BURKE MEDICAL RESEARCH INSTITUTE | Weill Cornell Medicine

Weekly Colloquium

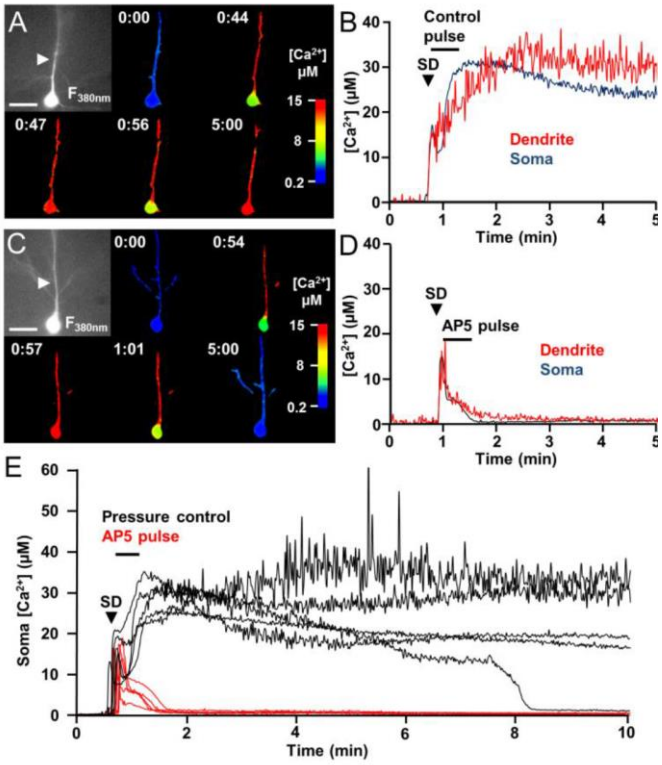
Tuesday, 9/12/2017, 12:30pm, Billings Building – Rosedale Conference Room

"Mechanisms of Spreading Depolarizations and Contributions to Acute Brain Injury"

Claude William Shuttleworth, PhD
Regents' Professor
Department of Neurosciences
Director, Center for Brain Recovery and Repair
Associate Director, Clinical and Translational Science Center
University of New Mexico Health Sciences Center
Albuquerque, NM

This talk focusses on slowly-propagating waves of profound and long-lasting depolarization, termed **"spreading depolarization" (SD).** SDs are quite unlike neuronal depolarizations observed in normal synaptic communication, and are also fundamentally different from seizures. The most important differences are the very slow propagation rates (~2-4mm/min), large amplitudes and the extraordinarily long periods of sustained depolarization (measured in minutes, rather than milliseconds) as individual waves sweep through a volume of brain tissue. The events are carried by extracellular accumulation of glutamate and/or K^+, and result in large amounts of ATP being expended to restore ionic gradients after SD. When they occur in otherwise healthy brain, SDs do not cause damage, as there is usually sufficient supply of metabolic substrates to restore membrane potentials. However, there is now very strong evidence that when SDs occur in injured brain, they are a key contributor to injury expansion. Breakthrough work in the last decade has revealed that SDs are a common feature after acute brain injury in humans and (as predicted from prior rodent studies) appear to be causative events, underlying stepwise expansion of injury in the days following injury. The talk will include work form our lab describing mechanisms underlying neuronal vulnerability and protection from SDs, and work with clinical collaborators testing interventions in the ICU.

Figure 6



Recent Publications:

Aiba, I. & Shuttleworth, C.W. Sustained NMDAR activation by spreading depolarizations can initiate excitotoxic injury in metabolically compromised neurons. Journal of Physiology (London) 590 (2012) 5877-5893. PMC3528997.

Lindquist, B.E. & Shuttleworth, C.W. Evidence that Adenosine Contributes to Leao's Spreading Depression *In Vivo.* Journal of Cerebral Blood Flow and Metabolism 37 (2017) 1656-1669. PMC5435284.

Hartings JA, Shuttleworth CW, Kirov SA, Ayata C, Hinzman JM, Foreman B, Andrew RD, et al., The continuum of spreading depolarizations in acute cortical lesion development: Examining Leão's legacy. J Cereb Blood Flow Metab. 37 (2017) 15711594. PMC5435288

For more information contact: dwhite@burke.org

Burke Medical Research Institute
Academic Affiliate of Weill Cornell Medicine
785 Mamaroneck Avenue, White Plains, NY 10605 | T. 914.597.2551 | burke.weill.cornell.edu