

Spinal Cord Injury Induced- Neuropathic Pain and the Gut Microbiome: A Review

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Spinal Cord Injury

- Spinal cord injury (SCI): “damage to the tight bundle of cells and nerves that sends and receives signals from the brain to and from the rest of the body” [1]
- Globally, 250,000 to 500,000 people experience an SCI each year with an average global incidence rate of 40 to 80 injuries per million population [1]
- Although almost full recovery is possible with minor SCI, many SCI have devastating and severe consequences, with many patients suffering from multiple chronic conditions post-injury including varying degrees of paralysis, bladder and bowel dysfunction, and pain [2]
- Despite the striking incidence rate and obvious health and economic implications, there is no current treatment to reverse the damage caused by an SCI, although regenerative treatments are currently being researched [3]



Spinal Cord Injury & Neuropathic Pain

Chronic Pain

Chronic pain is one of the most notable long term symptoms post-SCI [4]

An estimated 68% of SCI patients experience chronic pain post injury [5]

Neuropathic Pain

Neuropathic pain is defined as “pain caused by a lesion or disease of the somatosensory nervous system” [6]

Neuropathic pain has a 58% prevalence post-SCI [5]

Difficulties with Neuropathic Pain

SCI-induced neuropathic pain is difficult to diagnose [7]

Current treatment and therapies of SCI-induced neuropathic pain are inadequate and often ineffective [8]



The Gut Microbiome

- Complex ecosystem consisting of microorganisms involving viruses, archaea, bacteria, and fungi located within the gastrointestinal tract [9]
- Influences energy biogenesis, neurologic signaling, host cell proliferation, vascularization, immune maturation, and modulates biosynthesis and metabolism [10]
- Gut microbiome composition is thought to be highly reliant on both extrinsic and intrinsic factors [11]
- Diet is thought to be the main external modifier of gut microbiome composition [12]
- Increasing evidence suggests one's gut microbiome plays a role in various neurological disorders, including Alzheimer's disease, Parkinson's disease, traumatic brain and spinal cord injuries, among others [13, 14]
- The far reaching and complex impact the gut microbiome has on a variety of health outcomes sets it up to be an optimal target for new therapeutics and treatment techniques



The Microbiome-Gut-Brain Axis

The microbiome-gut-brain axis refers to the system of biological mechanisms that results in bidirectional communication between the gut microbiome and the brain [15]

Short-chain fatty acids

Neuronal signaling

Hypothalamic-pituitary-adrenal (HPA) axis



Spinal Cord Injury & the Gut Microbiome

Current evidence suggests that gut microbiome composition and diversity differs in patients with SCI as compared to able-bodied individuals [16, 17]

Lack of control over gastrointestinal tract function

Because of the lack of CNS control over the gastrointestinal tract, SCI patients frequently display neurogenic bowel dysfunction [18]

Alterations of colonic transit time

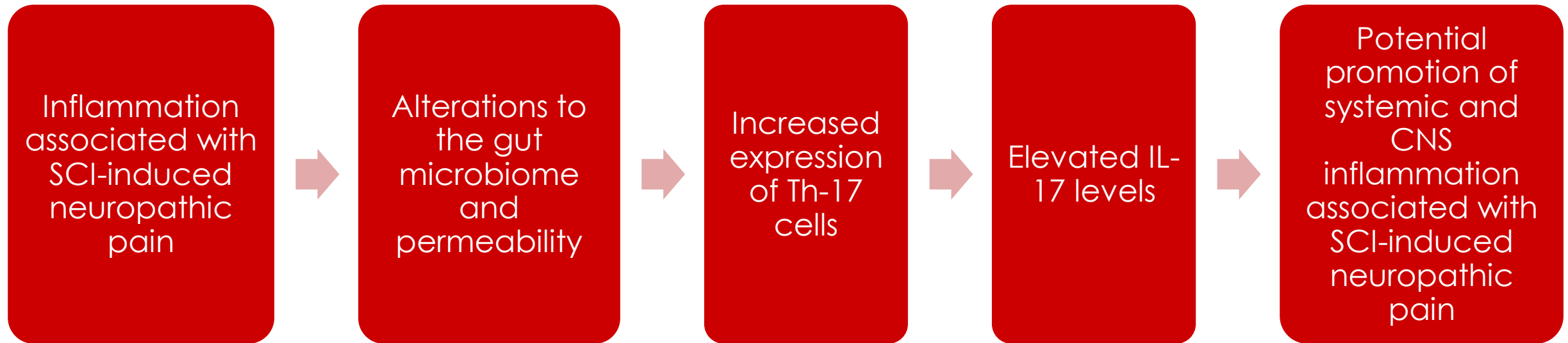
Drastic alteration of colonic transit time as well as other bowel functions, results in a significant change in gut microbiome composition [16]

Changes in gut microbiome

SCI-induced alterations to the gut microbiome are associated with impaired motor function and immune cell activation [19]

Data indicates that there is an interrelation between SCI, gut microbiome composition, and inflammatory effects on the entire body

Spinal Cord Injury-Induced Neuropathic Pain & the Gut Microbiome



Diet & Spinal Cord Injury-Induced Neuropathic Pain

Total Western Diet

- Considered detrimental to the gut microbiome
- Has been shown to increase inflammation in a mouse model [20]

Ketogenic Diet

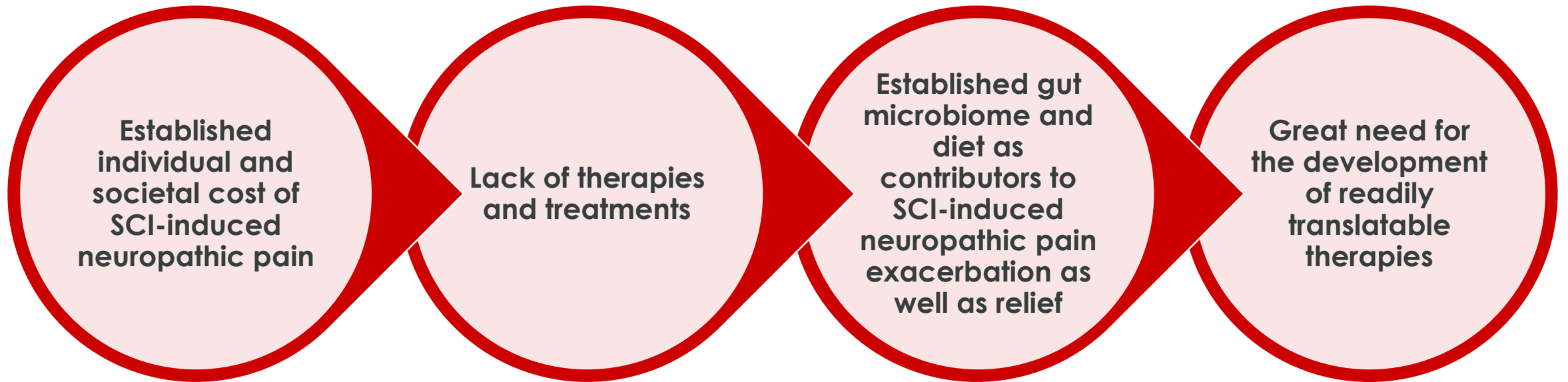
- Believed to be beneficial to the gut microbiome
- Has been linked to anti-inflammatory effects post-SCI [21]

Both preclinical and clinical literature indicate that alterations to one's diet can modify SCI-induced neuropathic pain and is thought to be associated with inflammation reduction in the CNS



Future Directions

Benefits of pig models



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