How a repurposed drug is helping patients with spinal cord injuries

Dr. Michael Fehlings and his team have discovered that the drug named riluzole has a protective effect, and they have launched a large-scale North American clinical trial

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If your brain is the computer that runs your body, then your spine is the cable that delivers the operating orders. So if your spine is damaged via injury or compression, then the entire communications network is compromised and in disarray.

"The outflow of the brain is through the spinal cord, so if you think of the spinal cord as being like part of a computer, then having a spinal cord injury is like disconnecting the cable from the computer," says Dr. Michael Fehlings, senior scientist at the Krembil Research Institute, vice-chair of research in the surgery department and head of the spinal program at Toronto Western Hospital and holder of the Gerry and Tootsie Halbert Chair in Neural Repair and Regeneration. Spinal cord injury (SCI) and its treatment is still a relatively new area of research. When the spine is damaged, says Dr. Fehlings, it affects every single organ system in the body.

Spinal cord compression is caused by injuries from accidents or conditions such as tumours that put pressure on the spinal cord, preventing messages from moving through the network cable. Spinal decompression is the term used for a variety of procedures that relieve the pressure placed on the spinal cord. Dr. Fehlings and his team have been able to determine why spine decompression surgeries can lead to neurological complications, and that a drug, riluzole, can have a protective effect. Based on these findings, the team has launched a large-scale North American clinical trial.

If you had an SCI, there weren't many treatment options 30 years ago.

"SCI will result in motor dysfunction, so, paralysis," Dr. Fehlings says. "It will result in sensory dysfunction. It will cause disordered sensory signalling, so you get neuropathic pain [chronic pain resulting from damaged nerve fibres]. It will cause autonomic changes [the unconscious control system that regulates bodily functions], so these are the changes that can occur in your cardiovascular control."

He also notes that "there can be immunological consequences, and patients will become immunosuppressed. It can affect your kidney function. It can affect your bladder function, your bowel function, your sexual functions. It essentially affects all parts of your body."

SCI typically is a two-step process, says Dr. Fehlings. The first is the original mechanical injury to the spinal cord, which he says commonly involves a fracture of the spine or a dislocation of the spine. "Then there are fractured bone elements that are putting compression on the spinal cord, and the vertical column is unstable. Then this initiates a process called secondary injury, which is a complex array of secondary molecular pathways that further exacerbate the extent of the injury."

He discovered in the 1990s that there was secondary degeneration of neurons around the injury, which often resulted from the surgery done to relieve spinal cord compression. He and his team theorized that surgery increased blood flow in the region, and this may cause further injury to the area – known as neuronal oxidative damage – from excessive sodium glutamate, an amino acid in the body. The theory was that this damage was most likely the cause for the neurological complications seen in SCI patients. This led Dr. Fehlings toward finding an agent that would protect these neurons from decline. Enter riluzole.

He was familiar with the drug, as it had been developed and marketed as an anti-epileptic to help treat seizures. The problem was, it just wasn't very good. "It's not a very good anti-epileptic, but it turns out that it's a dynamite neuroprotective agent," he says. "It blocks the right kind of sodium channels at the right dose."

The team started doing research with models of acute spinal cord injury, and later with models of non-traumatic injury. What they found is quite dramatic evidence of nerve protection in these models. Their work was subsequently validated in other laboratories.

The next step was conducting a Phase 1/2A clinical trial with 36 subjects with an acute spinal cord injury and 36 controls. They found significant improvement in the rates of neurological recovery and the extent of neurological recovery when riluzole is combined with surgery. Their current trial has some very promising results.

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– Dr. Michael Fehlings

"We're focused on patients with an acute cervical spinal cord injury," says Dr. Fehlings. "The neurological levels are between C4 and the C8 levels of the spinal cord [the lowest levels of the cervical spine, near the base of the neck and affect the arms and hands]. Patients have to have evidence of a severe spinal cord injury."

This means that patients who have an acute spinal cord injury can now see better outcomes in treatment versus 30 years ago.

"In the mid-1980s, the mortality rate for severe cervical spinal cord injuries was as high as 30 to 40 per cent. That's now been reduced to around 5 per cent. The outcomes for patients are much better. We're seeing far more incomplete injuries as a result of improved safety measures and prevention, but also in terms of improved medical and surgical treatment," says Dr. Fehlings. "There are more patients who are walking away from injuries. We have made strides, so the outcomes are dramatically better." ■