

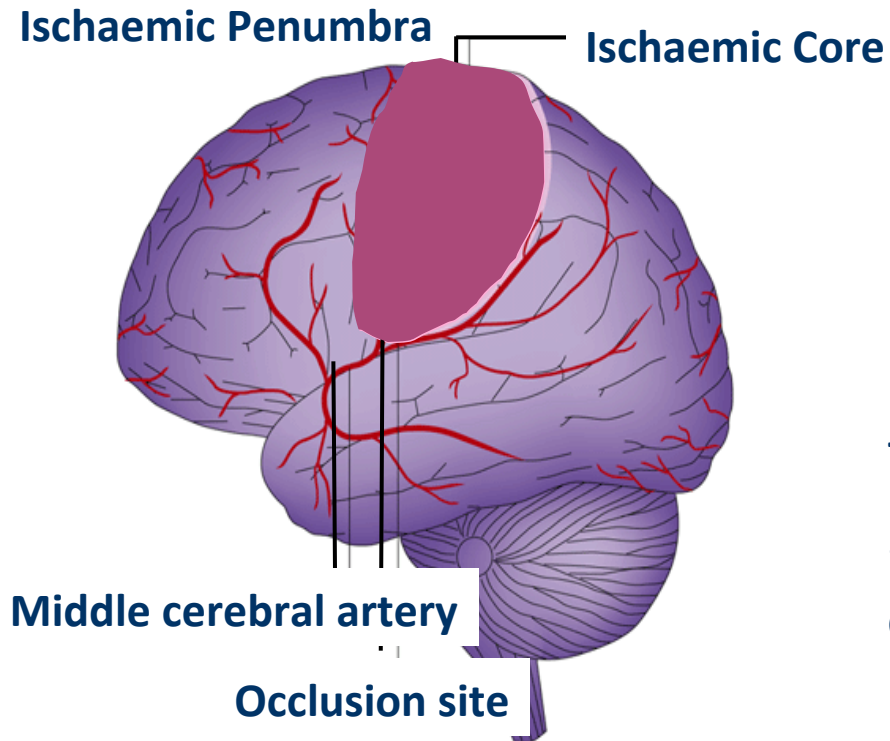
# Acute evolution of brain damage following stroke – influence of risk factors

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# Ischaemic stroke – Time is brain



## Ischaemic Core:

irreversibly damaged  
and cells are destined to die.

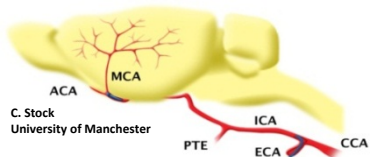
## Ischaemic Penumbra:

tissue does not function normally  
but is still viable and may recover  
if blood flow is restored or  
drugs given to support survival

