Module 9 – Neuroplasticity

Emerging Strategies That Leverage Neuroplasticity

Promoting neuroplasticity will be necessary and involved in successful future treatment approaches. Whether it is through intense rehabilitation after SCI to take advantage of spared circuitry, or by driving task-specific changes after the delivery of treatments that induce axon growth or regeneration, the connections within the nervous system will need to re-arrange to maximize function.

There are several ongoing clinical research efforts which leverage neuroplasticity for functional gain. These include functional exercise / activity-based therapy (ABT) in combination with:

- Acute Intermittent hypoxia (AIH)
- Stem Cell Therapies
- Inhibition of chrondroitin sulfate proteoglycans (CSPGs)
- Epidural and transcutaneous spinal cord stimulation (eSCS and tSCS)
- Brain Interfaces
- Vagus Nerve Stimulation (VNS)

Acute intermittent hypoxia (AIH) is an emerging rehabilitation technique that increases axon growth and plasticity. Repetitive consumption of low oxygen air followed by ambient room air breathing can induce a genetic response that primes neurons to grow. Intermittent hypoxia has been assessed by researchers for use in SCI as it may enhance walking function after the injury. There has been increasing evidence for AIH as a safe and efficacious method to improve motor function in people with SCI in combination with intense rehabilitation training.

Stem cell therapies, which we’ve discussed in module 8, can produce neuroplastic results. The introduction to new, healthy cells permits adaptations of the nervous system.

The use of intense activity-based therapy and locomotor training is also being incorporated into clinical trials involving stem cells or inhibition of CSPG. There is an emerging belief that rehabilitative training will act synergistically (or even be essential) with other treatment strategies that induce axon growth or abolish growth inhibitory molecules within the spinal cord.

Epidural and transcutaneous spinal stimulation utilizes electrical currents to stimulate the nervous system. An electrical stimulation paddle is placed on top of the spinal cord and used to deliver small and controlled amounts of electrical activity to the spinal cord below the injury. The difference between epidural and transcutaneous spinal stimulation is the former is invasive procedure as the electrode needs to be placed in the epidural space of the skin via surgery. The latter produces stimulation by having the electrode placed above the skin. Methods for using epidural stimulation vary. One method of use for epidural stimulation applies enough electrical activity to cause muscles to contract in a coordinated way to perform a function. Another method of use for epidural stimulation does not apply enough electrical activity to engage your muscles, but instead, just makes it easier for your own spared axons to activate your muscles.

Epidural stimulation has become one of the more recent advancements to treat human SCI as it has demonstrated the ability to restore some functional abilities even in individuals with chronic motor and sensory complete injuries. After turning on the epidural stimulators, what was an insufficient amount of signal to engage muscles becomes sufficient enough to drive small amounts of movement.

When coupled to intensive rehabilitation to drive plasticity, significant amounts of function can be restored, enough to observe weight supported stepping or upper limb movement in some people with injuries once classified as motor and sensory complete. After intensive rehabilitation, several individuals have reported a permanent return in some motor functions even when the stimulators are turned off.

The clinical implications of these findings are just as exciting as the basic science implications. Recovery effects observed after epidural stimulation have advanced our understanding of human SCI in the following ways: 1) we now know that many people with chronic motor and sensory complete injuries may not be anatomically complete (in other words people appear to have some spared axons that are just not enough to drive motor functions), 2) the ability for limited spared fibers to meaningfully improve functions can be leveraged in a clinically relevant manner, and 3) the ability to induce lasting plasticity is retained to some extent in chronic SCI.

Another emerging therapy is brain interface. As stated in video 2, the brain regions of the motor and sensory cortex are organized in a somatotopic manner where one region of the brain controls one body part. The magnitude and pattern of activity within these defined regions of the brain can predict the intention to move with high precision. Predicting how neural activity within the brain corresponds to movement in the body is termed “population coding”. Brain interface is an emerging tool that seeks to read and interpret neural activity though population coding, and use that information to allow an individual to interact with external devices. In a simple term, brain interface reads the brains intent to move and translates that into action in the environment. Brain interface has been used to interpret movements within the brain and translate that activity into robotic arms that can interact with the environment.

In order for brain interface to be successful learning must occur both in the side of the brain interface device, and the user. Plasticity is occurring within the motor cortex to enable the user to more appropriately interface with the brain interface. An example of the precision at which brain interface can be used comes from early experiments in monkeys back in the 2000s .

Recording electrodes are placed on the surface of the brain to record the monkey's intent to move, and after a training period, the monkey is able to control the robotic arm with its mind to feed itself. Use of brain interface has the potential to allow the user to interface with the environment in many ways including, engaging with computers, controlling robotic exoskeletons or robotic arms, and maybe even pair with epidural stimulators to directly control muscles.

Lastly, vagus nerve stimulation (VNS) is another emerging technology to enhance recovery after neurological injury. In studies with unilateral and bilateral cervical spinal cord injuries, scientists have been able to demonstrate the ability to strengthen connectivity from remaining motor networks to perform grasping functions in the upper limbs with the implementation of VNS. There are limited human clinical trials in spinal cord injury; however the intervention has regulatory approval for upper limb rehabilitation from a stroke.

There is an emerging understanding that using task-specific training to drive plasticity will be required alongside of emerging treatment strategies to maximize the prospects of functional recovery.