“Bite of Science”

Acute Therapies For Stroke
Translational Stroke Research

Louise McCullough MD, PhD
Department of Neurology at The McGovern Medical School
University of Texas Health Science Center at Houston
Louise.d.Mccullough@uth.tmc.edu
Types of Stroke

- Intracranial Hemorrhage
- Subarachnoid Hemorrhage
- Ischemic

Source: AHA Disease Statistics
Circulation 2012;125 (e2-e220)
Main Functional Areas of Cerebral Cortex
Complete MCA Territory

- MCA stem occlusion
- CL hemiplegia (F/A/L)
- CL sensory loss (F/A/L)
- Depressed level of consciousness with edema and herniation
- Global aphasia (dominant)
Parietal Neglect Syndrome

- Failure to recognize side of body contralateral to injury
- May not bathe contralateral side of body or shave contralateral side of face
- Deny own limbs
- Objects in contralateral visual field ignored
MERCI Trial = Mechanical Embolus Removal in Cerebral Ischemia; Concentric Retriever System

Thrombus Retriever x 5 Helical Loops

9-Fr Balloon Guide Catheter
20-year-old college sophomore in Holyoke, MA → Left hemispheric stroke, Symptoms onset, 9:40pm – Dense speech deficit and Right-sided weakness.

- EMS dispatched to dormitory →
- ED Eval @ Holyoke Medical Center (45mins) →
- Neurologist’s Eval @ Holyoke, contacting STROKE CENTER
- Started IV t-PA @ Holyoke (1hr, 40mins).

10/11/2006
- LIFE STAR dispatched (2hr, 10mins) →
- Arrival @ Hartford Hospital (3hr, 20mins), Severe deficits (NIHSS = 18 points) →
- Admit directly to Interventional Neuroradiology Suite →
- Catheter-based intervention (6hrs) →
- Extubated → Mild speech difficulty but sedated, right hand weakness.

10/12/2006
- Continues to improve – mild R hand weakness.

10/14/2006
- Discharged to Home.
Concentric Thrombus Retriever – *in vivo*
Mechanical Clot Retrieval

Pre Treatment

Post Treatment
MERCI ➔ Pathology
Final Results
Case

• 50 year old man with atrial fibrillation presents with left hemiparesis and neglect
• 3 hours since time of onset
• What vessel?
Early Imaging
Case

- 48 hours later the patient continues with dense left hemiparesis and eye deviation
- Still follows commands but becoming more somnolent
- Pupils initially reactive with normal Doll’s but develops aniscoria
Case

- 12 hours later
- Not arousable- comatose
- Still anisocoria, right pupil stops reacting

- Plan?
Case

Other options?
Issues in the use of animals in pre-clinical research

- Co-morbidities such as diabetes, obesity, high cholesterol, hypertension not modeled
- Lifestyle considerations (smoking, alcohol etc)
- Mimicking the actual “at risk populations”
- Interaction between risk factors and aging
Suture model (intra-luminal occlusion)

Hemorrhagic transformation (HT) after MCAO: blood marked by arrows.

Clot model MCA clot is stained with Evans Blue (arrows)
Cylinder test
Systemic Effects of Stroke

• Peripheral Effects

![Image showing SH and ST samples at 72 hr]

• Role of Peripheral Leukocytes/Myeloid Cells

• Local Response...

• Aging... T cell deficits? Infections?
Age and the Systemic Response to Stroke

Aged Stroke

Young Stroke

Neat $10^{-2}$

A

B

CFU/mL

Young Stroke  Aged Stroke
The amount AND the composition of systemic bacteria differ in young vs. aged mice

<table>
<thead>
<tr>
<th></th>
<th>Young Sham (%)</th>
<th>Young Stroke (%)</th>
<th>Aged Sham (%)</th>
<th>Aged Stroke (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLN</td>
<td>1/7 14.3</td>
<td>5/7 71.4</td>
<td>3/8 37.5</td>
<td>6/7 85.7</td>
</tr>
<tr>
<td>Spleen</td>
<td>0/6 0</td>
<td>4/10 40</td>
<td>1/8 12.5</td>
<td>6/7 85.7</td>
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<tr>
<td>Liver</td>
<td>0/7 0</td>
<td>8/10 80</td>
<td>2/8 25</td>
<td>7/7 100</td>
</tr>
<tr>
<td>Lung</td>
<td>0/7 0</td>
<td>3/10 30</td>
<td>1/8 12.5</td>
<td>5/7 71.4</td>
</tr>
</tbody>
</table>

**Diagram:**
- **Young Stroke**
  - Escherichia (50%) (50%)
  - Staphylococcus (31-33%) (31-33%)
  - Enterococcus (13-17%) (13-17%)

- **Aged Stroke**
  - Enterobacter (50%) (50%)
Aging and stroke impair GI barrier function and allow for bacterial translocation.

Stroke-induced loss of the gut hypoxic barrier, O2 sensing pimonidazole (green)
A principle component analysis (PCA) showed significant separation between age groups (ANOSIM p value = 0.005). Principle component 1 (PC1) explained 31.19% of variation seen in samples while PC2 (15.97%) further separated the different microbial populations from different microbiome. PCA plots were generated using the raw abundances of microbial groups after 16s rRNA sequencing.
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