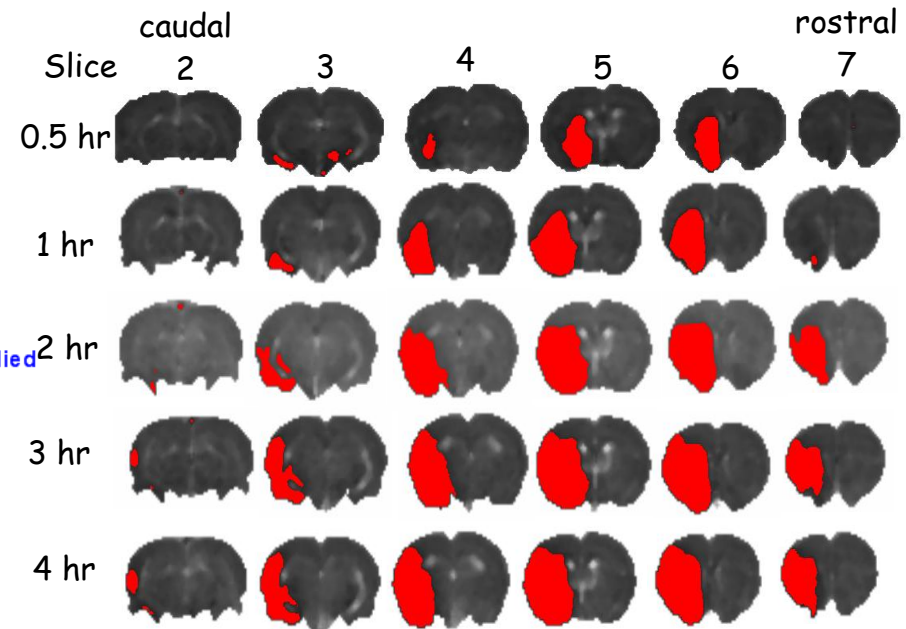
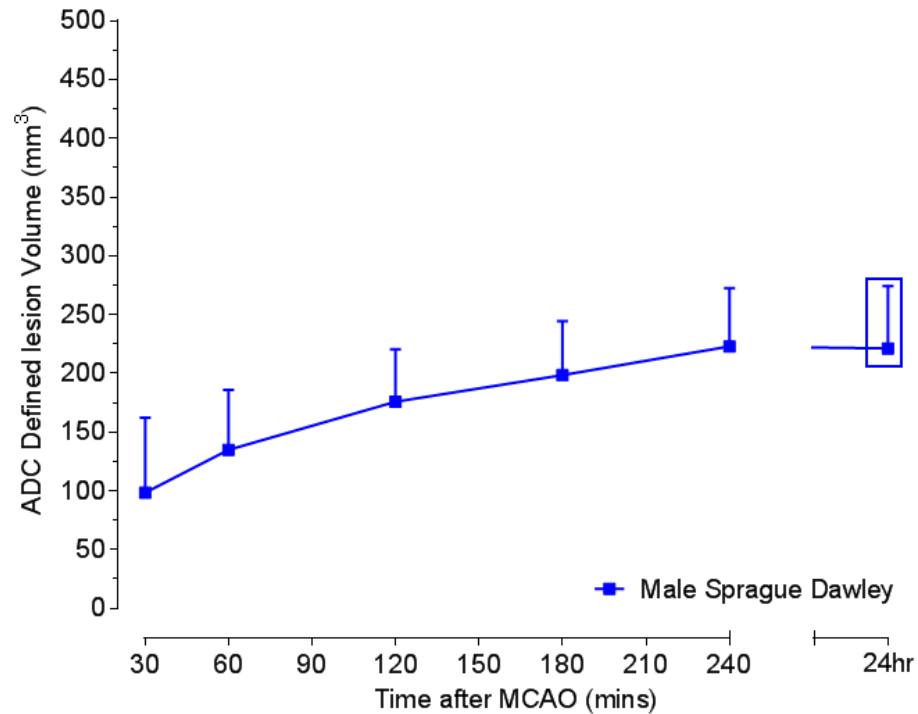
Nature Reviews | Neuroscience

*from Rothwell et al.*

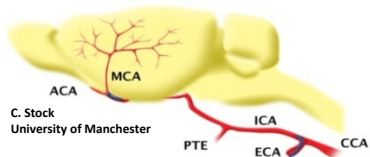
