WMIC Dublin, Sept 5, 2012

Pathophysiology and imaging of stroke

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Pathophysiology and imaging of stroke

Max-Planck-Institut für neurologische Forschung Köln

Understanding of pathophysiologic mechanisms

Evaluation of therapeutic strategies

Assessment of brain recovery

Pathophysiology and imaging of stroke

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The rapid loss of brain function(s) due to disturbance in the blood supply to the brain.

Pathophysiology and imaging of stroke

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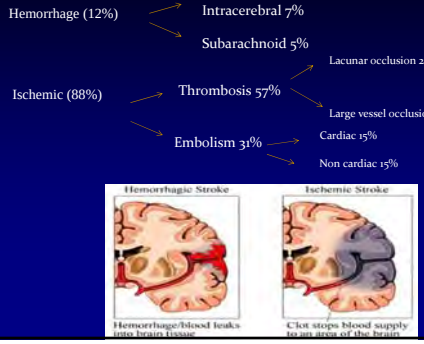

Stroke: pathophysiology and animal models

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Ischemia thresholds of CBF

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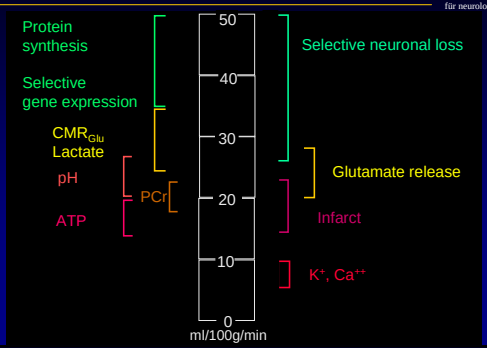

Outcome: severity of flow alterations

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Increasing severity of flow alteration

Inhibition of protein synthesis

↓

Transient increase of glucose consumption
Anaerobic glycolysis => lactate accumulation
tissue acidosis

↓

Breakdown of energy metabolism
=> anoxic depolarization of cell membranes

Outcome: duration of flow alterations

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Increasing duration of flow alteration

Persistent restriction of blood flow

↓

Tissue damage becomes more severe /
eventually irreversible

↓

Tissue becomes necrotic

Outcome: recirculation

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Quality of reperfusion

↓

Influence on success of tissue recovery

Recirculation

↓

Secondary functional and
metabolic disturbances

Cascade of pathophysiological events

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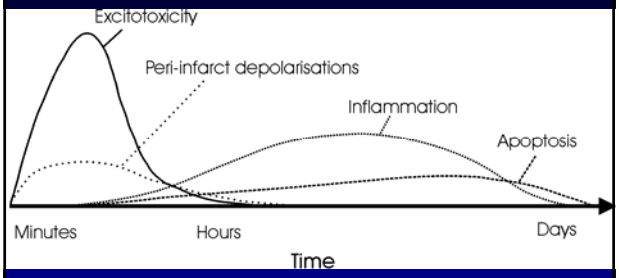

U. Dirnagl et al. 1999

Animal models of stroke

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Occlusion of the middle cerebral artery (MCA) by:

Electrocoagulation
Intraluminal suture occlusion technique / Withdrawal
Clot embolization / Lysis of clots

Permanent occlusion

↓

Evolution of focal cerebral
ischemia in space and time

Transient occlusion

↓

(potential) tissue recovery /
pathophysiological events induced
by reperfusion itself

Non-invasiveness of NMR

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Evolution of disease in space in time
Evolution of disease in relation to severity of lesion

MRA:	Vascular patency during MCA occlusion, after recanalization
PWI:	Tissue perfusion status
31P-/1H MRS:	metabolic alterations during ischemia and reperfusion (ATP, PCr, lactate, pH)
DWI:	Demarcation of ischemic injury (reflects earliest step of ischemic disturbances)
T2*:	Metabolic activity of reperfused tissue
T1/T2:	Increase of tissue water; spread of vasogenic edema
CE-T1WI:	Disturbance of BBB

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(Mike O'Neil, Eli Lily)

Severity in blood flow decrease

Depending on the Duration of occlusion

Collateral blood supply

3 days

Subcortical

Subcortical + cortical

2, 3, 5-triphenyltetra-zolium chloride (TTC)

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Stroke evolution and evaluation of therapeutic strategies

