Quantitative electroencephalogram as an objective biomarker of deep brain stimulation

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Introduction

DBS leads are often programmed for individual patients using qualitative data points such as differences in motor function following the stimulation of certain regions of the brain. This has proven to be a highly effective way to make sure the leads of the DBS are placed in the proper locations and to determine which contacts to use in long term stimulation. Sometimes, however, the brain responds to stimulation inconsistently and relying on the patients' visible changes in motor function alone can be not only confusing but also subject to error, resulting in sub-optimal performance of the DBS. This becomes more critical in newer targets such as cognitive nuclei where there is no immediate behavioral response. Thus, we hypothesized that if we stimulate certain contacts in particular nuclei of the brain, then this will create a Quantitative Electroencephalogram (QEEG) signature of stimulation associated with those nuclei. In addition, we will be able to differentiate between the effective and ineffective contacts within the target area, which can be used as reliable markers for future Deep Brain Stimulation (DBS) brain mapping. The analysis of this QEEG data during the electrode mapping sessions, in addition to motor responses, will provide objective, consistent, and useful data so as to provide each patient with individualized stimulation locations that maximize the efficacy of their DBS.

Methods

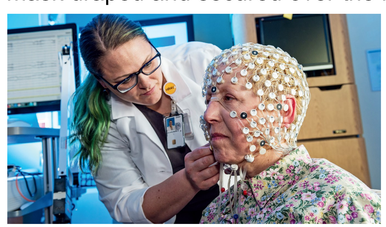
- Subjects: Patients that have been implanted with DBS and are returning for programming were offered participation in this study. Inclusion criteria include patients who have an existing DBS and are capable of giving informed consent. Patients with Parkinson's disease and essential tremor who were implanted with DBS leads in three different brain nuclei: globus pallidus interna (Gpi), subthalamic nucleus (STN), and ventral intermediate (VIM) thalamus.
- Experimental setup: Patients were fitted with a EEG cap that contains 256 electrodes (Fig 1) suspended in an elastomer mask draped and secured over the head (Geodesic).
- 

Fig. 1. Patient setup of the dense array (256 electrode) cap. Photo published in NEXT MCV magazine (Winter 2018-2019)

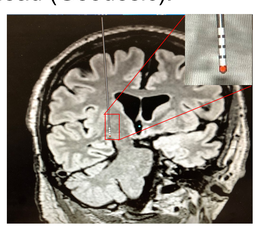


Fig. 2. Representative MRI of a DBS patient showing the location of the DBS lead in the GPi. Inset: magnified DBS lead

- Data collection: Dense array EEG was recorded during a resting condition under the following conditions 1) on and off optimal settings at rest 3) Separate activation of the contacts not in clinical use with both optimal frequency.
- Data Processing: The background activity was initially screened/ corrected for any non-physiologic artifacts, power line interferences, baseline wandering, and movement artifacts.
- Filtered data was then epoched based on stimulation configuration.
- General processing: Power spectral density (PSD), time-frequency analysis, coherence, topographical plots, and source localization at different time points of the recording will be assessed
- Various supervised and unsupervised machine learning algorithms were employed to classify different patient categories.

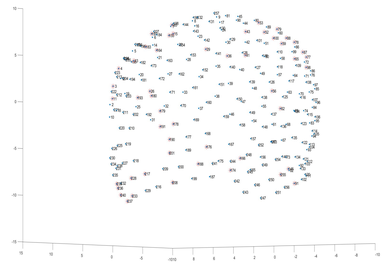


Figure 3: Location of Dense Array Electrodes. This image is a 2D rendering of a 3D model of the 256 dense array electrodes on the cap that was placed on each patient

Results

Discriminate between DBS ON and DBS OFF state

Algorithm	Train Accuracy	Class Precision		Class Recall		Test Accuracy
		DBS_ON	DBS_OFF	DBS_ON	DBS_OFF	
LR	92.00	94.59	89.47	89.74	94.44	97.22
DL	97.33	97.44	97.22	97.44	97.22	100

Table 2: Results for Supervised ML Techniques: The data above proved that it is possible to distinguish between ON and OFF state with 100% accuracy using Deep Learning and 97.22% accuracy using Logistic Regression

Cluster	Count from each target	
	DBS ON	DBS OFF
Cluster 0	57	0
Cluster 1	0	4
Cluster 2	0	50

Table 2: Results for Unsupervised ML Techniques: The data above indicated that not only can the software distinguish ON vs. OFF, but also it can subclassify the ON and OFF data into clusters.