# Acute evolution of brain damage following stroke



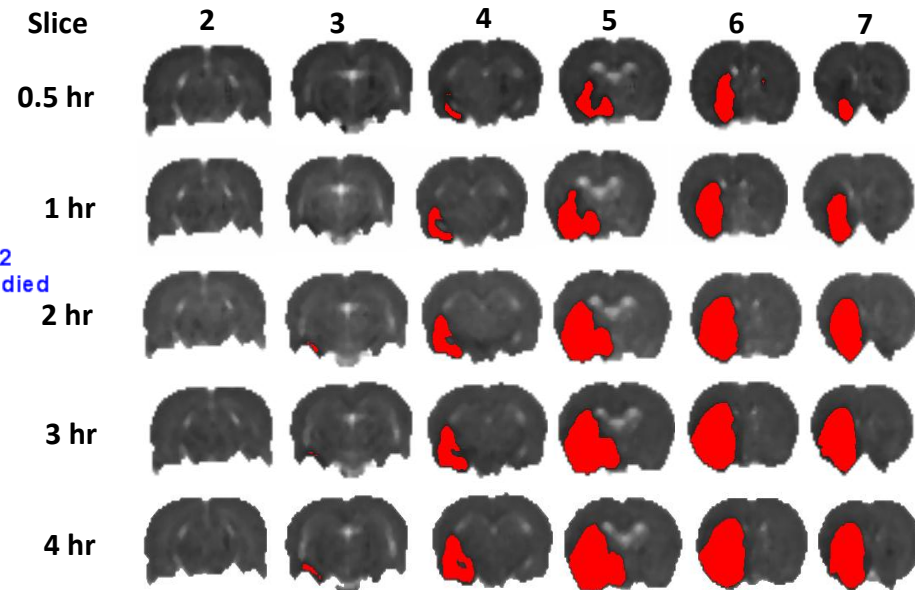
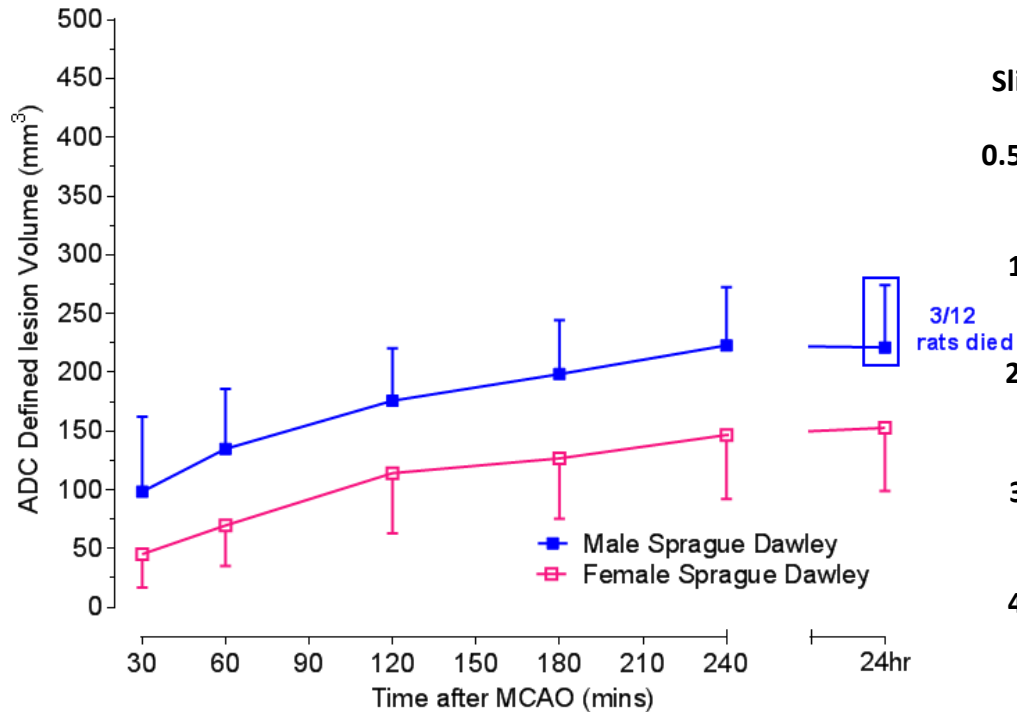
## Permanent MCAO



