Using a modified cannula delivery system to implant sural nerve grafts into the rhesus macaque midbrain

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Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by a loss of dopaminergic function. There is currently no effective treatment to slow or prevent its progression. Studies have shown that neurotrophic factors can promote dopaminergic function in areas like the substantia nigra, which is affected in PD. It has also been shown that Schwann cells in peripheral nerves might be a source of growth factors, including GDNF, NDF, BDNF, and NT-3. An FDA- approved Phase I clinical trial is currently ongoing at the University of Kentucky to assess the safety and efficacy of implanting an autologous sural nerve graft into the substantia nigra of PD patients. While functional improvements have been seen in these participants post-implantation, how the sural nerve graft interacts with the surrounding brain tissue is unclear. To address this knowledge gap, similar procedures were performed in two normal, adult female rhesus macaques to study the histological and neurochemical effects from the implanted nerve grafts into the substantia nigra. A modified cannula/stylet assembly and modified Nexdrive system were implemented. First, the tip of a stainless steel 18G cannula/stylet was cut to have a tapered blunt end. Then, a 1 x 5mm side window was created, 4mm from the cannula tip to load the sural nerve tissue. Next, a Nexdrive system was adapted to hold the cannula while allowing both the cannula and stylet to be individually locked down for insertion into the brain parenchyma. MRI-guided sural nerve grafts were performed in both animals without post-surgical complications. Animals were monitored for 8 weeks post-implant for changes in motor function and/or body weight, at which point they were necropsied and brain tissue collected for analysis. No significant changes in body weight or locomotor activity were observed over the course of the study. Histological analyses indicated sural nerve tissue delivery to the substantia nigra with tyrosine hydroxylase (TH) immunoreactive cells innervating the graft. Neurochemical analyses showed that in the ipsilateral side to the graft, dopamine content in the caudate was 21400 ± 1290 ng/g and in the putamen was 19800 ± 4660 ng/g while in the contralateral side the caudate was 12400 ± 2180 ng/g and in the putamen was 12800 ± 2950 ng/g (mean ± SD). We conclude that our modified surgical hardware can be safely used to successfully deliver sural nerve tissue to the rhesus midbrain to further understand the associated mechanisms of action and support further clinical development of this promising therapy.