BURKE MEDICAL RESEARCH INSTITUTE

Weekly Colloquium

Tuesday, 4/17/2018, 12:30pm, Billings Building – Rosedale Conference Room

"Treating weakness in critically ill patients"

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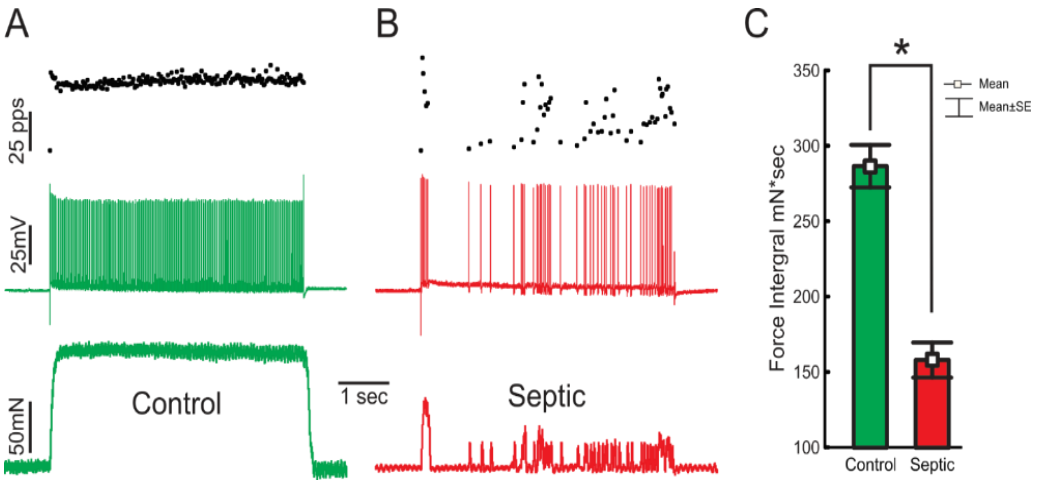
Abstract:
Weakness induced by critical illness (intensive care unit acquired weakness) is a major cause of disability in patients and is currently untreatable. We recently identified a defect in repetitive firing of lower motor neurons as a novel contributor to intensive care unit acquired weakness. In order to develop therapy for intensive care unit acquired weakness, it was necessary to determine the mechanism underlying the defect in repetitive firing. Both computer simulation and in vivo dynamic voltage clamp of spinal motor neurons in septic rats were employed to explore potential mechanisms underlying defective repetitive firing. Our results suggested alteration in subthreshold voltage-activated currents might be the mechanism underlying defective repetitive firing. It has been shown previously that pharmacologic activation of serotonin receptors on motor neurons increases motor neuron excitability, in part by enhancing subthreshold voltage-activated inward currents. Administration of a food and drug administration approved serotonin agonist (lorcaserin) to septic rats greatly improved repetitive firing and motor unit force generation. Our findings suggest activation of serotonin receptors with lorcaserin may provide the first ever therapy for intensive care unit acquired weakness.



Publications:

Hawash AA, Voss AA, Rich MM. (2017) Inhibiting persistent inward sodium currents prevents myotonia. Annals of Neurology. 82:385-395. PMID: 28833464.

Nardelli P, Powers R, Cope TC, Rich MM. (2017) Increasing motor neuron excitability to treat weakness in sepsis. Annals of Neurology. 82(6):961-971. PMID: 29171917.

Wang X, McIntosh JM, Rich MM. (2018) Muscle nicotinic acetylcholine receptors may mediate trans-synaptic signaling at the mouse neuromuscular junction. Journal of Neuroscience 38(7):1725-1736. PMID: 29326174.

Weill Cornell Medicine