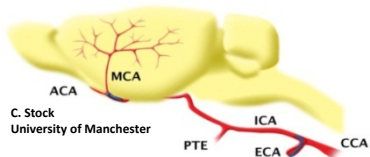
# Acute evolution of brain damage following stroke – gender differences



## Permanent MCAO



# Acute evolution of brain damage following stroke – influence of hypertension



C. Stock  
University of Manchester

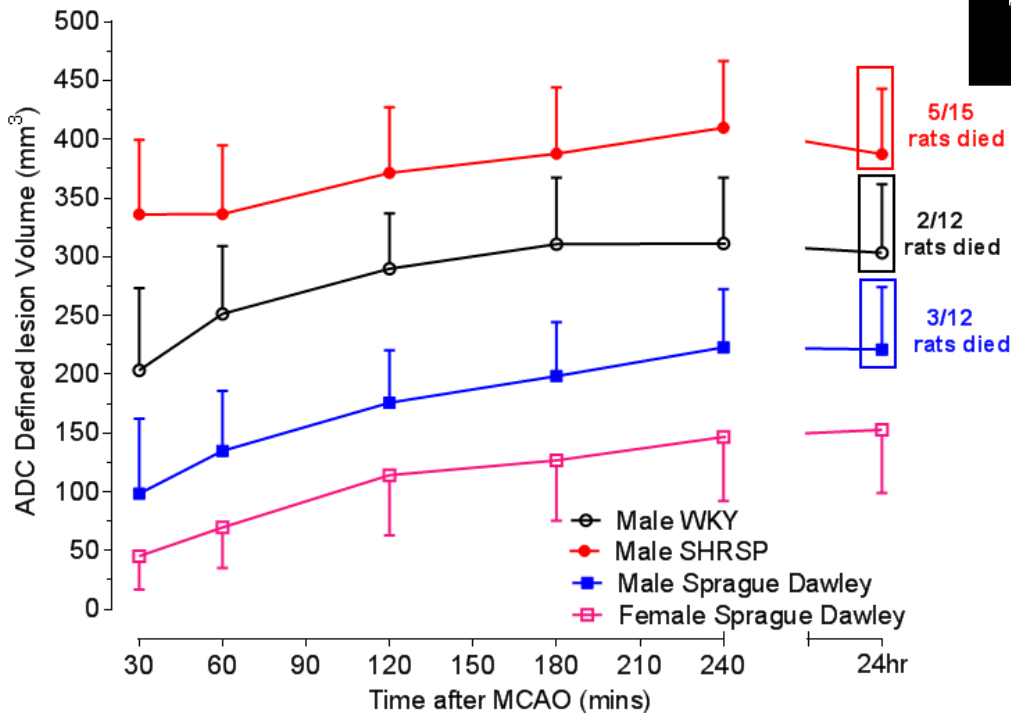
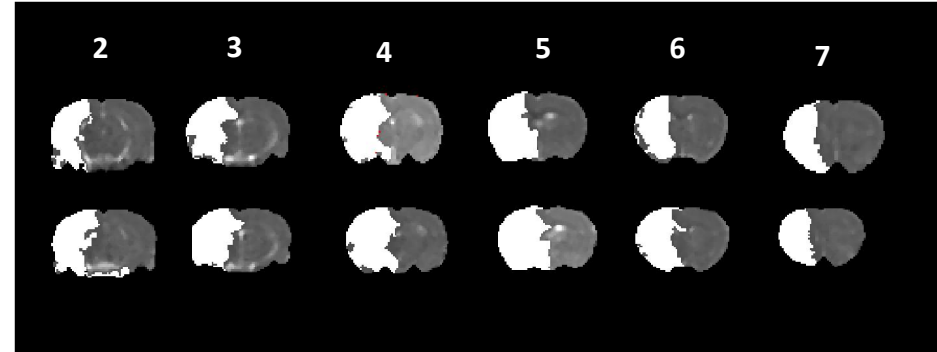
## Permanent MCAO

