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

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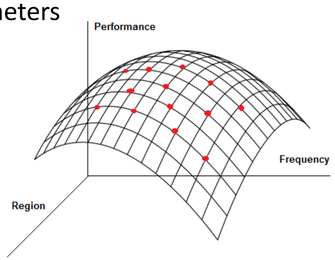
Rationale

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 additional potential to enhance memory in these patients. One of first challenges to enhance memory using neurostimulation is to identify optimal stimulation parameters. We present a modeling approach to predict 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.

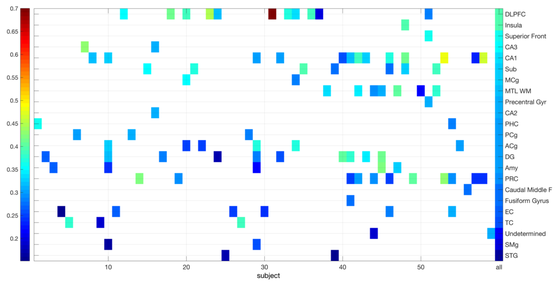
- Each stimulation recorded: pre-stimulation biomarker, frequency, duration, amplitude, and post-stimulation change in biomarker
- Each location: fit linear least-squares model to predict change in biomarker from combination of pre-stimulation biomarker and stimulation parameters



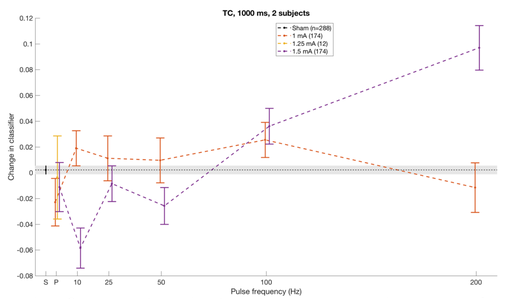
In first analysis, we looked at prediction using stimulation alone, pre-stimulation biomarker, and a combination. Mean squared error (MSE) between predicted and actual biomarker change was used to judge performance with leave-one-out cross-validation. In second analysis, we looked at influence each predictor had on change in biomarker by examining t-stat p-value of each term after fitting model. We again used MSE but with k-folds (k=30) cross-validation.

Results

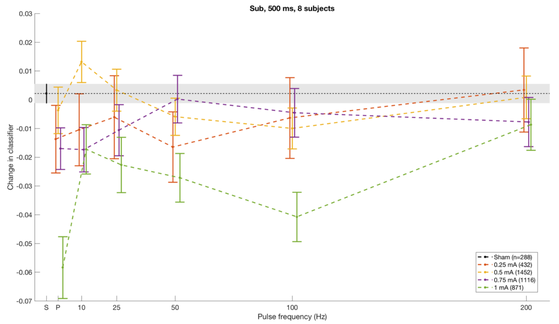
- 21 unique anatomic locations
- Not all subjects able to complete same sequences so sparse grid sampling
- 81,716 total stimulation observations



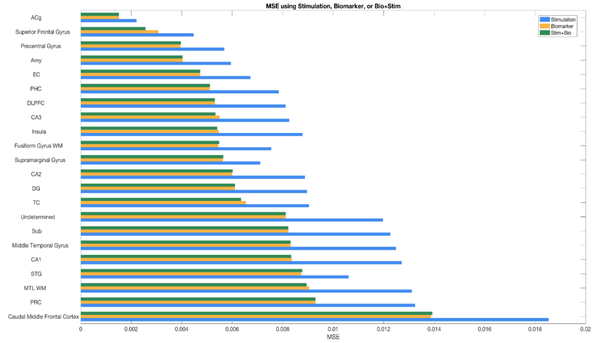
Location (y-axis) sampling across subjects (x-axis). Colored squares indicate r^2 of linear model from data sampled.



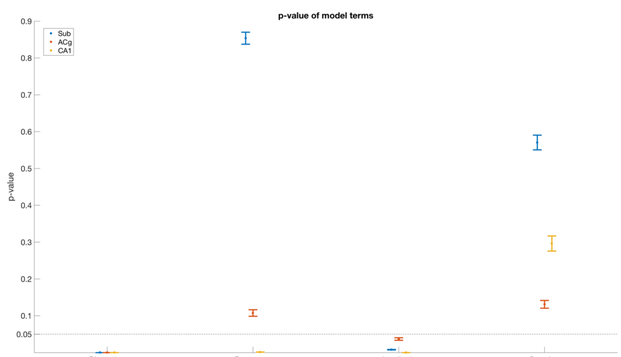
Results from stimulating in Temporal Cortex (TC) for 1000ms duration at various amplitudes (trend lines) and frequencies (x-axis) and resultant change in biomarker classifier performance (y-axis, mean and standard error bars). Stimulation at 1.5 mA (purple) appears to have an interesting effect with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



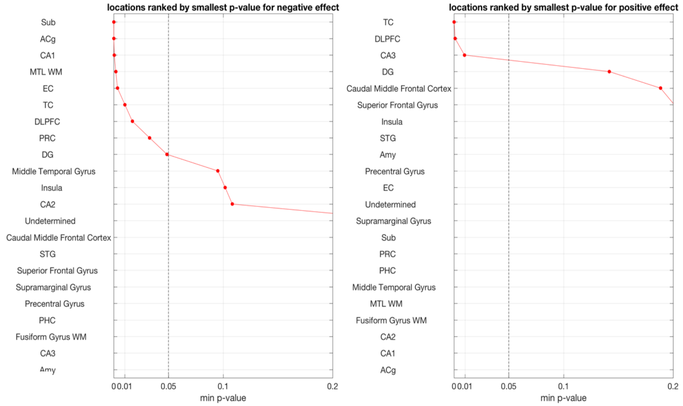
Results from stimulating in Subiculum (Sub) for 500ms. Interesting effects are observed for 1mA (green).



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



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



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

Conclusions

This presents a predictive modelling approach for exploring 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 neurostimulation parameter space.

Acknowledgement

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