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IMPROVE SUBTHALAMIC NUCLEUS LOCALIZATION DURING DEEP BRAIN STIMULATION SURGERY

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ABSTRACT

Deep brain stimulation (DBS) is a treatment for movement disorders (e.g., Parkinson's Disease, or PD) in patients who cannot manage their symptoms with medications. DBS efficacy depends on optimal DBS electrode placement which is achieved by a laborious search of putative electrode sites requiring serial expert analysis of microelectrode recordings. Target localization can be made faster and more accurate with automation powered by machine learning. Faster and more accurate electrode placement can reduce surgical complications and improve patient outcomes.

INTRODUCTION

High-frequency DBS of the subthalamic nucleus (STN) is a treatment for the affective and motor symptoms of Parkinson's disease in patients who can no longer manage their symptoms with medications. STN-DBS surgery involves the permanent placement of DBS electrodes in the STN. STN is a small lens-shaped nucleus surrounded closely by other structures, including substantia nigra, red nucleus, and zona incerta.

Precise and accurate DBS target localization is typically done in four stages: 1) initial trajectory planning based on the co-registration of magnetic resonance images and X-ray computed tomography images; 2) stereotactic localization and functional localization via microelectrode recordings (MER); 3) microstimulation to identify structures around the electrode based on stimulation-induced side effects; and 4) post-operative CT scans to confirm the proper placement of the DBS electrodes.

This paper starts by stating how precise localization and the laborious process of functional localization are used in STN-DBS surgery. Then the state of the art research for automatic and optimized STN localization techniques are reviewed. Finally, we proposed an algorithm that enables automated and optimized localization in real time.

PROBLEM STATEMENT

DBS efficacy and patient tolerance to stimulation depends greatly on the precise placement of the DBS electrodes in the motor aspect of the dorsal STN [1]. Side effects can arise from the stimulation spread to the structures surrounding the STN [2]. Moreover, sub-optimal positioning of DBS electrodes accounts for up to 40% of cases of inadequate efficacy of stimulation post-operatively [3, 4]. Thus, precise localization of the STN is a critical component of DBS surgery for optimal patient outcome.

DBS target localization is currently a laborious process entailing detailed surgical

planning and functional localization via MER mapping. MER mapping can take an extended amount of time due to the requirement for serial assessment of the neurophysiological signals from an expert. Increased surgical time doing MER-based target refinement can be costly in terms of hospital resources and the increased chance for complications [5].

PROBLEM RESOLUTION

MER-based localization is costly in time and resources because it requires one or more experts to analyze neurophysiological waveforms and make determinations based on somewhat intangible signal features. This process can be automated, and therefore sped up and potentially improved, with the application of machine learning. A corpus of neurophysiological signals and anatomical labels obtained retrospectively from clinical data can be used to train a model that can then predict anatomical labels intraoperatively on new data. This is an area of active research with most approaches labeling and predicting sites as being within or outside the STN [6, 7].

Automatic STN Localization

Over the last decade, researchers have attempted to quantitate the MER-based STN localization process. Early strategies matched single neuron spiking patterns for neurons of various subcortical nuclei [8]. This approach is limited due to the requirements of stationary recording of unit activity, and the spiking characteristics of STN and surrounding nearby subcortical structure can have significant overlap.

With the rising popularity of machine learning, enabled by recent gains in data storage and compute power, researchers have attempted pattern matching with multidimensional feature sets. Researchers have attempted using unsupervised learning and supervised learning with a 13-dimensional feature set including spike-dependent and spike-independent statistics [3, 6]. The multidimensional features approach (both full-sets combination or sub-set combination) has been reported to have approximately 80%-90% prediction accuracy. This result is not good enough to be relied on exclusively for clinical decisions, but it is sufficient for assisting the neurosurgeon's decision of selecting the location for electrode placement. This method is also limited due to the expensive computational power required for higher dimensional feature space.

Optimizing STN Localization

Another useful application from quantifying the STN localization process with MERs is the ability to optimally determine the STN location for the best therapeutic outcome. There are currently two methodologies proposed and investigated that can be used to determine the optimal trajectory for DBS electrode placement.

One methodology is done with an extension from the technique for automatically locating STN. Typically, three to five trajectories of electrode sites are used for functional localization. The trajectory that has the longest continuous span of labelled STN sites is selected as the optimal trajectory [7].

Second, features of the MERs recorded during the STN implantation surgery are implicated in disease pathophysiology, are indicative of anatomical structure, and their magnitude correlates with the efficacy of the DBS electrode contacts [9, 10]. This implies that it is possible to determine an electrode site placement that can deliver optimal therapeutic outcomes based on MER features independent of or in addition to anatomical labeling.

For example, in PD, the basal-ganglia thalamocortical circuit is observed to exhibit enhanced neuronal synchronization in the beta frequency band (13-30 Hz) that is proportional to motor symptom severity [9, 10]. Also in PD, abnormal phase-amplitude coupling (PAC) between the phase of beta frequency band and the amplitude of neuronal spiking activity has been implicated in disease pathophysiology, and PAC magnitude correlates post-hoc with optimal placement of DBS electrodes for the treatment of PD [11, 12].