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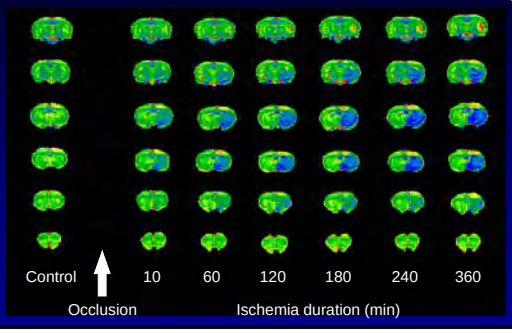
Evolution of focal ischemia / ADC



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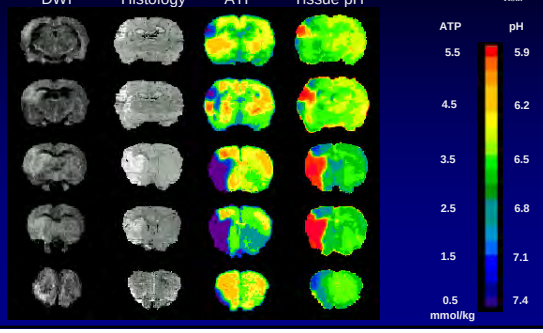
Focal cerebral ischemia at 6 hours



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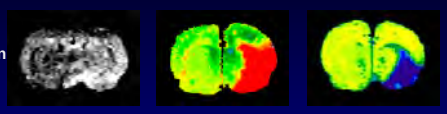
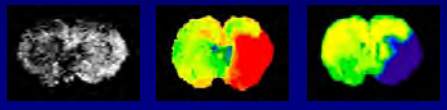
Focal cerebral ischemia at 30 min and 2 hrs

30 min Occlusion



DWI Tissue pH ATP

2 h Occlusion



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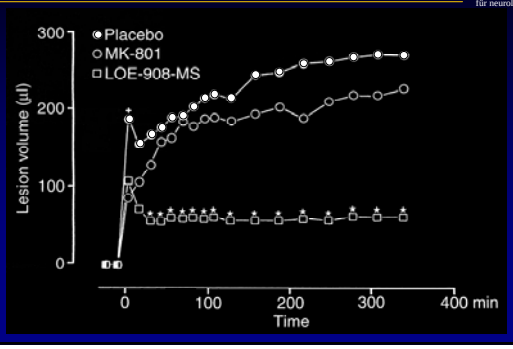
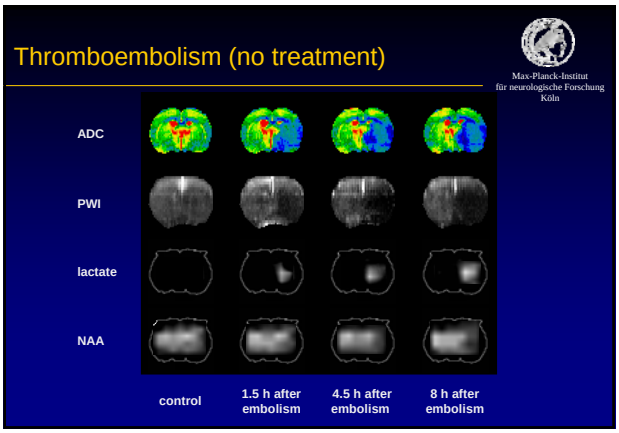
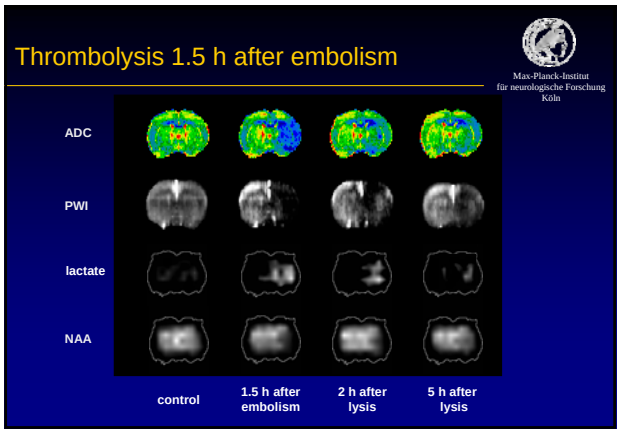
Lesion growth w./wo. treatment



