USING A MULTIMODAL PLATFORM TO INVESTIGATE THE ROLE OF SPREADING DEPOLARIZATIONS AND HEMODYNAMICS IN NEUROLOGICAL RECOVERY

Christian Crouzet, Beckman Laser Institute and Medical Clinic, University of California, Irvine, ccrouzet@uci.edu
Robert H. Wilson, Beckman Laser Institute and Medical Clinic, University of California, Irvine
Donald Lee, Department of Medicine, University of California, Irvine
Afsheen Bazrafkan, Department of Neurology, University of California, Irvine
Ayushi Patel, Department of Biomedical Engineering, University of California, Irvine
Bruce J. Tromberg, Beckman Laser Institute and Medical Clinic, University of California, Irvine
Yama Akbari, Departments of Neurology and Medicine, University of California, Irvine
Bernard Choi, Beckman Laser Institute and Medical Clinic, University of California, Irvine

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Acute brain injury, such as traumatic brain injury, stroke, and subarachnoid hemorrhage exhibit spreading depolarizations (SDs). SDs have been associated with worsening neuronal injury and are thought to contribute towards overall worse neurological outcome. SDs during global cerebral ischemia and its implications on neurological recovery following reperfusion are poorly understood. We investigated the role of SDs in a global cerebral ischemia model of cardiac arrest (CA) and cardiopulmonary resuscitation (CPR).
To induce SD, rats underwent asphyxial CA (ACA) for 5-, 7-, or 8-min, which was followed by CPR. Previous studies used electrocorticography (ECoG) to detect SDs. We used a multimodal platform of ECoG, laser speckle imaging (LSI), and spatial frequency domain imaging (SFDI) to continuously monitor rats during SD and recovery. We measured brain electrophysiology, cerebral blood flow (CBF), tissue scattering, and cerebral metabolic rate of oxygen (CMRO2). Neurological outcome was measured 90min post-CPR using quantitative ECoG (i.e. information quantity (IQ)) and 24h post-CPR using behavioral tests (i.e. Neurological Deficit Score; NDS). SDs were manually detected after applying a 1Hz low-pass filter on ECoG (Fig 1A, red number 2) and with tissue scattering from SFDI (Fig 1B, bottom, spatial increase in tissue scattering from right to left).
SDs typically occurred within 2-3min after onset of asphyxia, during which vasoconstriction of cerebral vessels, waves of spreading ischemia and scattering, and abrupt changes in CMRO2 were visualized. Interestingly, rats with earlier SD showed better neurological recovery (NDS) (Fig 1C). In addition to earlier SD being associated with better neurological recovery, we also found that less total CBF prior to SD (Fig 1D) and a smaller change in tissue scattering (Fig 1E) during SD were associated with better neurological recovery (ECoG IQ).
Although SDs have typically been perceived to be harmful and detrimental to neurological outcome, our data provides evidence that earlier SDs may have neuroprotective potential. These data provide support for the earliest known biomarker of neurological outcome post-CA. These findings may lead to novel therapies to modulate SDs during CA and acute brain injury that improve neurological outcome.