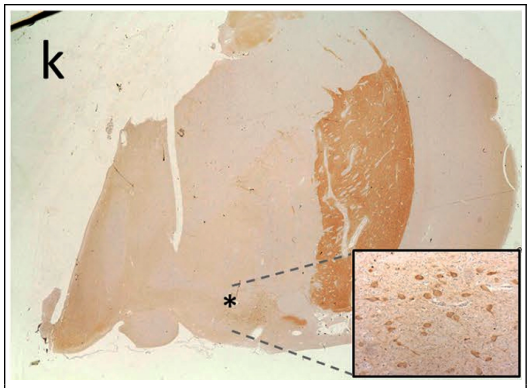
A Pilot Clinical Trial Evaluating Autologous Peripheral Nerve Grafts Implanted Into the Nucleus Basalis of Meynert in Patients with Parkinson's Disease and Mild Cognitive Impairment

Craig van Horne MD PhD; Amelia Anderson PhD; George Quintero; Julie Gurwell PAc, PhD; Rich Lamb MD; Andrew Welleford; John Slevin MD; Greg A Gerhardt

University of Kentucky

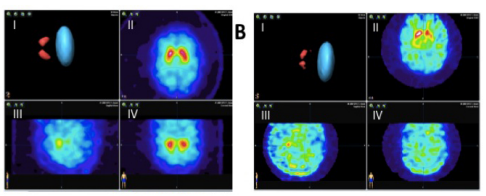


Location of cholinergic neurons in NBM

Introduction

No treatment halts or modifies the course of clinical decline of motor and non-motor symptoms in Parkinson's disease (PD). Cognitive impairment is one of the most troubling non-motor symptoms and is associated with a loss of cholinergic neurons in the nucleus baslalis of Meynert (NBM). Nerve growth factor (NGF) has been shown to support the cell maintenance and survival of cholinergic neurons in experimental models. We tested the safety and feasibility of transplanting autologous peripheral nerve grafts (APNGs), containing Schwann cells which have been shown to produce NGF, into the NBM in PD patients with mild cognitive impairment (NCT02369003). Grafts were placed at the time of bilateral deep brain stimulation (DBS).

Methods: DaT scan

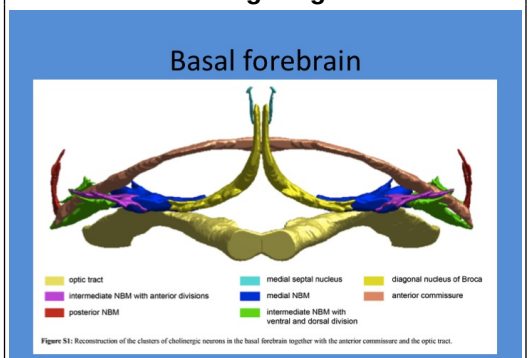


Normal, Left. PD subject, right. I = volumetric analysis of striatum

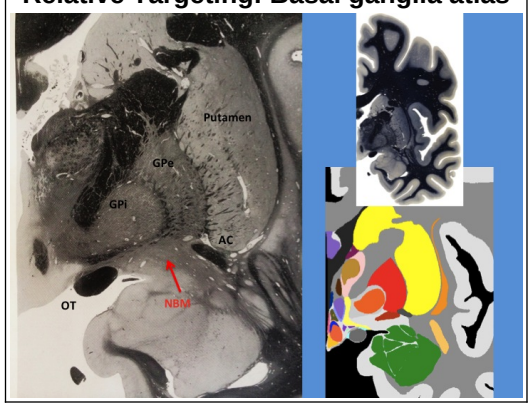
Methods

Six subjects have participated currently. All had a diagnosis of idiopathic PD with MCI, demonstrated from a comprehensive pre-operative neurocognitive exam. Subjects were good candidates for bilateral DBS of the globus pallidus internus. APNGs were harvested from the sural nerve and deposited unilaterally into the NBM, targeted electrophysiologically, contralateral to the most symptomatic side. Subjects were followed clinically for adverse events. Post-op MRIs were obtained within 24 hours.

