From Paralysis to Regrowth—Inducing Breathing Motor Recovery After Cervical Spinal Cord Injury

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Abstracts will be considered for both poster and platform presentations

Neurotrauma (TBI, spinal cord injury, etc.)

In the human population, spinal cord injury (SCI) most commonly occurs at the cervical level. Interruptions of the pathways within the cervical spinal cord can result in breathing motor deficits through paralysis of the diaphragm, necessitating mechanical ventilation for survival and greatly decreasing patients' quality of life. To promote recovery, two wide treatment categories emerge: the enhancement of remaining synaptic connections and the compensatory sprouting or regeneration of spared or damaged axons. For newly formed connections to become functional, axons must both project to their targets and subsequently form active synapses. This first step of sprouting or regeneration can be targeted through treatment with Gabapentin (GBP), a drug commonly prescribed to patients for the alleviation of neuropathic pain or epileptic symptoms. GBP blocks the alpha-2-delta-2 subunits of neuronal Voltage Gated Calcium Channels which have been shown to mechanize the switch from developmental axonal elongation to synapse formation at maturity. After cervical-level spinal cord injury, such treatment could promote breathing motor recovery if latent circuits such as the Crossed Phrenic Pathway sprout or damaged axons extend past the lesion to form or strengthen connections to phrenic motorneurons. We therefore hypothesize that systemic intraperitoneal Gabapentin injection following C2 Hemisection (C2H) injury in rat models will induce functional recovery in the hemidiaphragm ipsilateral to the injury greater than recovery in saline-treated control. At a timepoint 4 weeks after C2H rats were intraperitoneally injected with GBP at a dosage of 276 mg/kg body mass every 8 hours for 7 consecutive days. After this was completed, a latency period of one week was instituted to allow the disassociation of the drug from its receptors and promote synapse formation. Animals were then urethane anesthetized and diaphragmatic EMG recordings were conducted to measure breathing motor activity post-treatment. Preliminary results suggest that GBP treatment increases breathing motor activity in the hemidiaphragm ipsilateral to the lesion when compared to control. Immunohistochemical analysis of spinal cord issue is underway and will focus on markers for axonal sprouting, regeneration, and functional synaptic formation. Future directions for this study include novel post-injection treatment to optimize baseline utilization of available axons and evaluation of the drug's effect on animals at various time points post-injury.