

OPTICAL IMAGING OF INTRACELLULAR PH CHANGES WITH SPREADING DEPOLARIZATION IN THE INTACT AND ISCHEMIC RAT BRAIN

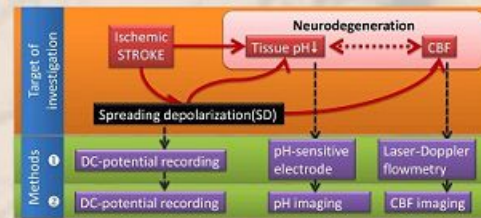
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BACKGROUND AND GOAL

Spreading depolarization (SD) is a slowly propagating wave of near-complete depolarization of neural and glial cells followed by a transient suppression of the brain's spontaneous electrical activity. The massive depolarization consumes energy generating an increased metabolic need for ATP and glucose. In an energy compromised tissue (e.g. ischemia) spontaneously occurring SDs may exacerbate ischemic injury via related atypical hemodynamic responses, but their consequences on tissue pH changes are not yet understood. The regulation of pH changes of neurons is crucial because acid loading makes them susceptible for injury. We propose that acid loading associated with SDs is superimposed on ischemia-related lactic acidosis, which would contribute to injury and cell death. Therefore we set out to compare tissue pH changes associated with SDs propagating across the intact and the ischemic cortex of rats, visualized by live optical brain imaging.

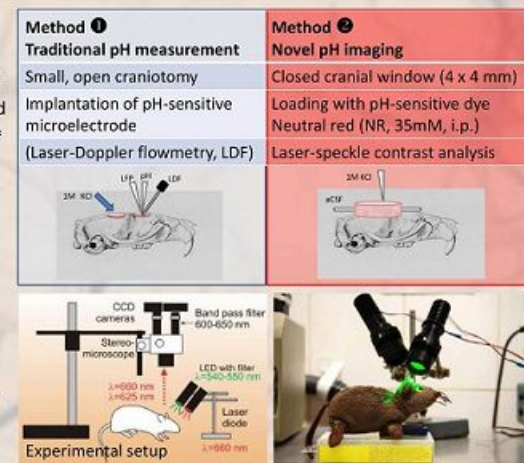
MATERIALS AND METHODS

- Animals: Adult, male Sprague-Dawley rats (n=13)
- Anesthesia: isoflurane (1.5-2.2% in N₂O:O₂/2:1)
- Monitoring mean arterial pressure and arterial blood gases (left femoral artery catheter)
- Transient global forebrain ischemia induction: bilateral occlusion of the common carotid arteries ("two-vessel occlusion", 2VO)
- SD elicitation: topical 1M KCl
- Experimental protocol →
- Experimental design ↓

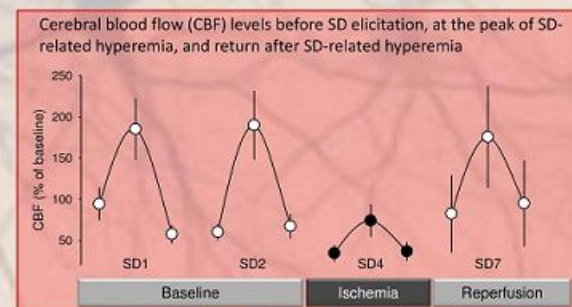
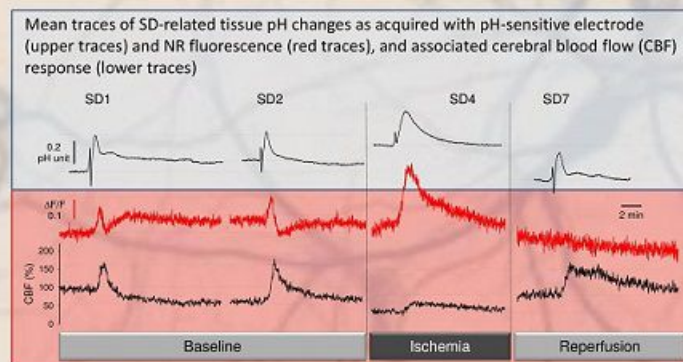
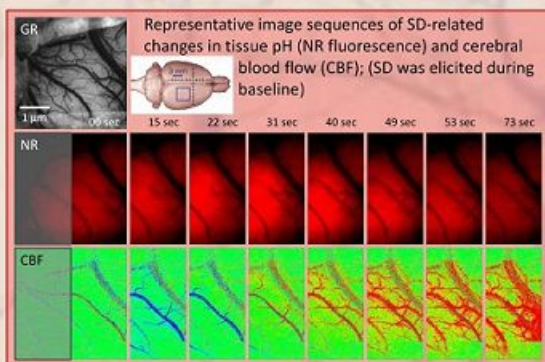


Tissue pH indicator ⇒
fluorescent pH sensitive dye
(Neutral red)

alkaline Tissue pH acidic
low Fluorescence intensity high

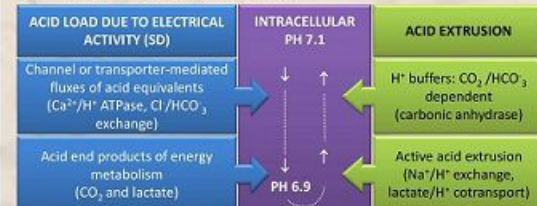


RESULTS



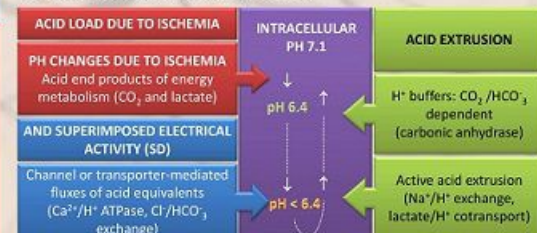
CONCLUSIONS

SD OCCURRENCE IN INTACT CORTEX:



- SD is associated with moderate acidosis
- Acidosis suppresses neuronal excitability and synaptic transmission
- THE SD-RELATED ACIDOSIS MAY BE PROTECTIVE BY INHIBITING THE OCCURRENCE OF SUBSEQUENT SDs

SD OCCURRENCE IN ISCHEMIC CORTEX:



- Acidosis due to SD and ischemia is additive (higher amplitude of acidosis)
- Acid extruders work against higher acid load (longer duration of acidosis)
- Exaggerated acid load makes the neurons susceptible for injury
- SDs DURING ISCHEMIA HAVE HIGH INJURIOUS POTENTIAL

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