Slice

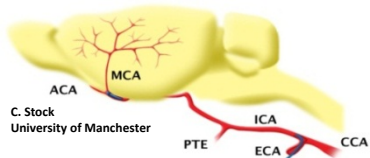
2 3 4 5 6 7

1 hr

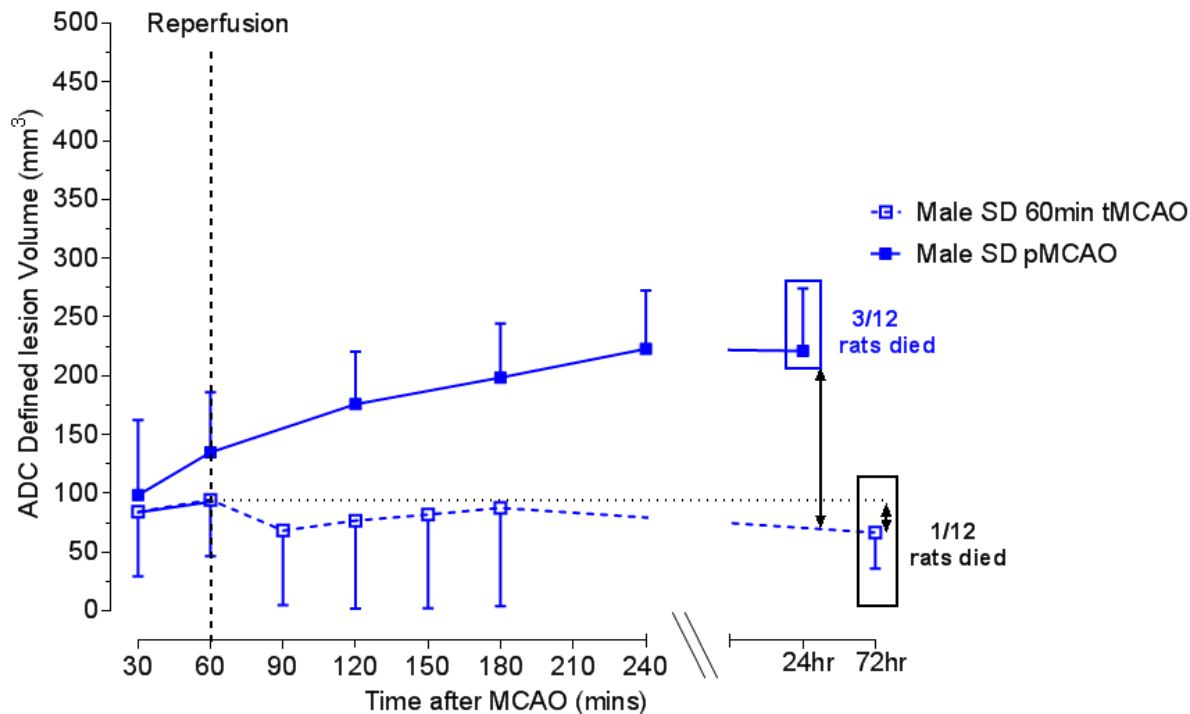
4 hr

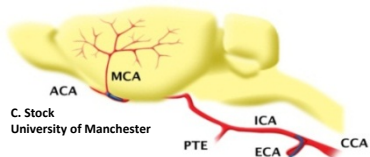


# Early reperfusion at 60 min can salvage brain tissue...

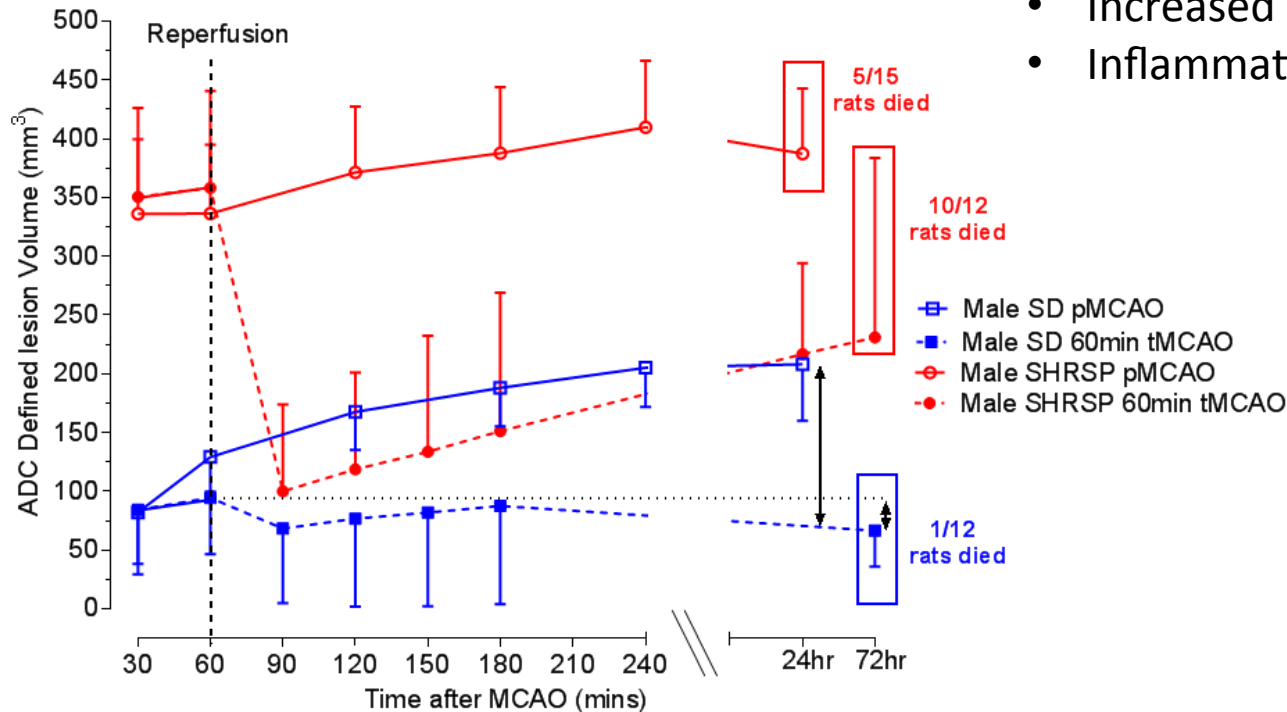


## Transient MCAO





## Transient MCAO



## Factors involved in worse outcome?

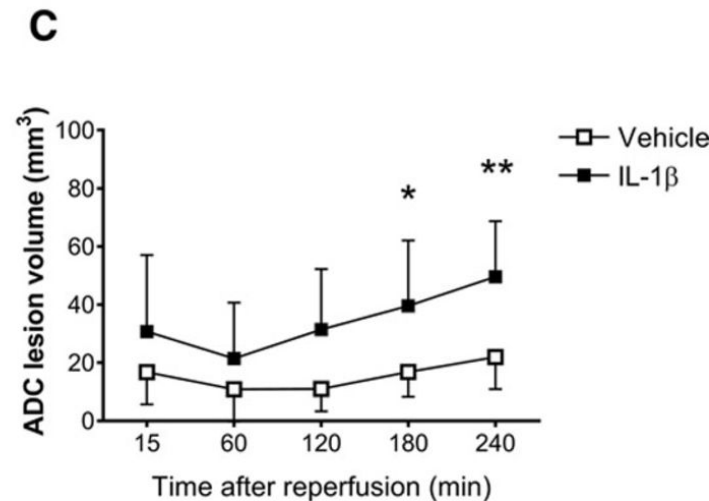
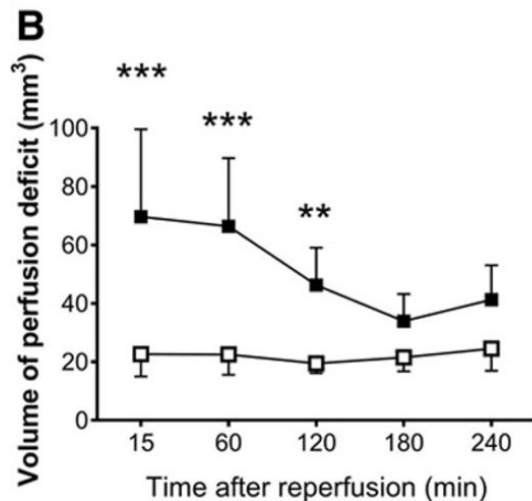
- Poorer collateral flow and perfusion following recanalisation
- Increased oxidative stress
- Inflammation – systemic &/or central