More recent research [13] has explored whether beta power, high frequency oscillation (HFO: 150-400 Hz) power, and beta-HFO PAC can be used as independent data features for fine tuning DBS localization. However, it is observed that not all STN recording sites exhibit abnormal beta power, HFO power, and PAC. It has since been hypothesized that the

Figure 1: Block diagram overview of the automatic labelling using the MER signals.

abnormalities of these data features exist only in a small localized region within the STN [14].

PROPOSED APPROACH

Figure 1 shows a flow chart representation of our proposed approach. Unlike the state of the art research, this approach is designed to label the MER signal recording site with an anatomical identity in an intraoperative setting. The signal features (i.e., the 13 dimensional set of features, beta power, HFO power, PAC, etc) are extracted from the MER signal in real time. The machine learning model is trained and tested offline using past recorded MER signals and the pre-labelled data.

This approach allows the determination of the anatomical identity of the microelectrode site immediately as it passes by. An optimal STN location can be determined from the STN labelled by this approach, since disease-related features (clinical features) are applied.

However, signal features like PAC have high computational complexity, which makes real-time extraction of such features difficult. It has been shown that PAC with low magnitude of loss can be computed quickly with compressed MER signal [15]. It has also been shown that modulations in PAC is observed in the MER signal of the same recording site [15].

CONCLUSION

In conclusion, STN-DBS surgical procedure can be greatly improved by automatically labelling of anatomical identities, and the determination of optimal location on DBS electrode contact efficacy for successful therapeutic outcome via analysis on MERs.

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REFERENCES

1. M.L. Kringelbach, N.Jenkinson, S.L.F. Owen, and T.Z. Aziz, "Translational Principles of Deep Brain Stimulation," *Nature Reviews Neuroscience*, vol. 8 (8):623-35, 2007. https://doi.org/10.1038/nrn2196.
2. R.M. Richardson, J.L. Ostrem, and P. Starr, "Surgical repositioning of misplaced subthalamic electrodes in Parkinson's disease: location of effective and ineffective leads," Stereotact. Funct. Neurosurg. 87, 297–303, 2009. doi: 10.1159/000230692
3. V. Rajpurohit, S.F. Danish, E.L. Hargreaves, S. Wong, "Optimizing computational feature sets for subthalamic nucleus localization in DBS surgery with feature selection," Clinical Neurophysiology, vol. 125, pp. 975-982, 2015.
4. M.S. Okun, M. Tagliati,M. Pourfar, H.H. Fernandez, R.L. Rodriguez, R.L. Alterman, "Management of referred deep brain stimulation failures." Arch. Neurol. vol. 62, pp. 1250–1255, 2005. doi: 10.1001/archneur. 62.8.noc 40425.
5. A.J. Fenoy, and R.K. Simpson. "Risks of Common Complications in Deep Brain Stimulation Surgery: Management and Avoidance." Journal of Neurosurgery

vol. 120, pp.132–39, 2014. https://doi.org/10.3171/2013.10.JNS131225.
6. S. Wong, G.H. Baltuch, J.L. Jaggi, S.F. Danish, "Functional localization and visualization of the subthalamic nucleus from microelectrode recordings acquired during DBS surgery with unsupervised machine learning," Journal of Neural Engineering, 2009.
7. I. Telkes, J. Jimenez-Shahed, A. Viswanathan, A. Abosch and N.F. Ince, "Prediction of STN-DBS Electrode Implantation Track in Parkinson's Disease by Using Local Field Potentials." Front. Neurosci. vol. 10, 2016. doi: 10.3389/fnins.2016.00198
8. W.D. Hutchison et al., "Neurophysiological identification of the subthalamic nucleus in surgery for Parkinson's disease," *Annals of Neurology*, 1998.
9. P. Brown, "Making use of pathophysiological synchrony in Parkinson's disease," Clinical Neurophysiology, 2013.
10. A. Kühn, A. Kupsch, G.H. Schneider, P. Brown, "Reduction in subthalamic 8-35 Hz oscillatory activity correlates with clinical improvement in Parkinson's disease," European Journal of Neuroscience, vol. 23, pp. 1956-1960, 2006.
11. C. de Hemptinne *et al.*, "Therapeutic deep brain stimulation reduces cortical phaseamplitude coupling in Parkinson's disease." Nat. Neurosci. 18: 779–86, 2015.
12. A.I. Yang, N. Vanegas, C. Lungu, K.A. Zaghloul. "Beta coupled high frequency activity and beta locked neuronal spiking in the subthalamic nucleus of Parkinson's disease." J. Neurosci. vol. 34 pp. 12816–12827, 2014.
13. B.C.M. van Wijk *et al.* "Localization of beta and high-frequency oscillations within the subthalamic nucleus region," NeuroImage: Clinical, vol. 16, pp. 175-183, 2017.
14. A. Horn *et al*. "Toward an Electrophysiological 'sweet Spot' for Deep Brain Stimulation in the Subthalamic Nucleus." Human Brain Mapping, 2017. https://doi.org/10.1002/hbm.23594.
15. D. C.C. Lu, C. Boulay, A. D.C. Chan, A. J. Sachs, "Realtime phase-amplitude coupling analysis of micro electrode recorded brain signals," *submitted to IEEE Transactions on Biomedical Engineering*, 2018.