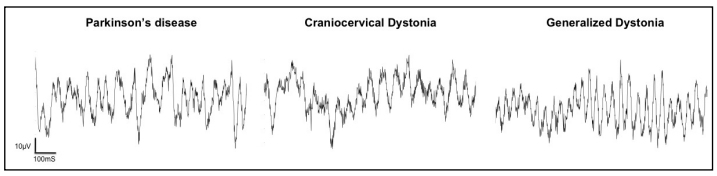
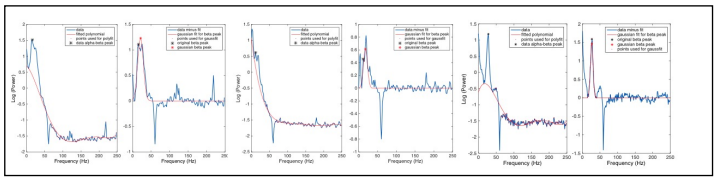


Figure 2

Results

Figure 1



Peak power analysis showing presence of spectral power increase in beta frequency. Left panels show log LFP power spectral density (blue line) with background power fitted using a polynomial function (red line). Right panel shows power peak graph (blue line) calculated by subtracting the baseline power and fitted using a Gaussian function (redline).

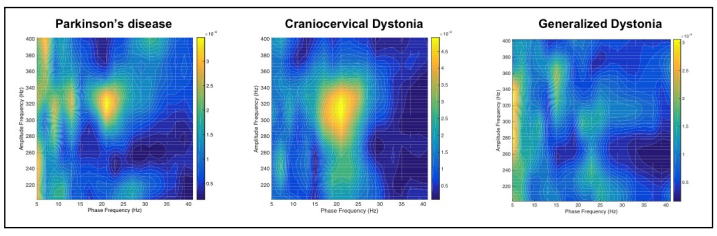


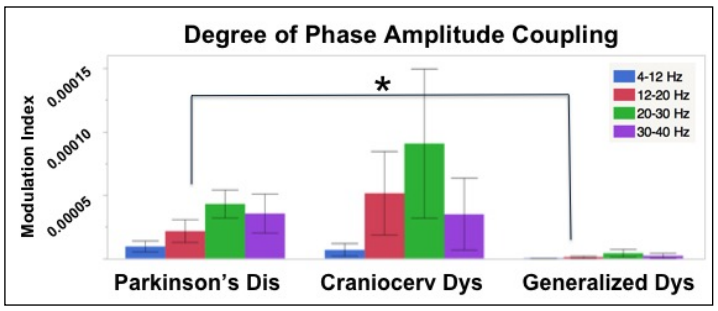
Figure 3

Summary

Comodulograms calculated by finding the modulation indices between phase of the alpha-beta band (5-40 Hz) and amplitude of high gamma (200-400 Hz) frequency. Warmest colors represent the strongest coupling.

	Parkinson's Disease	Craniocerv. dystonia	Generalized dystonia
N	14	7	4
Beta peak freq (hz)	19.0 ± 5.8	21.3 ± 6.7	18.6 ± 9.1
Beta peak amp (log a.u)	0.9 ± 0.4	0.7 ± 0.4	0.9 ± 0.5
Beta peak width (hz)	5.2 ± 2.5	4.5 ± 2.0	3.5 ± 1.9

GPi LFPs demonstrated similar peak frequencies, amplitudes, and widths for the alpha-beta spectral peak in PD, craniocervical dystonia, and generalized dystonia patients ($p>0.05$ for all groups).



Calculated modulation indices showing prominent high frequency amplitude coupling to beta phase for all disease states. PD patients show greater degree of PAC in the low beta frequency phase compared to those of generalized dystonia patients ($p=0.04$)

Conclusions

- Direct comparison of GPi LFPs in PD, craniocervical, and generalized dystonia shows that all patients have peak spectral power in the beta band, casting doubt on the view that excessive beta band power is a specific biomarker of the parkinsonian state.
- Cross frequency interactions are also found in GPi and are not specific for disease state.
- The study reveals potential similarities between abnormal neural network activity and synchronization in PD and dystonia.

References

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Lopez-Azcarate J, Tainta M, Rodriguez-Oroz MC, Valencia M, Gonzalez R, Guridi J, Iriarte J, Obeso JA, Artieda J, Alegre M. Coupling between beta and high-frequency activity in the human subthalamic nucleus may be a pathophysiological mechanism in Parkinson's disease. Journal of Neuroscience. 2010;30(19):6667-77.

Connolly AT, Jensen AL, Bellow EM, Netoff TI, Baker KB, Johnson MD, Vitek JL. Modulations in oscillatory frequency and coupling in Globus Pallidus with increaseing Parkinsonian severity. Journal of Neuroscience. 2015 35(15): 6231-40.