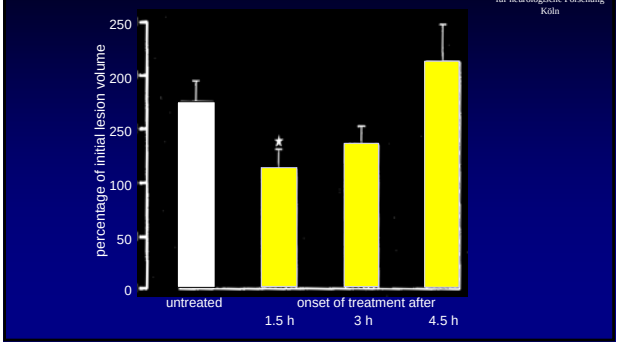
Thromboembolism (no treatment)



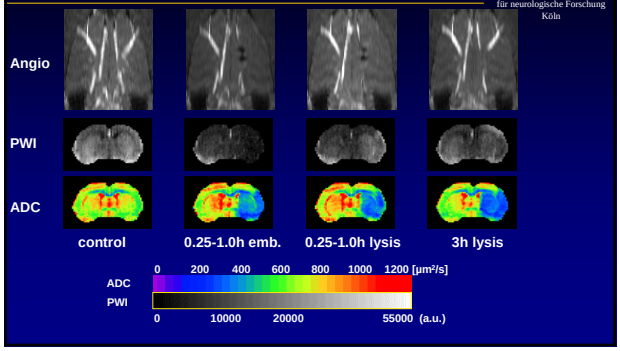
Thrombolysis 1.5 h after embolism



Lesion volume after rt-PA thrombolysis

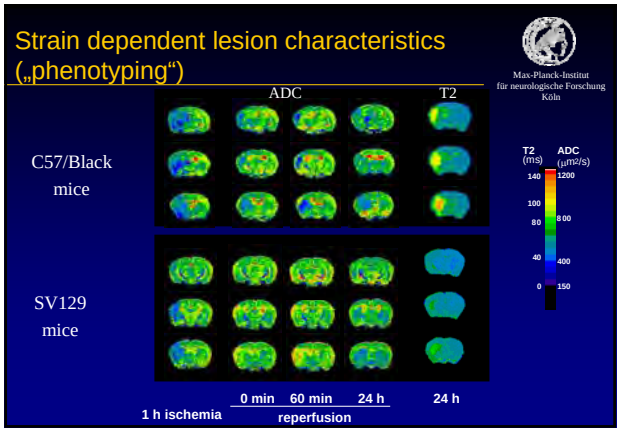


Thrombolysis after 60 min occlusion



Morphological and functional changes: Chronic phase

Strain dependent lesion characteristics („phenotyping“)



Brain Vasculature of C57Bl and SV129 Mice

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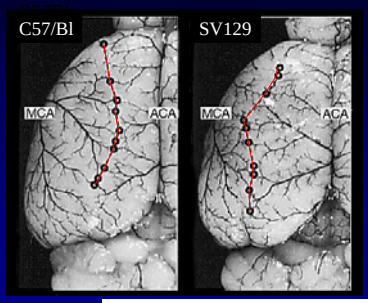

Maeda et al. (1998), Neuroreport **9**, pp 1317-1319

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Molecular imaging / Regeneration

fMRI: functional recovery after stroke

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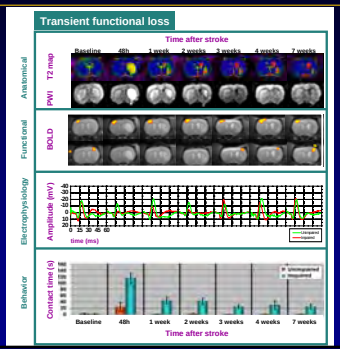

fMRI: functional recovery after stroke

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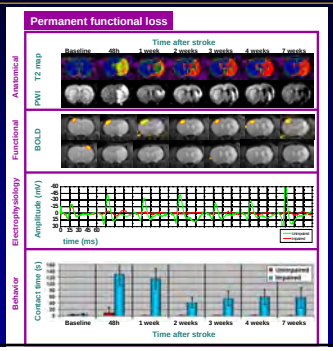

Stem cell mediated functional recovery

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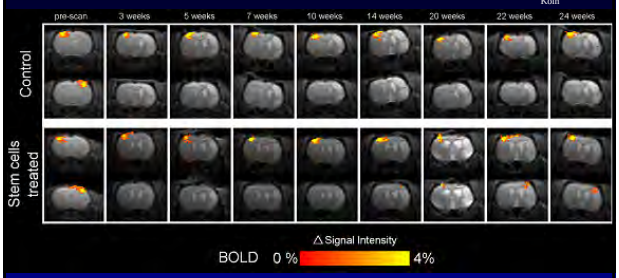

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