Acute Global Anoxic Brain Injury

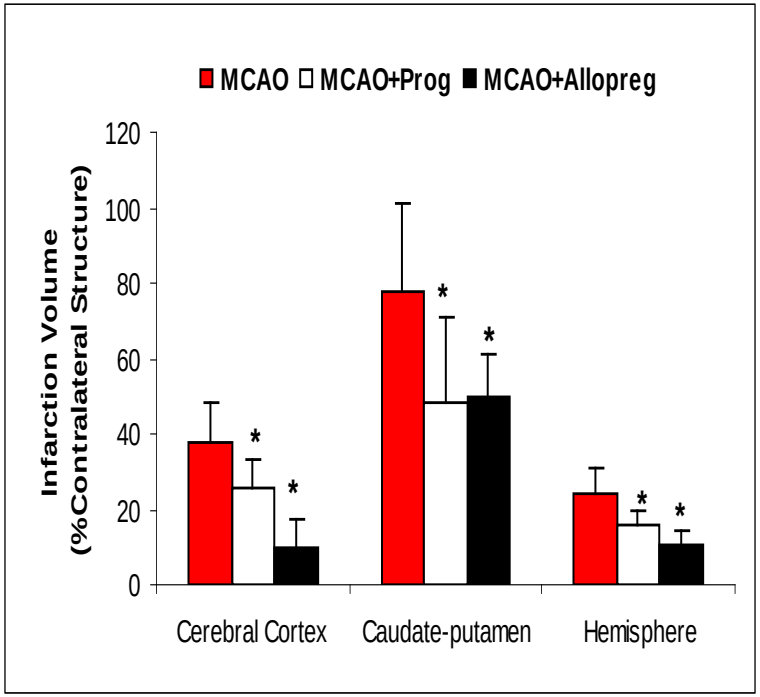
Mike Frankel

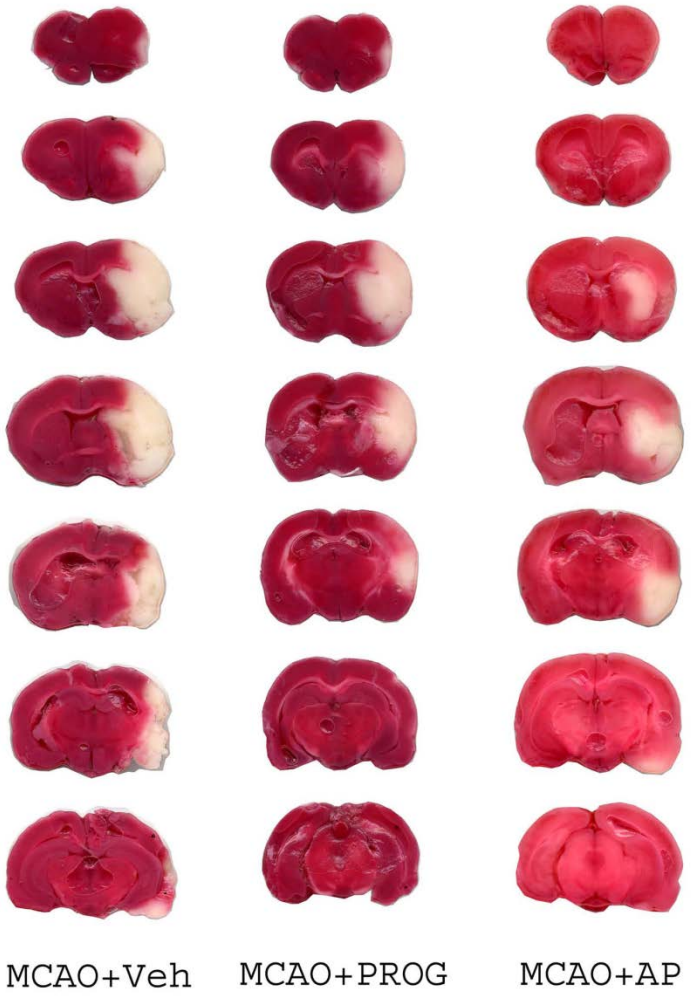
Anoxic Brain Injury

- *The biggest stroke you can have…* Walter Koroshetz

- NETT focus is a neurological emergencies
- Circulatory arrest and subsequent global cerebral anoxia is a major public health problem for emergency physicians.
- Out of hospital cardiac arrest causes 300,000 deaths per year in US
- Survivors are often devastated with cognitive and physical disability