Stroke co-morbidities such as age, hypertension, atherosclerosis, obesity & diabetes all have a strong inflammatory component

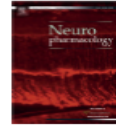
# Systemic inflammation impairs reperfusion

- Inflammation associated with increased risk of stroke and worse outcome following stroke
- Systemic inflammation induced with IL-1 resulted in hypoperfusion following reperfusion and increased infarct volume
- Hypoperfusion was due in part to an upregulation of the vasoconstrictor ET-1

Recanalisation in the presence of stroke co-morbidities (i.e hypertension, age, atherosclerosis) may result in impaired perfusion partly through effects of inflammation on the cerebrovasculature







## RESEARCH PAPER

### Suppressing inflammation by inhibiting the NF- $\kappa$ B pathway contributes to the neuroprotective effect of angiotensin-(1-7) in rats with permanent cerebral ischaemia

Teng Jiang<sup>1</sup>, Li Gao<sup>2</sup>, Jun Guo<sup>3</sup>, Jie Lu<sup>2</sup>, Yao Wang<sup>2</sup> and Yingdong Zhang<sup>1</sup>

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Dr Yingdong Zhang, Department of Neurology, Nanjing First Hospital, Nanjing Medical University, PO Box 210006, No. 68 Changde Road, Nanjing 210006, China. E-mail: j1870918@163.com; zhangyingdong@yahoo.com.cn

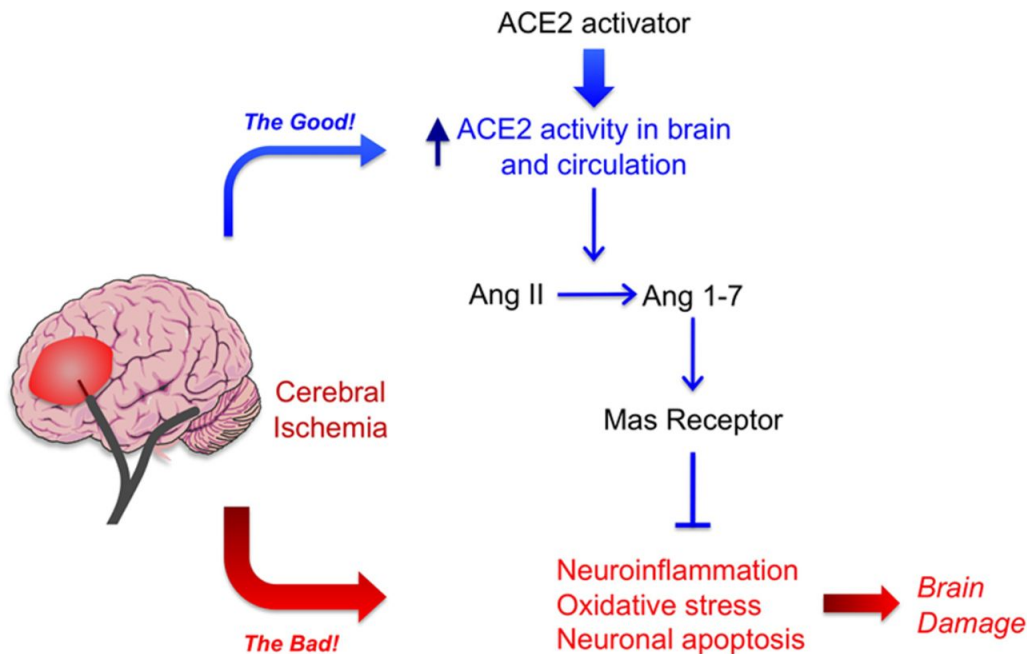
**Keywords**  
stroke; inflammation; Ang-(1-7); A-779; NF- $\kappa$ B

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2 July 2012  
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8 July 2012

### Anti-inflammatory effects of angiotensin-(1-7) in ischemic stroke

Robert W. Regenhardt<sup>a,b</sup>, Fiona Desland<sup>a,b</sup>, Adam P. Mecca<sup>a,b</sup>, David J. Pioquinto<sup>a,b</sup>, Aqeela Afzal<sup>c</sup>, J. Mocco<sup>c</sup>, Colin Sumners<sup>a,b,\*</sup>

Brain ischemia induces neuroinflammation, apoptosis, and oxidative stress and causes brain damage.

