Technical Considerations for Surgical Targeting of the Substantia Nigra

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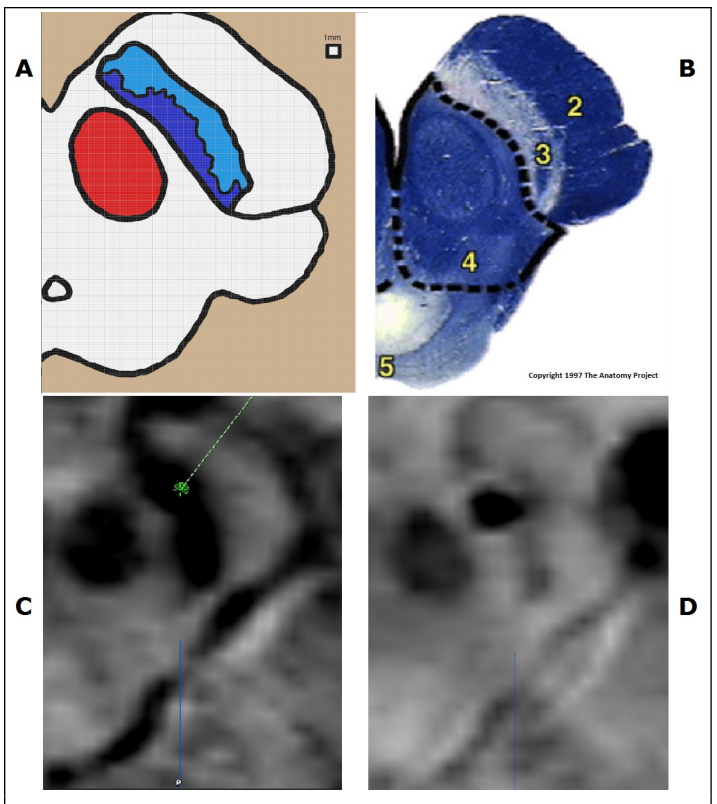
Introduction

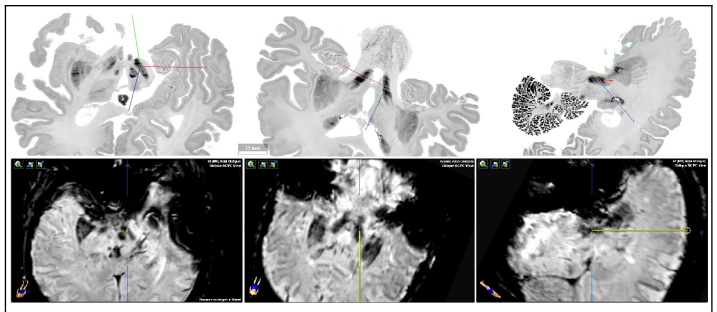
The subatantia nigra has recently gained traction as a target for deep brain stimulation (DBS) in clinical trials for Parkinsonian gait improvement as well as gene therapy delivery and cell therapy strategies in Parkinson's Disease (PD). The potential electrophysiologic variability of the substantia nigra due to its inherent heterogeneity and its potential alteration in PD progression have made mapping throughout the nucleus more difficult and less defined than other basal ganglia nuclei. We report our experience in PD study participants with peripheral nerve grafts targeting the substantia nigra using visual based targeting both with and without microelectrode recording (MER).



Left midbrain at the level of substantia nigra: A. illustration B. Histology C. SWI 3T MRI with nigral target plan D. SWI 1.5T MRI after implant

Methods

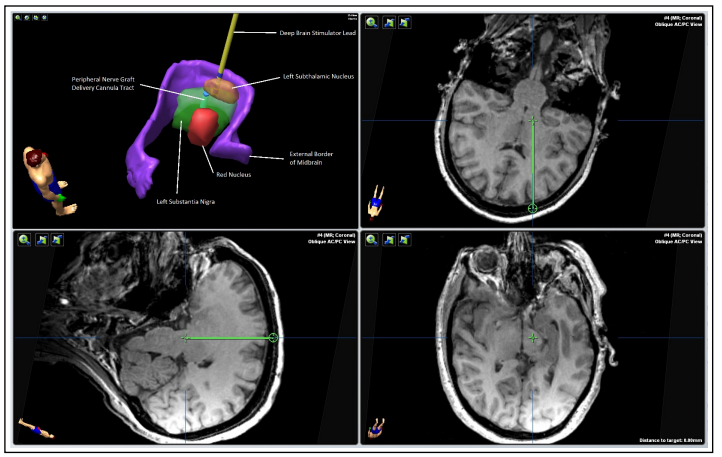
Thirty participants were included in our study with a total of 47 different peripheral nerve graft implantations into the substantia nigra. Each participant underwent a pre-operative 3T MRI which was imported into Brainlab for identification of the substantia using relative hypointense structues on SWI including the red nucleus, subthalamic nucleus, and midbrain border. A safe trajectory through the middle frontal gyrus similar to a typical entry point for GPI DBS leads, which allows for adequate clearance of the lateral ventricle, and through long axis of the substantia nigra was planned using T1 contrasted and T2 sequences. Participants underwent nerve graft implantation at the time of DBS lead implantation using of a CRW headframe. Intraoperative MER was used to aid in confirming 18 of the 47 targets intraoperatively.



Typical trajectory plan through long axis of substantia nigra as seen on 3T MRI SWI sequence using Brainlab software (bottom) with analagous histologic views obtained from Big Brain database (top)

Results

Post-operative MRI review and trajectory mapping after 47 peripheral nerve graft implantations within the substantia nigra demonstrated no occurrences of graft material or delivery cannula tract outside of the substantia nigra. Accuracy was not significantly impacted by the use of MER. Side effect profiles with graft implantation were not significantly different from DBS alone. Early data shows improvements in UPDRS part III scores but is still being collected.



Conclusions

Visual based targeting is a safe and accurate method for the purpose of intranigral therapeutic trial delivery in PD. MER can be used to identify the nigral -STN border, but may not provide additional benefit in all intranigral targeting applications.

Future Considerations

Additional follow-up for study patients will be needed to determine clinical efficacy, dose response, and optimal placement of nerve grafts within the substantia nigra and to compare the effects. The Brain Restoration Center also has ongoing studies regarding implantation in other brain structures as well as efforts to determine gene/protein expression and graft fate in animal models.

References

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