

Module 6 – Neuroprotection

Understanding the Balancing Act

Inflammation, free radicals, and glutamate signaling all play important roles in maintaining health and physical function, but too much of any one of them can cause damage.

- Inflammation is the immune system’s response to infection or damage. It is necessary to fight off bacteria and viruses, clear cellular debris, and promote wound healing following an injury.
- Free radicals, which include reactive oxygen and nitrogen molecules, are important for cell signaling and other normal and necessary biological processes.
- Glutamate is a neurotransmitter that is required to transmit signals from one neuron to another.

Usually our bodies regulate the amount of inflammation, free radicals, and glutamate through an elaborate network of cells and molecules that coordinate with each other to provide checks and balances.

For example, “danger” signals from damaged cells or tissues activate the **inflammatory process**, including the production of molecules that recruit immune cells to injured tissues and stimulate them to remove debris and start wound healing. At the same time, this repair process stimulates anti-inflammatory parts of the immune system to work on restoring order so that inflammation doesn’t take over. These pro-inflammatory and anti-inflammatory components of the immune system communicate through molecular signaling pathways to maintain the proper balance.

In a similar way, the body has complementary processes for producing free radicals and the antioxidants that neutralize them, and for producing and using up glutamate so that proper balance is maintained.

After an SCI, however, the balance in all three of these systems is upset, so that they become self-perpetuating. And because they are linked, they also exacerbate each other.

The next several videos will talk about each these processes in more detail. But, to illustrate, here are just a few of the ways we know these biological processes interact:

- Free radicals spill out from injured cells and damage surrounding cells and tissues, which stimulates more inflammation; meanwhile, immune cells that are responsible for inflammation also release free radicals.

- Free radicals can also stimulate glutamate release.
- Excess glutamate raises the concentration of calcium inside cells, which can cause the cells to rupture, and also causes organelles inside the cells called mitochondria to produce even more free radicals.
- The remnants of cells that have ruptured because of glutamate excitotoxicity further fuel the inflammation process.

Because inflammation, free radicals, and glutamate are necessary for the body, neuroprotection therapies must be able to reduce their harmful effects without shutting down their necessary functions. Because these biological processes are intertwined, it will probably be necessary to target them with multiple therapeutic mechanisms to restore balance, protect neurons, and improve function after an SCI.

The following videos in this module describe some of the approaches that researchers are working on to bring these processes back into balance.