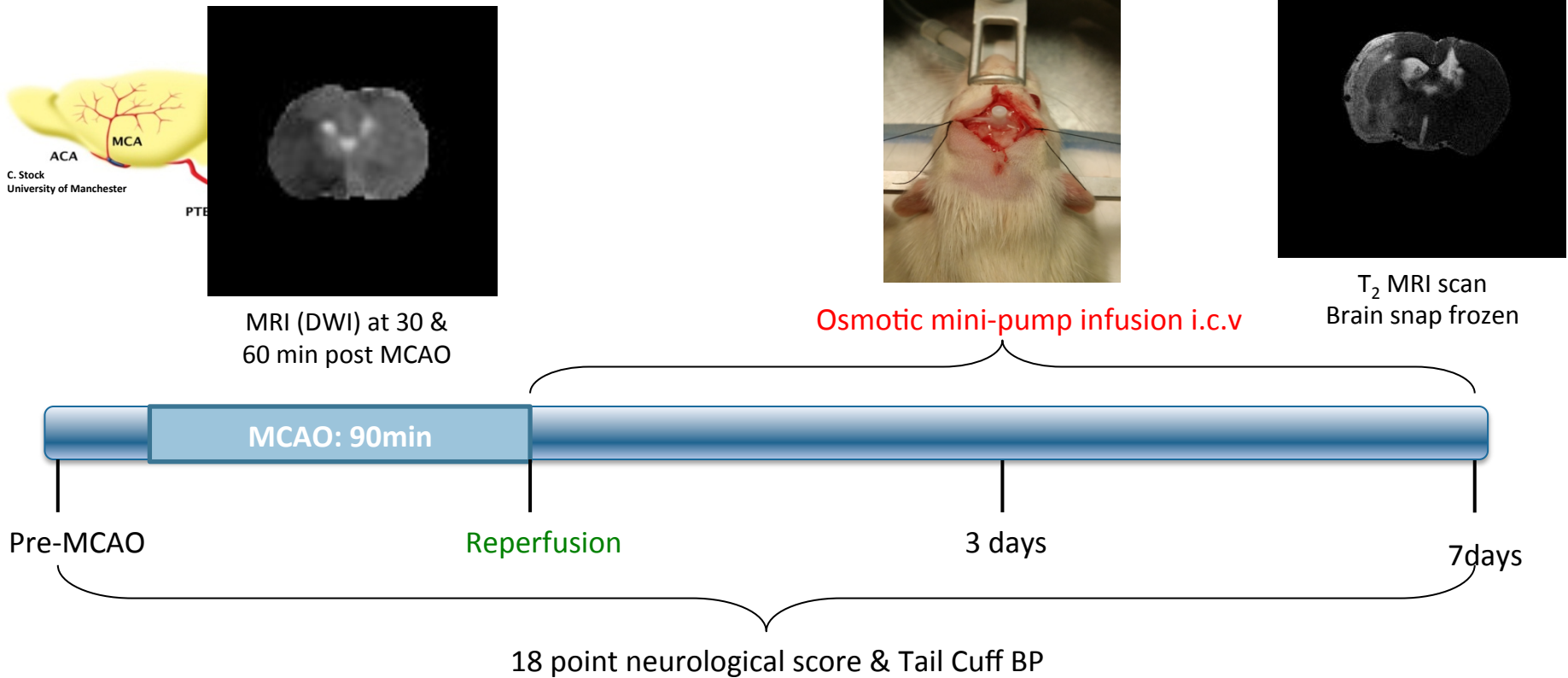


- Ang(1-7) attenuated the increased expression of iNOS, IL-1a, IL-6, CXCR4 & CD11b 24hr post ET-1 MCAO.

