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Technique to promote nerve regeneration after spinal cord injury restores bladder function in rats

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Using a novel technique to promote the regeneration of nerve cells across the site of severe spinal cord injury, researchers have restored bladder function in paralyzed adult rats, according to a study in the June 26 issue of *The Journal of Neuroscience*. The findings may guide future efforts to restore other functions lost after spinal cord injury. It also raises hope that similar strategies could one day be used to restore bladder function in people with severe spinal cord injuries.

For decades, scientists have experimented with using nerve grafts as a way of bridging the spinal cord injury site in an attempt to recover lost function following spinal cord injury. However, coaxing these cells to grow and form connections capable of relaying nerve signals has been elusive. In the current study, Yu-Shang Lee, PhD, of the Cleveland Clinic, together with Jerry Silver, PhD, of Case Western Reserve Medical School, and others, used a chemical that promotes cell growth along with a scar-busting enzyme to create a more hospitable environment for the nerve graft at the injury site.

"Although animals did not regain the ability to walk, they did recover a remarkable measure of urinary control," Silver explained. This basic function is one that many spinal cord injury patients rank as one of the most important to regain following injury. "This is the first time that significant bladder function has been restored via nerve regeneration after a devastating cord injury," Lee added.

When a spinal cord injury takes place, extensions of nerve cells from the brainstem—the region of the brain where the command and coordination for urination takes place—become disconnected from cells in the spinal cord that control the muscles that squeeze or relax the bladder and open and close the urethra. The body's natural response to form a scar at the injury site reduces the spread of inflammation but deters the growth of severed nerve fibers. With no way for the cells between the brain stem and spinal cord to regenerate or reconnect, the injury often results in the permanent inability to empty the bladder.

The team of researchers delivered an enzyme called chondroitinase to disrupt scar formation in tandem with a chemical called fibroblast growth factor used to promote cell survival as they performed nerve graft surgery at the site of the injury. After three and six months, the scientists discovered that the rats that received this combination of treatment saw a significant return of bladder function, as indicated by measurements of urine output. Researchers also saw the regrowth of some brainstem cells across the injury site.

"What was especially surprising and exciting was that a subset of nerve cells situated largely in the brainstem could slowly re-grow far down the spinal cord once a permissive environment that allowed them past the site of the scar was provided," Silver said. "What endows these particular neurons with such an innately high re-growth capacity is unknown but will be an extremely important area of research in the future."

Elizabeth Bradbury, PhD, a spinal cord injury researcher at King's College London who was not involved with this study, cautioned that several challenges must be overcome before this type of therapy could be tested in people. "Nevertheless, this remarkable advance offers great hope for the future of restoring bladder function to spinal cord injury patients," she said.