Pathophysiology and imaging of stroke

Mathias Hoehn
In-vivo-NMR-Laboratory
Max Planck Institute for Neurological Research
Cologne

WMIC Dublin, Sept 5, 2012

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

Pathophysiology and imaging of stroke

Understanding of pathophysiologic mechanisms
Evaluation of therapeutic strategies
Assessment of brain recovery

Hemorrhage (12%)
Ischemic (88%)
Intracerebral hemorrhage (12%)
Subarachnoid hemorrhage (5%)
Thrombosis (57%)
Embolism (31%)
Cardiac (15%)
Non-cardiac (15%)
Lacunar occlusion (26%)
Large vessel occlusion (31%)

Ischemia thresholds of CBF

Protein synthesis
Selective gene expression
CMRglu
Lactate
pH
ATP
PCr
Glutamate release
Infarct
K+, Ca++

Stroke: pathophysiology and animal models
Outcome: severity of flow alterations

- 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

- Persistent restriction of blood flow
- Tissue damage becomes more severe / eventually irreversible
- Tissue becomes necrotic

Outcome: recirculation

- Quality of reperfusion
- Influence on success of tissue recovery

Cascade of pathophysiological events

U. Dirnagl et al. 1999

Animal models of stroke

- Occlusion of the middle cerebral artery (MCA) by:
  - Electrocoagulation
  - Intraluminal suture occlusion technique / Withdrawal
  - Clot embolization / Lysis of clots

- Permanent occlusion
- Transient occlusion

Evolution of focal cerebral ischemia in space and time

Evolution of disease in space and 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

Non-invasiveness of NMR
Stroke evolution and evaluation of therapeutic strategies

Evolution of focal ischemia / ADC

Focal cerebral ischemia at 6 hours

Focal cerebral ischemia at 30 min and 2 hrs

Lesion growth w./wo. treatment
**Thromboembolism (no treatment)**

<table>
<thead>
<tr>
<th>ADC</th>
<th>PWI</th>
<th>Lactate</th>
<th>NAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>1.5 h after embolism</td>
<td>4.5 h after embolism</td>
<td>8 h after embolism</td>
</tr>
</tbody>
</table>

**Thrombolysis 1.5 h after embolism**

<table>
<thead>
<tr>
<th>ADC</th>
<th>PWI</th>
<th>Lactate</th>
<th>NAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>1.5 h after embolism</td>
<td>2 h after lysis</td>
<td>5 h after lysis</td>
</tr>
</tbody>
</table>

**Lesion volume after rt-PA thrombolysis**

<table>
<thead>
<tr>
<th>Percentage of initial lesion volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>untreated</td>
</tr>
</tbody>
</table>

**Thrombolysis after 60 min occlusion**

<table>
<thead>
<tr>
<th>Angio</th>
<th>PWI</th>
<th>ADC</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>0.25-1.0h emb.</td>
<td>0.25-1.0h lysis</td>
</tr>
</tbody>
</table>

**Morphological and functional changes:**

**Chronic phase**

<table>
<thead>
<tr>
<th>ADC</th>
<th>T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>C57/Black mice</td>
<td>SV129 mice</td>
</tr>
</tbody>
</table>

**Strain dependent lesion characteristics (“phenotyping”)**
Brain Vasculature of C57Bl and SV129 Mice

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

C57Bl

SV129

Molecular imaging / Regeneration

fMRI: functional recovery after stroke

T2 map

Baseline          48h           1 week       2 weeks      3 weeks       4 weeks       7 weeks

Time after stroke

fMRI: functional recovery after stroke

T2 map

Baseline          48h           1 week        2 weeks      3 weeks       4 weeks       7 weeks

Time after stroke

Stem cell mediated functional recovery

In-vivo-NMR-Laboratory

fMRI: functional recovery after stroke

T2 map

Baseline          48h           1 week        2 weeks      3 weeks       4 weeks       7 weeks

Time after stroke

fMRI: functional recovery after stroke

T2 map

Baseline          48h           1 week        2 weeks      3 weeks       4 weeks       7 weeks

Time after stroke