Integration of Tractography with Deep Brain Stimulation Modeling

Kyle Taljan[1,2], Angela Noecker[2], Ken Sakaie[3], Mark Lowe[3], and Cameron McIntyre[2]

[1]*Biomedical Engineering, Case Western Reserve University, Cleveland, OH, United States,* [2]*Biomedical Engineering, Cleveland Clinic Lerner Research Institute, Cleveland, OH, United States,* [3]*Cleveland Clinic Imaging Institute, Cleveland, OH, United States*

Introduction: Deep brain stimulation (DBS), the gold standard treatment for refractory movement disorders such as Parkinson's disease, can cause cognitive and motor side effects in patients (1). It is commonly believed that stimulation of tissue connected to motor cortex is beneficial whereas stimulation of tissue connected to non-motor cortex leads to side effects. Previous work showed a reduction in side effects by optimizing the stimulation voltages so that the volume of tissue activated (VTA) was limited to motor regions of the subthalamic nucleus (STN), a deep brain structure commonly targeted in DBS (2). We use probabilistic tractography to compare the cortical connections between the VTA associated with side effects and the VTA that limited side effects. The VTA associated with side effects showed greater anatomical connectivity to non-motor cortical regions than the model-based VTA. This result points to the potential power of integrating tractography with stimulation modeling in DBS procedures to improve patient outcomes.

Methods: One patient with advanced Parkinson's disease was implanted bilaterally with a STN DBS system under an IRB approved protocol. Two sets of stimulation parameters were developed. For VTA-clinical the patient performed a series of motor tasks as a technician manually adjusted the applied voltages until the best performance on the tasks was obtained. For VTA-model the stereotactic locations of the electrodes were imported into the Cicerone Deep Brain Stimulation software and registered into a standard atlas space. The stimulation voltages were then adjusted on this atlas to focus stimulation on motor regions of the STN (3). VTA-clinical and VTA-model were coregistered to a standard FSL diffusion brain to investigate differences in anatomical connectivity from each VTA to cortex (4). Tractography was run from VTA-clinical and

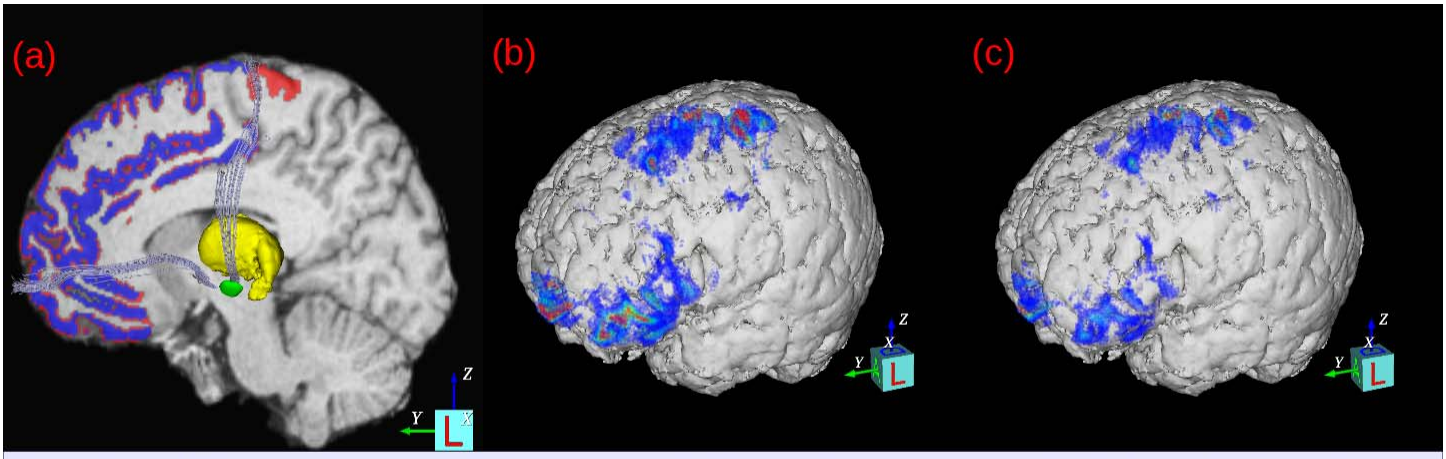

Figure 1: (a) VTA-clinical (green) with fibers to frontal (blue) and motor cortex (red). Thalamus (yellow) shown for context. (b) Cortical connections for VTA clinical (red highly connected). (c) Cortical connections for VTA-model. Regions of high anatomical connectivity in frontal cortex in (b) almost disappear in (c).

VTA-model to motor and frontal cortex using FSL's probtrackx in single-fibre mode (5).

Results: Use of the model-based stimulation parameters led to a substantial reduction in side effects without a reduction in therapeutic benefit (3). Figure 1a shows VTA-clinical in green with fibres going to motor and frontal regions of cortex. Figure 1b shows high anatomical connectivity from VTA-clinical to the frontal pole and lateral frontal cortex, regions believed to be associated with side effects. Figure 1c shows reduced anatomical connectivity to the frontal pole and lateral frontal cortex.

Conclusion:

Integration of tractography with VTA models shows promise for reducing the occurrence of side effects in DBS procedures. We show one example of a difference in anatomical connectivity to non-motor regions of cortex which may account for differences in clinical results. This method may be useful for treatment of OCD and depression, for which the targets and mechanisms are unclear. Visualizing the fibre paths and anatomical connectivity of VTAs to cortex may be one method of discovering stimulation targets.

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References:

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