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INCONTINENCE

Novel grafting technique restores bladder function after spinal cord transection

Researchers from Ohio, USA, have shown for the first time that bladder function can be restored via nerve regeneration after complete spinal cord transection, using a modified version of a classic peripheral nerve grafting (PNG) technique.

In this rodent study, Lee *et al.* were able to regenerate brainstem and propriospinal axons across spinal injury sites and restore urinary function by injecting fibroblast growth factor (FGF) and chondroitinase into the spinal cord immediately after inserting intercostal nerve segments into the gap and fixing the vertebral column in the dorsiflexed position with steel wires.

In total, 112 rats were randomly assigned to receive either sham treatment (laminectomy only), T8 spinal cord transection only, or T8 transection with various combinations of PNG, FGF, and chondroitinase. Although rats treated with the triple combination therapy (PNG, FGF, and chondroitinase) didn't regain the ability to walk, they recovered urinary control. At 3 months after surgery, the frequency of micturition in these rats was significantly higher than for rats in all other treatment groups. The volume per micturition was also significantly lower in the rats that received PNG, FGF, and chondroitinase than for the other groups.

At 6 months after surgery, rats treated with the triple combination therapy continued to show improvements in bladder function, with more voids and lower volumes per micturition than at 3 months, suggesting a reduced need to store excessively large volumes of urine in the bladder to void. By contrast, rats from the other groups showed significantly increasing volumes per micturition over time, indicating ongoing pathology within the bladder.

In addition, rats receiving the triple therapy demonstrated the greatest reductions in frequency of detrusor-sphincter dyssynergia and nonvoiding bladder contraction amplitudes, as well as displaying a characteristic phasic external urethral sphincter electromyography bursting activity that was well coordinated with bladder contractions during voiding.

Although nerve grafts have been used to bridge spinal cord injury sites in previous studies, nerve cells have failed to grow or form connections capable of relaying nerve signals. Chondroitinase disrupts scar formation—a process that is known to reduce inflammation but retard the growth of severed nerve fibres—and FGF helps by promoting nerve cell survival.

“We have shown that nerve regeneration can restore a significant measure of urinary function after the most severe of spinal cord injuries—a complete gaping transection lesion,” says Jerry Silver, who led the study. “A subset of neurons, located mostly within the brainstem, has a remarkable intrinsic capacity for long-distance, albeit slow, regeneration once guided past the glial scar.” However, before this strategy can be brought to clinics, the authors stress that “similar results must be obtained in larger animals with distances for regeneration and urinary physiology more closely related to humans.”

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Original article Lee, Y. S. *et al.* Nerve regeneration restores supraspinal control of bladder function after complete spinal cord injury. *J. Neurosci.* doi:10.1523/JNEUROSCI.1116-12.2013