Dissertation Defense

"Electrical Activation and Analysis Paradigms for Restoration of Breathing"

Rehabilitation Science
Dissertation Defense

Public oral examination for the degree of Doctor of Philosophy

Michael Sunshine

FUTURE PLANS
Michael will pursue a post-doctoral fellowship in spinal cord injury research. His career goal is to direct his own research laboratory.

Doctoral Committee:
David Fuller, PhD
Gordon Mitchell, PhD
Emily J. Fox, PT, DPT, PhD, NCS
Kevin J. Otto, PhD

Thursday, November 5, 2020
3:00pm
Via Zoom

UF College of Public Health and Health Professions
Rehabilitation Science
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Respiratory insufficiency is a leading cause of death due to drug overdose or neuromuscular disease. We hypothesized that a novel stimulation paradigm using temporal interference (TI) could restore breathing in such conditions. Following opioid overdose in rats, two high frequency (5000 Hz and 5001 Hz), low amplitude waveforms delivered via intramuscular wires in the neck immediately activated the diaphragm and restored ventilation in phase with waveform offset (1 Hz or 60 breaths/min). Epidural TI stimulation robustly activated the paralyzed hemi-diaphragm after chronic spinal cord injury. We conclude that TI stimulation can activate spinal motor neurons after SCI and prevent fatal apnea during drug overdose by restoring ventilation with minimally invasive electrodes.

Further, I investigated how TI stimulation recruits and activates diaphragm motor units. Breathing requires repeated periodic contraction of the diaphragm muscle, which is impaired by neurologic injury or disease. Appropriate motor unit recruitment is essential to produce these repeated bursts without muscle fatigue. Using a custom multi-electrode array, I was able to record numerous diaphragm motor units during endogenous and evoked bursts. TI stimulation recruited motor neurons at similar rates, and in a similar order to endogenous bursts. Additionally, TI stimulation but not square-wave stimulation, recruited more units in the center of the burst resulting in a modulated breath pattern. Collectively, these data suggest that TI stimulation has the potential to restore breathing in conditions of severe hypoventilation.

I then developed a method to assess whole body plethysmography waveforms as these provide information about breathing and related are impaired by injury and disease. Respiratory waveforms vary in timing and amplitude, however, this information is lost with conventional approaches to data analysis. Here I developed an unbiased approach for evaluating the dynamically changing waveforms that typify breathing. The analyses was then validated on a data-set testing a pharmacological rescue to opioid overdose. We conclude that the respiratory waveform cluster analysis developed herein allows for rapid, unbiased assessment of stochastic breathing patterns during hypoventilation. Further, ampakine CX1942 increases breath variability following opioid overdose. This analysis can provide insight into how the neuromotor respiratory system is affected by drugs, disease, or injury.


Sunshine MD, Ganji CN, Fuller DD, Moritz CT. (2020). Respiratory resetting elicited by single pulse spinal stimulation. Respiratory Physiology & Neurobiology; 14;274:103339

Streeter KA, Sunshine MD, Brant JO, Sandoval AGW, Maden M, Fuller DD. (2019). Reduced wounding and enhanced neurogenesis following spinal cord injury in spiny mice, Acomys cahirinus. Journal of Comparative Neurology.;528:1535–1547.


SELECTED HONORS AND AWARDS

F31-HL145831 Ruth L. Kirschstein Predoctoral Individual National Research Service Award. Title: A new method of spinal stimulation to activate the diaphragm - NHLBI (PI: M. Sunshine)

T32 HD043730 Interdisciplinary Training in Rehabilitation and Neuromuscular Plasticity Pre-Doctoral Training Fellowship (PI: K Vandenborne ;2016-2018; D Fuller, 2018-2019)