The Role of Vascular Endothelial Growth Factor in Spinal Cord Injury
Michelle Puma*, Sreyashi Samadder**, Zaghoul Ahmed#

*Department of Biology, College of Staten Island, City University of New York, New York
**Department of Physical Therapy/ Center of Developmental Neuroscience and Developmental Disabilities, College of Staten Island, City University of New York, New York

Abstract
Trans-spinal direct current stimulation (tsDCS) is a neuro-modulatory technique, extensively used to positively effect spinal plasticity and motor function in Spinal Cord Injured patients. tsDCS causes immediate and long-term effects in spinal excitability (Ahmed, 2011, 2013; Ahmed and Wierszko, 2012). Spinal cord injury (SCI) is a condition that affects physiological, psychological, emotional, social, economic and sexual aspects of a patient’s life. Scientists around the globe are working towards deciphering a remedy that might be able to impart a better quality of life to these patients. The objective of this study is to understand the effect of tsDCS on the expression a specific growth factor, vascular endothelial growth factor (VEGF). VEGF, a potent angiogenic factor, also plays a significant role in bone formation, hematopoiesis, wound healing, development, neur al migration and neuroprotection. Our experimental paradigm will consist of injured, Injured-stimulated, non-injured-non-stimulated and non-injured-stimulated along with appropriate controls to compare the expression of VEGF. Analyzing this growth factor may help us in developing future therapeutic measures for spinal cord injured patients.

Literature Review Findings
Vascular Endothelial Growth Factor (VEGF), is a growth factor which was initially identified to be associated with angiogenesis. VEGF at present is also known to play a major role in neuro-protection, neurite extension in spinal cord explants and even enhance neurogenesis in the hippocampus. Furthermore, VEGF is also known to possess mitotic effects on Neural Stem Cells (NSCs), via the VEGF Receptors (VEGFRs). Here, we will discuss two very interesting studies discussing the role of VEGF following Spinal Cord Injury (SCI). Liu, et al. in 2018 has shown that VEGF promotes NSCs proliferation and self-renewal. Further investigation showed VEGF mediates Epidermal Growth Factor Receptor (EGFR) through VEGF Receptor 2 (VEGFR2) to promote NSC proliferation. Experiments with exogenous VEGF spinal injections confirm the role of VEGF-VEGFR2-EGFR signaling cascade in NSC proliferation as shown in Figure 1 and Fig 2 below. In another interesting study by Nesic, et al in 2010, an isoform of VEGF has been shown to be instrumental in non-specific axonal sprouting and development of mechanical allodynia following SCI.

Methods
A. Immunohistochemistry: Spinal cords are perfused with 0.1M phosphate-buffered saline (PBS), followed by 4% paraformaldehyde. Once spinal cords are removed, they are then immersed in 30% sucrose-phosphate-buffered saline (0.1M PBS) for 2–3 days at 4°C (Nesic et al., 1794). Cryostat was used to make section of 35 m that would later be stored in a storing medium at -20°C (Nesic et al., 1794). B. Western Blotting: Spinal cord tissue is lysed into protease inhibitor buffer, put on ice and then centrifuged at 4°C (Liu et al., 779). Probing with antibodies detects the expression of the protein. C. Real-time qPCR: RNA was extracted from Spinal cord samples. Reverse transcription was done to produce cDNA, followed by real time quantitative PCR for measuring RNA expression across different samples following direct current stimulation.

Significance
- VEGF is a growth factor that stimulates the formation of blood vessels and is being used to understand how it can affect chronic pain and spinal cord injuries (SCI).
- The role of this neurogenic factor allows us to better understand how it can be used therapeutically for SCI patients.
- SCI can be debilitating once there is damage to motor and neuron functioning, however functional recovery of motor neuron through proliferation of neural stem cells by VEGF creates new hope of potential therapeutics.

References

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