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Module 4 – SCI Biology Part I: How an SCI Causes Loss of Function

What Happens During and After an SCI

The research on SCI that is being done today is based on an understanding of what happens inside the body during and after a spinal cord injury, and how those events lead to loss of function. Therefore, as a research advocate, learning about what happens during and after an SCI can help you better understand current SCI research.

When the spinal cord is injured, two types of damage occur: the primary injury and the secondary injury. The primary injury is the physical injury to the spinal cord itself. The secondary injury includes a range of after-effects that cause further damage as the body responds to the primary injury.

The secondary injury unfolds over a long period of time that is divided into three phases: the acute phase, the subacute phase, and the chronic phase.

The acute phase begins immediately after the injury and can last days. In the acute phase, neurons and glial cells are physically injured and/or dying because of direct trauma. The injury causes spinal shock, in which neurons are stunned and stop signaling.

If blood vessels were damaged by the injury, blood supply may be interrupted, leading to additional cell death. Damage to blood vessels also can lead to bleeding, or hemorrhaging, into the spinal cord, which can allow inflammatory cells to enter the spinal cord, and cause swelling and compression that lead to further damage.

The subacute phase follows the acute phase and lasts for weeks. In this phase, injured and dying cells release substances that start a chain reaction of inflammation and cell death.

For example, neurotoxins released by injured cells kill healthy neurons and oligodendrocytes in the area near the injury. As those cells die, they in turn release more neurotoxins, which go on to kill other healthy cells in the area.

At the same time, additional substances released by injured cells activate microglia, which begin to clean out debris and damaged cells, and cause inflammation. Inflammation is an essential process that allows our body to fight infection and repair injury, but when inflammation is severe, it becomes a self-perpetuating cycle that causes damage to healthy cells and tissues that are near the site of injury. We will discuss this in more detail in Neuroprotection Module.

Another cycle of damage during the subacute phase is caused by the neurotransmitter glutamate spilling out of damaged neurons. Excess glutamate leads to “excitotoxicity,” a cycle in which over-stimulation causes neurons to burst. The bursting neurons spill more glutamate into the area, causing the cycle to repeat itself and also perpetuating inflammation. We will discuss this in more detail in the Neuroprotection Module.

Another key development during the subacute phase is the mobilization of astrocytes, which multiply and move to surround the site of injury, forming a “glial scar.” The glial scar is a physical barrier around the damaged area that separates healthy cells from injured ones.

This barrier protects the healthy cells outside the scar from toxins and inflammatory cells, which remain inside the scar. But the astrocytes that form the scar also produce molecules called chondroitin sulfate proteoglycans (CSPGs), which inhibit the growth of axons inside the damaged area.

Damaged tissue and cells enclosed by the glial scar get broken down, leaving a cavity, or “cyst.” The cyst is filled with fluid that contains inhibitory molecules that prevent nerve regeneration and block axonal growth.

The scar and the cavity also are physical barriers to axon growth, because axons cannot easily penetrate the scar, and the cyst lacks the physical structures necessary to support and protect axons, and hold them in place.

The subacute phase is followed by the chronic phase, which begins months after the injury and continues indefinitely. By this time, the inflammatory response and neuronal injury have plateaued at a low level.

Some natural recovery of neural signaling occurs, which can improve function but also can lead to secondary complications of pain and spasticity. Dysfunction of parts of the nervous system and the immune system begin to cause secondary complications that affect other parts of the body, and continue to progress with age. We will discuss secondary complications in more detail in the Aging with a Spinal Cord Injury Module.

As you can see, the body’s response to an SCI is very lengthy and complex. It is characterized by an escalating cycle of damage and cell death, coupled with changes to the environment around the injury that stop neurons from regrowing. The death and damage to neurons blocks essential communication between the brain and body, leading to a loss of function.

Based on that knowledge, scientists are working on four main types of research that could lead to SCI treatments.

One approach, called “neuroprotection,” is focused on protecting surviving nerve cells from further damage during the acute and subacute phase. Neuroprotection therapies try to stop or reverse the damage by blocking the molecules or cells that cause it.

A second approach is called “neurorepair.” In neurorepair research, the goal is to stimulate the growth of axons during the subacute or chronic phase of injury. Neurorepair therapies seek to remove the barriers to axon growth, to block cells and molecules that prevent it, and/or provide support to axon growth.

“Neuroreplacement,” sometimes called cell replacement, is a third approach. Neuroreplacement therapies involve replacing lost and damaged cells with new ones during the subacute or chronic phase of SCI.

Finally, “neuroplasticity” research seeks to retrain neural circuits that remain intact to restore function during the chronic phase.

We will discuss each of these approaches in detail in the Neuroprotection, Neurorepair, Neuroreplacement, and Neuroplasticity modules.