PROGESTERONE AND ALLOPREGNANOLONE ATTENUATE DIRECT INJURY VOLUME AFTER 2 H MCAO

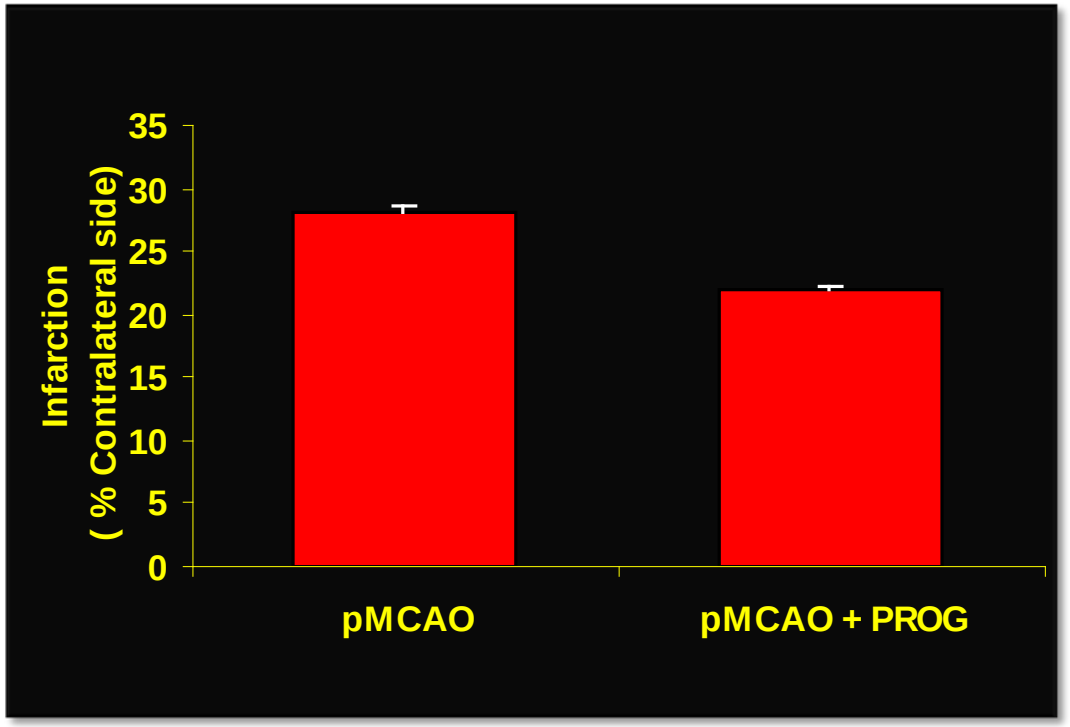




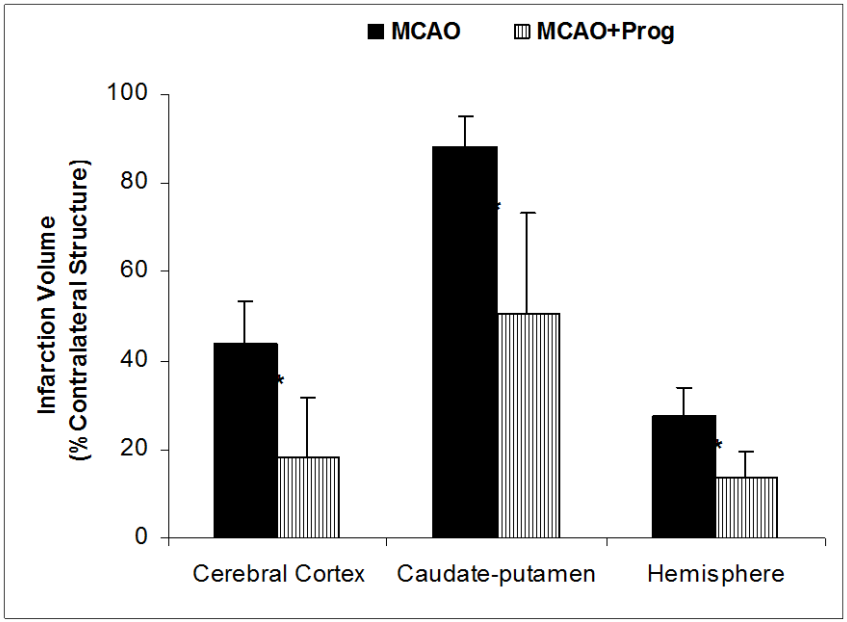
Cortical, caudate putamen and hemispheric infarct volumes (% contralateral hemisphere) in male Sprague-Dawley rats treated with 0 (n=7), 8 mg/kg (n=6) progesterone, and 8 mg/kg (n=5) allopregnanolone i.p. 5 min prior to reperfusion followed by s.c. injection 4h post-reperfusion. All values are mean ± SD.

Sayeed et al., *Ann Emerg Med. 2006* Apr;47(4):381-9.

Progesterone treatment delayed for 6h after injury substantially reduces infarct size



PROGESTERONE DECREASES DIRECT INJURY VOLUME AFTER pMCAO (Intraluminal suture method)



Sayeed et al., *Restor Neurol Neurosci*. 2007;25(2):151-9.

- Determine whether IV Progesterone reduces long term disability from anoxic injury to the brain
  - Phase II- III Adaptive design
  - Define an optimal dose and duration
  - Out-of-hospital cardiac arrest PROG vs. Placebo
  - Exception From Informed Consent
  - Initial bolus pre-hospital setting
  - Initiating study drug infusion within 30 minutes of the onset of circulatory
  - The primary outcome measure - *proportion* of patients *with pre-arrest modified Rankin Score* (mRS) of $\leq$ 1 who achieve an *mRS score of 3 or better* (moderate disability, slight disability or no disability) *at 6 months*.