Predictive Modeling the Effect of Neurostimulation on Memory Biomarkers in Epileptic Patients

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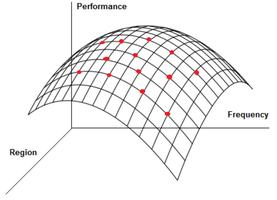
Rationale

Many epileptic patients suffer from memory dysfunction. Neurostimulation has emerged as a novel treatment option for seizure control in patients with medically refractory epilepsy, and it has the additional potential to enhance memory in these patients. One of the first challenges to enhance memory using neurostimulation is to identify optimal stimulation parameters. We present a modeling approach to predict the effect of different stimulation parameters and locations on memory biomarkers.

Methods

- 64 patients undergoing intracranial EEG
- Experimental sessions of free recall memory tasks
- Calculated EEG band power, memory performance fed into classifier
- Classifier used to produce scalar biomarker measure of performance
  - Positive => enhanced memory
  - Negative => diminished memory
- In each experiment, different brain region stimulated
- Stimulation parameter grid search:
  - Frequency: pulse (P), 10, 25, 50, 100, 200Hz
  - Amplitude: 0.25-3.0mA, 0.25mA steps
  - Duration: 250, 500, or 1000ms.



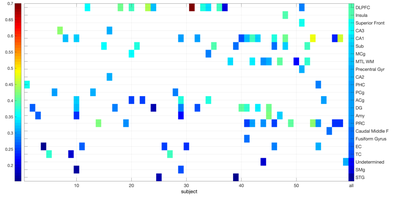
- Each stimulation recorded: pre-stimulation biomarker, frequency, duration, amplitude, and post-stimulation change in biomarker
- Each location: fit linear least-squares model to predict change in biomarker from combination of pre-stimulation biomarker and stimulation parameters

In the first analysis, we looked at prediction using stimulation alone, pre-stimulation biomarker, and a combination. Mean squared error (MSE) between predicted and actual biomarker change was used to judge performance with leave-one-out cross-validation.

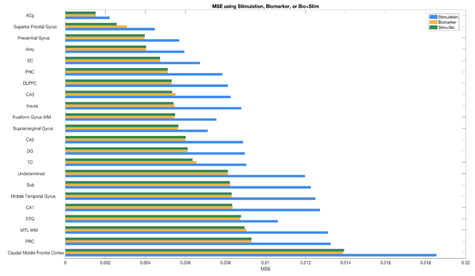
In the second analysis, we looked at the influence each predictor had on change in biomarker by examining the t-stat p-value of each term after fitting the model. We again used MSE but with k-folds (k=30) cross-validation.

Results

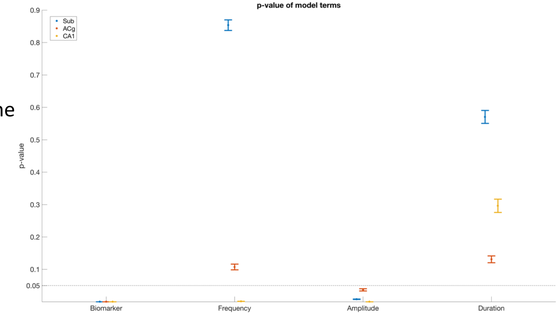
- 21 unique anatomic locations
- Not all subjects able to complete same sequences so sparse grid sampling
- 81,716 total stimulation observations



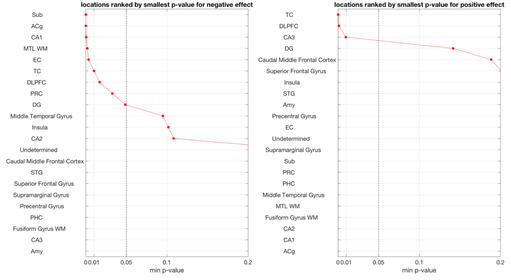
The location (y-axis) sampling across subjects (x-axis). Colored squares indicate r^2 of linear model from data sampled.



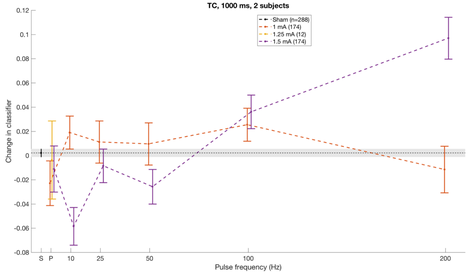
The predictability of the post-stimulation changes in the memory biomarker as a function of the anatomical location, stimulation parameters, and the biomarker before stimulation. X-axis MSE, Y-axis location. Combining stimulation parameters and the pre-stimulation value of the biomarker (green) is the best predictor of the changes in the memory biomarkers after stimulation.



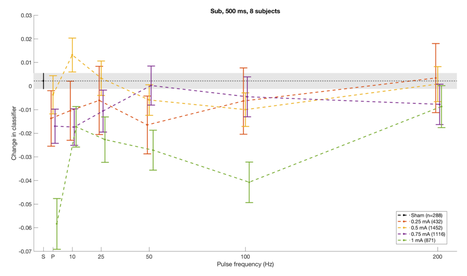
The influence that each of the predictors has on change in biomarker at three locations. The biomarker itself is most significant followed by amplitude, while duration appears to have no significant influence.



The ranking of each location by effect size and direction (positive, negative). Most significant negative effect was in the Subiculum (Sub) while the most significant positive effect was in the Temporal Cortex (TC).



The results from stimulating in the Temporal Cortex (TC) for 1000ms duration at various amplitudes (trend lines) and frequencies (x-axis) and the resultant change in biomarker classifier performance (y-axis, mean and standard error bars). Stimulation at 1.5 mA (purple) appears to have an interesting effect with respect to frequency.



The results from stimulating in the Subiculum (Sub) for 500ms. Interesting effects are observed for 1mA (green).

Conclusions

This presents a predictive modelling approach for exploring the effects of stimulation on electrophysiological biomarkers of cognitive performance in epileptic patients. Preliminary results indicate certain locations and stimulation parameters have more influence. These findings will inform subsequent experiments to determine potential anatomical targets and interesting areas in the neurostimulation parameter space.

Acknowledgement

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