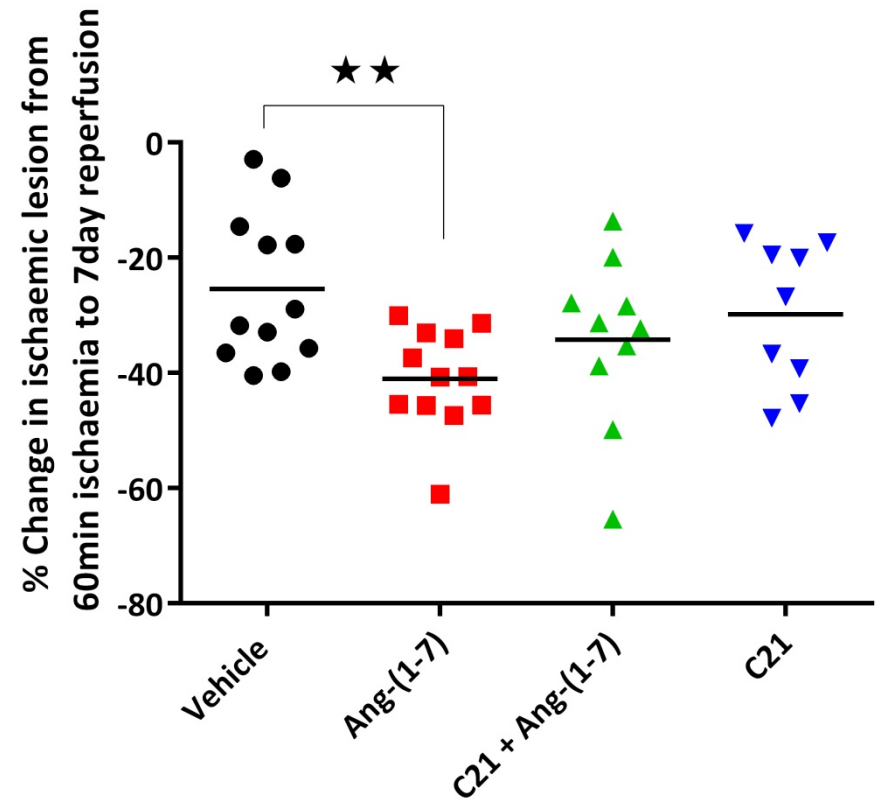
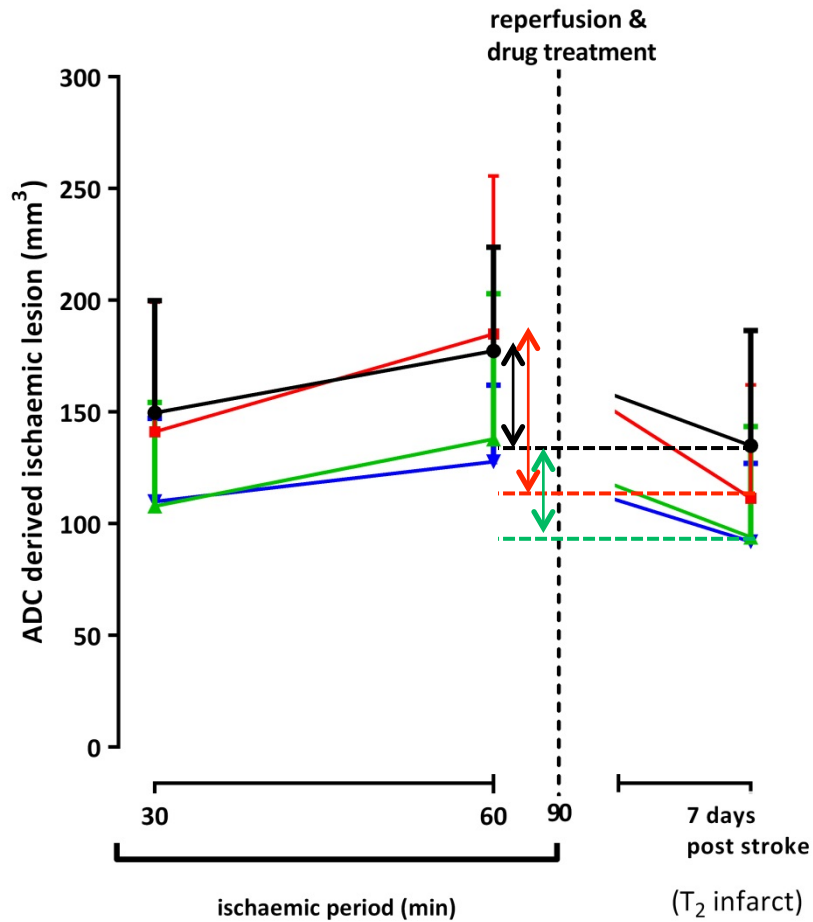
- ↓ NF- $\kappa$ B

- Mas Receptor immunoreactivity present in neurons in rat cerebral cortex and striatum as well as macrophages/microglia.

# Does Angiotensin-(1-7) improve outcome following reperfusion?



# Ang-(1-7) increases tissue salvage following reperfusion



- Temporal changes in Cerebral blood flow – laser doppler/speckle imaging
- Methods of detecting and measuring inflammatory mediators post stroke? Blood samples, brain tissue..
- BBB breakdown, Haemorrhagic transformation

## Ongoing & Future studies

- Investigating the role of Ang(1-7) on the acute evolution of brain damage in the presence of stroke co-morbidities (**Mariana Arroja, PhD student & Dr Emma Reid**)
- Potential of inhaled NO as a therapeutic strategy to improve CBF following stroke (**Joachim Biose, PhD student**)
- Understanding the role of Alpha 5 Beta1 Integrin on BBB integrity and outcome following stroke (**Biav Kittani, PhD student**)

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- **Dr William Holmes**
- **Mr Jim Mullin**
- **Dr Lorraine Work**



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