Computational Modeling of Brainstem Stimulation

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Introduction

Modulation of the **Pedunculopontine nucleus (PPN)** using deep brain stimulation (DBS) is thought to improve gait disturbances in people with medication-refractory Parkinson's disease. However, previous studies have been inconclusive [1,2], with only some showing improvement in parkinsonian motor symptoms [3,4]. One of the primary challenges of PPN-DBS is avoiding activation of adjacent fiber pathways, which can evoke untoward side effects, including sensory discomfort. In this study we developed a **computational model of PPN-DBS** to predict the fiber pathways modulated by each stimulation setting. We developed a 3D model through reconstruction of the PPN, medial lemniscus (ML), lateral lemniscus (LL), and superior cerebellar peduncle (SCP) from non-human primate histological images. This anatomical framework was coupled with 1) a finite element model simulating the voltage field in the brain during DBS, and 2) a multi-compartment neuron model environment simulating the effects of DBS on PPN neurons and adjacent fiber pathways. These models provide a framework to predict how the implantaton trajectory, lead position, and stimulation settings affect neural pathways in the brainstem.

Computational Methods

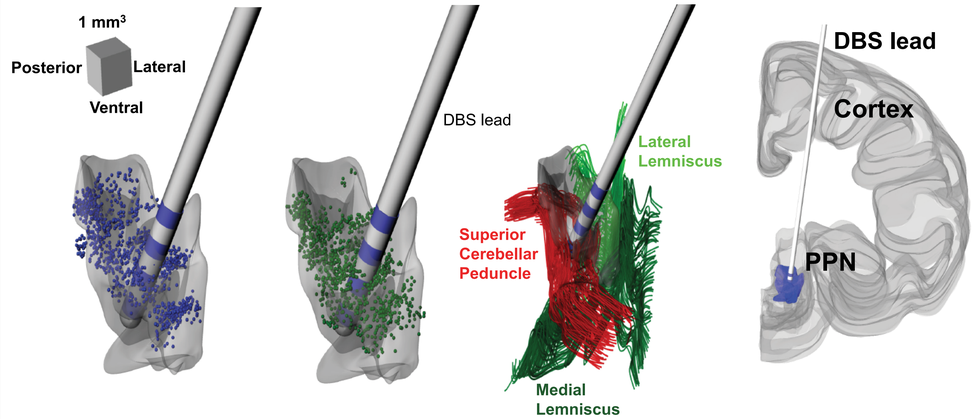


Fig. 1. The PPN is a challenging neurosurgical target for deep brain stimulation, given:
1) Its location deep within the brainstem (far right)
2) Its amorphous morphology (above)
3) Its variable distribution of cell types (above)
4) Its proximity to fibers of passage (above right)

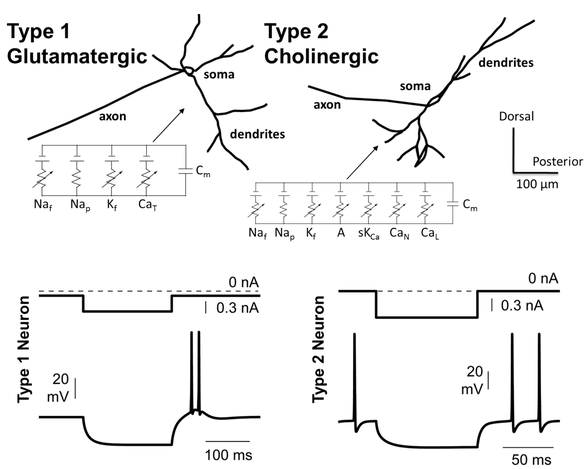


Fig. 2. PPN neuron models extended to the substantia nigra pars compacta, thalamus, and caudal brainstem [5,6]. Ion channel conductances were adapted in both PPN neuron models to reproduce the salient features of each cell type [7].

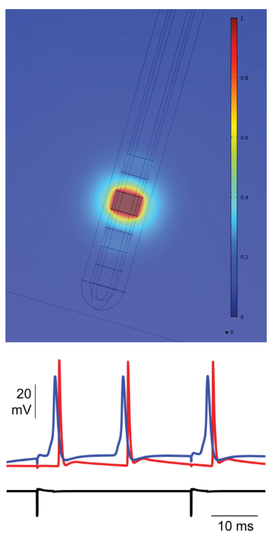


Fig. 3. Model dynamics were simulated for a range of electrode configurations and stimulation voltages using a 3D finite element model [8,9].

Results

Fig. 4. Simulation results from a DBS lead implantation trajectory, showing activation plots (right) and fibers activated at 3 V (left).

