Nerve Growth Factor and Lysophosphatidylcholine in Peripheral Nerve Repair

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Introduction: One of the responses following a traumatic injury to the peripheral nervous system (PNS) is an increased expression of nerve growth factor receptors (NGFR), which helps to stimulate the regeneration of the nerve. In a normal, healthy PNS, NGFRs are rarely found. Following damage to the nerve, NGFRs can be found in high levels around the damaged area.

Materials and Methods: We used two treatment models in rats that simulate traumatic injury: a crush model and a focal demyelination model. In the crush model, we examined the degeneration effects of crushing the extracellular matrix (ECM) of the nerve and its subsequent regeneration. In the focal demyelination model, we examined the degeneration effects of local demyelination through the application of Lysophosphatidylcholine (LPC) and subsequent regeneration of the nerve. We tested seven experimental groups: Sham, Crush, LPC, Crush + LPC, LPC+ NGF, Crush + NGF, and Crush + LPC+ NGF. In three of our experimental groups, we performed intraneural injections of NGF into the sciatic nerve one week after the local crush or focal demyelination injury. We examined the nerves both qualitatively using SEM and immunohistochemistry, and quantitatively using electrophysiology.

Results and Discussion: We were able to see the effects of the crush model in our preliminary experiments through electrophysiology recordings. These nerve conduction tests demonstrated that crushed nerves have sustained damage for a few weeks following the crush. We also monitored the gait of the rats to help us understand their rate of healing. There was a measurable decrease in nerve conduction after crush that persisted for 6 weeks, and the lasting effects of the crush was observed on the action potential, although all the rats regained full gait by week 6. In conjunction with the monitoring of the gait, the electrophysiology suggested that after three weeks the rats only recovered about a third of their limb function. Our next step was to perform immunohistochemistry to determine the extent of nerve recovery. We examined residual damage to the nerve ECM and found intact nerve bundles that demonstrated regeneration. The rats receiving no NGF helped to establish the rate of normal degeneration and regeneration. The models were then combined and LPC was applied to crushed nerves. Adding NGF to LPC-crush nerves did not provide a significantly faster result or any significant change in the percentage of functioning nerve fibers compared to crushed nerves that were not treated with NGF.

Conclusions: Although there was no significant difference in the rate of recovery between rats receiving only NGF and those receiving both NGF and LPC in the combined model, we have established a methodology that can be used in similar studies and believe that the concept of accelerating the degenerative process to improve regeneration still shows potential. We believe that a single injection of NGF was insufficient to provide the desired outcome and are currently studying the effects of multiple treatments of NGF in the same combined model.