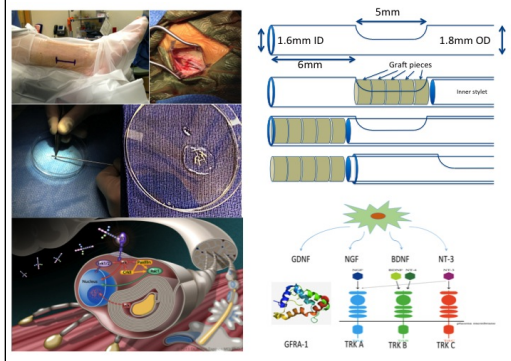
Targeting



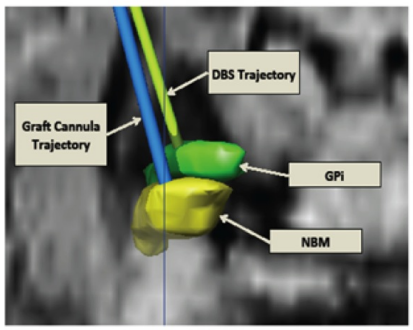
Relative Targeting: Basal ganglia atlas

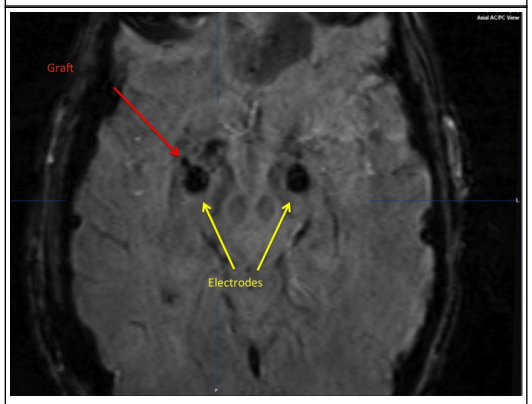


Methods: Surgery and graft prep



Methods: Targeting





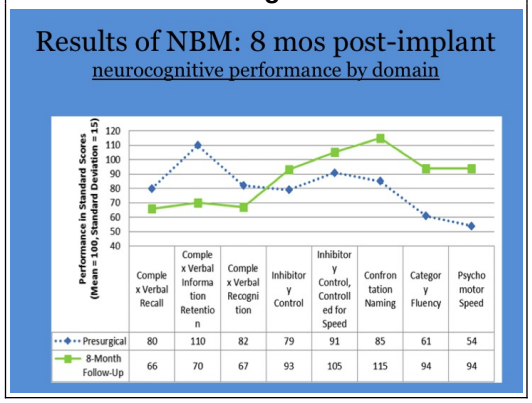
SWI MRI 24 hours post-op. DBS electrode artifact, yellow arrows. Graft target trajectory, red arrow.

Results: The 8 month post-op neurocognitive analysis was compared to the pre-op evaluation. Decreases in verbal scocres were observed, which are consistent with changes seen in our DBS patients without grafts and with changes reported in the literature. We also found improvements in areas of executive function compared to pre-op, which are not typically observed in normal DBS patients.

Results: Adverse events

Subjects were successfully implanted with APNGs to the NBM. MRIs demonstrated safe graft implantations without hemorrhage or edema. There were no significant adverse effects related to graft implantation within the perioperative period.

Results: Neurocognitive evaluation



	Complex Verbal Recall	Complex Verbal Information Retention	Complex Verbal Recognition	Inhibitory Control	Inhibitory Control, Controlled for Speed	Confrontation Naming	Category Fluency	Psychomotor Speed
Presurgical	80	110	82	79	91	85	61	54
8-Month Follow-Up	66	70	67	93	105	115	94	94

Conclusions

Evidence is provided that our DBS Plus approach is safe and feasible. This is in agreement with our previous studies of APGNs implanted into the substantia nigra (n=19). Results are preliminary. Full evaluations will be performed through 24 months.