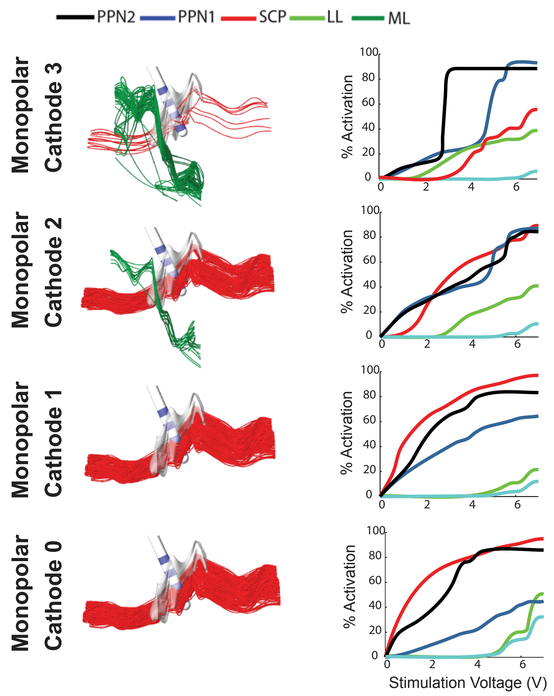
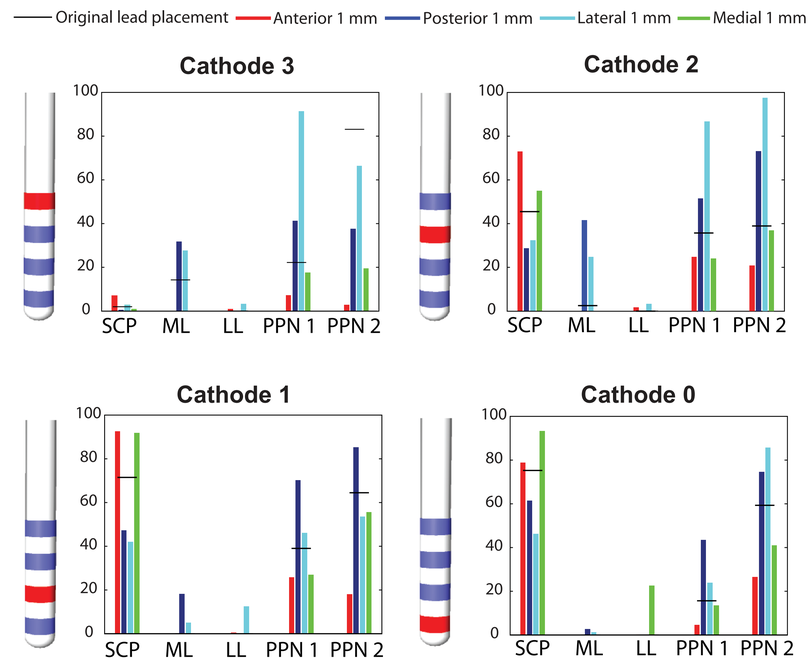
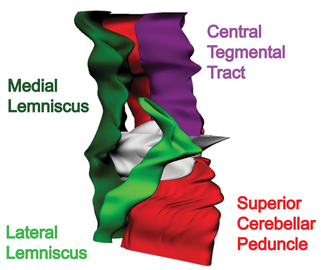


Fig. 5. Simulating implantation error. Results from moving lead implantation trajectory by 1 mm, displayed at 3 V activation voltage.



Future Work

Fig. 6. The PPN, ML, LL, SCP, and the central tegmental tract pathways were reconstructed from human histological images. Future studies will compare **human PPN-DBS** to the model predictions shown above.



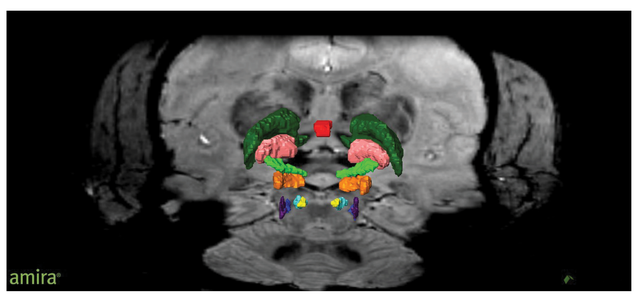
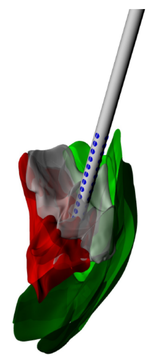


Fig. 7. Using 7T susceptibility-weighted imaging (SWI) of a non-human primate, we have segmented brainstem structures in order to model PPN-DBS using these reconstructions as a more accurate anatomical framework.

Fig. 8. A **radially-segmented lead** design can allow for current steering to more selectively activate PPN.



Conclusions

Computational neuron models of PPN-DBS provide a theoretical framework by which to prospectively evaluate the effects of a range of DBS settings. Using an implant trajectory and lead design consistent with previous studies, we found:

- Both PPN cell types are affected by PPN-DBS, though to different degrees.
- Voltage thresholds for activating the SCP, ML and LL pathways ranged from (0.08-2.3 V), (1.6-4.2 V), and (4.0-5.6 V), respectively.
- Variations in the lead trajectory by 1 mm can have a large effect on activation profiles.
- Use of a radially-segmented lead design may allow for more selective stimulation of PPN.

References

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