Improving Collateral Circulation During Focal Ischemia

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What Is Stroke?

- Two major types
  - Ischemic stroke (occlusion of a major artery going to the brain—majority of stroke)
  - Hemorrhagic stroke (bleeding on or inside the brain caused by the breakage of an aneurysm, vessel dissection, etc.)
- Usually related to preexisting conditions
  - Hypertension, prior head injury, embolism
- In focal ischemic stroke, the pial circulation provides collateral blood flow to the core and penumbra regions.


MRI of a stroke in the left hemisphere of the brain
Research Questions

- How do focal ischemia and reperfusion affect cerebral circulatory responses?
- What may contribute to the recovery of brain perfusion during and after ischemia?
Lab Objectives

- Observe the effects of induced focal stroke on rats
  - Male, female, hypertensive/aged (risk factors for stroke)
  - Use either a suture or a thrombin clot to occlude the MCA

- Enhance collateral blood flow using vasodilators, including:
  - Adenosine/adenosine kinase inhibitor
  - Nitric oxide/phosphodiesterase inhibitor
  - Carbon dioxide/hypercapnia

A silicon-coated suture occludes the MCA by filling the ICA.

Image courtesy of Dr. Al C. Ngai
Methods

- Anesthetized using isoflurane gas
- Cannulation of femoral artery for BP monitoring; tracheal intubation
- Creation of cranial window
- MCAO using suture or clot
- Topical administration of vasodilator/IV application of AKI
- Monitoring of blood flow/dilation
  - LDF
  - Laser Speckle Imaging
  - Vessel diameter measurement

Processed Laser Speckle contrast image

Image courtesy of Dr. Al C. Ngai
Results

RAW IMAGE

LASER SPECKLE CONTRAST

CEREBRAL BLOOD FLOW

Images courtesy of Dr. Al C. Ngai
Adenosine

- Breakdown product of ATP
  - Adenine (purine) and ribose sugar
  - Lack of $O_2$, glucose to core of stroke; cellular respiration cannot occur
  - ATP breaks down to Adenosine and 3 $P_i$
- Adenosine acts as a potent vasodilator of collaterals, but is quickly broken down by adenosine kinase.
  - Adenosine kinase inhibitor

Image from: http://www.patientsville.com/labels/adenosine-structure.JPG
Conclusion

- Primary results are encouraging
  - Adenosine/AKI administration attenuates ischemic damage
- Future studies
  - Phenylephrine
- Development of collateral flow-enhancing drugs with minimal side effects
References


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