Topographical plots of EEG activation in different locations

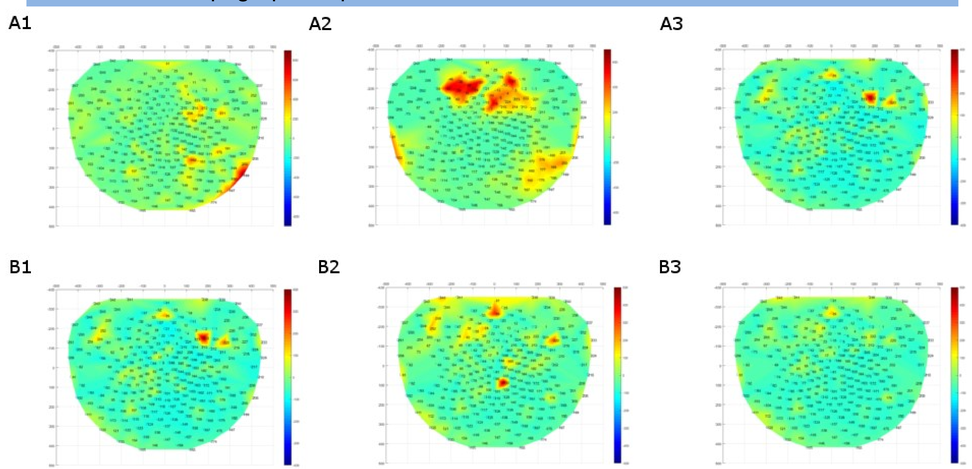


Figure 4: These topographical plots of QEEG data represent DBS in various nuclei of 3 different patients. Gpi (A1), STN (A2), VIM (A3) while stimulating the optimal contact 1,2 (B1), contact 0 (B2), contact 3 (B3)

Classifier for inter-nucleus discrimination

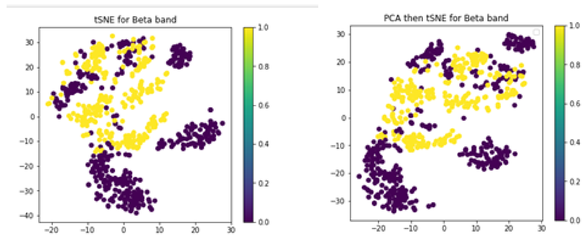


Figure 5: This figure represents a clustered data set of beta band (12-30 Hz) activity of GPi (yellow) and Non-GPi (purple).

Summary of Results

1. Most of the patients were able to tolerate long term OFF stimulation state indicating the feasibility of the recording paradigm.
2. Using our ML algorithms on EEG based beta modulation, we were able to differentiate between On and OFF state of stimulation (Table 1 and 2).
3. Beta modulation topographical subtraction map demonstrates differential unique activation patterns in different nuclei (Fig 4)
4. Despite the relative proximity of these contacts, their differential activation resulted in clearly different cortical beta activity, suggesting that the EEG may be useful in differentiating the utility of each contact within a lead (Fig 4, B).
5. EEG features from the dense array were extracted using ML and tested to provide 75% test accuracy for inter-nucleus classification.
6. Further classification tended to cluster all of the beta features of GPi patients together but doesn't efficiently separate them from non-GPi patients (fig 5). Further pre-processing and normalization of data is needed for robust classification.

Conclusions

This study demonstrated that electrical stimulation of various nuclei generates EEG activation patterns which are unique to the sub-circuitry activated by the DBS. Thus, these topographical patterns can be used as a biomarker to identify the stimulation location. This is particularly important for confirming novel stimulation targets. However, a robust classifier would require a more comprehensive pattern analysis sand feature extraction.

Acknowledgements

I would like to thank my PI Dr. Kathryn Holloway. I would also like to thank Dr. Deepak Kumbhare, as well as Dr. Milos Manic's team for analyzing and testing the ML classifiers for this EEG data. I would also like to thank Dr. Ken Ono, and Rachel Van Aken for their help with data acquisition and patient setup. This project would not have been possible without their guidance and mentorship.