NASCIC
SCI RESEARCH
ADVOCACY COURSE

Module 6 – Neuroprotection

Introduction to Neuroprotection Research

"Neuroprotection" is a treatment strategy that aims to protect the neurons and axons that survive the primary injury to the spinal cord, but may become damaged during the secondary injury. The strategy involves stopping or reversing the biological processes that cause continued damage in the days to weeks after the initial injury.

This approach includes the use of drugs, medical devices, surgeries, and other treatments that:

- Restore or increase **blood flow** to ensure the normal delivery of oxygen and nutrients to neurons;
- Relieve **pressure** on the spinal cord and/or spinal nerves that was caused either by the primary injury, or by swelling and inflammation;
- Reduce **inflammation** that causes damage to cells and tissues;
- Reduce the amount or activity of excess **free radicals and oxidants** that are released after an SCI; or
- Prevent neurons from becoming over-excited by the neurotransmitter **glutamate**, which is released in excessive amounts during a trauma and causes nearby neurons to die.

Two examples of neuroprotection treatments that are used to treat SCI include decompression surgery, and methylprednisolone. Decompression surgery is used to relieve pressure on the spinal cord and/or spinal nerves by removing bones, discs, or soft tissue that are pressing on the cord and nerves. Methylprednisolone is a potent steroid that reduces inflammation.

Even though these neuroprotection therapies have been used for many years, research is still being done to answer questions about the best ways to use them. For instance, one of the unanswered questions about decompression surgery is how soon after an injury it should be performed.

Most of clinical studies that have tested whether "early" surgical decompression results in better recovery than "late" decompression used 24 hours from injury as the cut-off between early and late. But an analysis of published reports from several studies that used different cut-offs suggested that recovery may be best when surgery is done within 8 hours of injury. More clinical trials are needed to answer this question.

Similarly, there is controversy about whether and how much methylprednisolone improves function, how soon it needs to be given in order to improve function, and how to weigh the risks of infection and gastrointestinal bleeding against the potential benefits. We will discuss this example in more detail at the end of this module.

Many other neuroprotection strategies are being explored in basic and translational research, preclinical studies, and clinical trials. These experimental approaches require a delicate balancing act, because the biological processes that cause harm after an SCI also have necessary functions in the body.

Specifically, inflammation, free radicals and oxidants, and glutamate are required for the healthy functioning of cells, tissues, and organs in our bodies. But after an SCI, they increase to excessive levels. Neuroprotection strategies targeting these processes therefore need to be able to turn them down, but not turn them off.

In this module, we will describe these biological processes and discuss how they become overactivated after an SCI. We will also describe selected examples of neuroprotection research that illustrate key research principles and questions that apply to other experimental approaches not covered here.

You will learn:

- Some of the biological mechanisms that are important in neuroprotection strategies;
- Why and how scientists think different neuroprotection strategies could prevent secondary damage to neurons;
- Why it is challenging to target these mechanisms without causing unwanted side effects;
- Some of the research questions that still need to be answered; and
- Some of the unique challenges in neuroprotection research.

The lessons in this module will be easiest to understand if you have already completed “SCI Biology Part 1: How an SCI Causes Loss of Function.” If it’s been a while, you may want to review that module for a refresher, especially the video on “What happens inside the body during and after an SCI.”