Cerebral Blood Flow after Concussion: Implications for Model Systems Patients

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UTSouthwestern Medical Center

UTSouthwestern was founded in 1943 and became part of The University of Texas System in 1949.

World renowned for its research with 6 Nobel Prize winner on our faculty over the years.
We train nearly 3,600 medical, graduate, and health profession students, residents, and postdoctoral fellows each year.
Our 17,000 employees provide care to more than 105,000 hospitalized patients, almost 370,000 emergency room cases, and oversee approximately 3 million outpatient visits annually.

Clements University Hospital

Opened in December 2014 and currently undertaking a $480 million expansion of the hospital that will open in 2020 consisting of a third tower that will serve as the clinical home for the Peter O’Donnell Jr. Brain Institute.

Zale Lipshy University Hospital – neuroscience hospital that will soon become our Rehabilitation and Wellness Hospital
Physical Medicine and Rehabilitation Department

- 58 Faculty Members (by Oct 1, 2019)
  - 2 University hospitals, Parkland Hospital, Children's Medical Center, Dallas VA Medical Center, Simmons Cancer Center
  - Clinics: Sprague, Aston, Moncrief/Fort Worth, Las Colinas, Richardson, Frisco
  - 33 PMR residents, Brain Injury Medicine/Spine/MSK/Ped Rehab fellows (4), Rehabilitation Psychology postdoctoral fellowship
  - Biomechanics and Neuromodulation laboratories
  - North Texas Burn Model System
  - Research funding from NIH, NIDILRR, TIBIR, PCORI, Foundation for PMR, AOTF
  - Top 25 for NIH funding for rehabilitation departments
  - School for Health Professions (PhD Applied Research, DPT, Master’s P&O, Rehab Counseling)

Acknowledgement

TIBIR Pilot Grant 2016-2018
Sydney Lyng
Emma-Kate Brown
SMU Athletics Department
University Research Council Grant
Autonomic Nervous System – Role in Health and TBI


What is a Concussion?

Estimated Number of Athletes

3.8 million concussions annually
Shearing of endothelial cells ↓ CBF Regulation

Disruption of axon transportation

Deregulated ion flux

Proteolytic enzyme activation

Energy crisis

↓ Neuron Function

Poor Outcome

Signs & Symptoms

<table>
<thead>
<tr>
<th>Physical Features</th>
<th>Cognitive Features</th>
<th>Behavior Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Impaired concentration</td>
<td>Sleep disturbances</td>
</tr>
<tr>
<td>Gait Disturbances</td>
<td>Memory problems</td>
<td>Emotional lability</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Confusion</td>
<td>Nervous or Anxious</td>
</tr>
<tr>
<td>Nausea</td>
<td>Feeling in a &quot;fog&quot;</td>
<td>Easily distracted</td>
</tr>
<tr>
<td>Impaired playing ability</td>
<td>Delayed</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Photophobia</td>
<td>Responsiveness</td>
<td>Irritability</td>
</tr>
</tbody>
</table>

Animal Studies

Structural integrity of microvessels compromised
- Acute loss of microvasculature with TBI
- Reductions in capillary number & diameter of vessels at injury site

Functional Integrity compromised
- Impaired CBF regulation
- Decoupling between CBF and glucose metabolism

Control TBI Patient

Reduced rCBF compared to the controls
Meier, T et al. 2015. JAMA Neurol. 72 (5): 530-538
Symptomatic patients presented with reductions in CBF.

Meier, T et al. 2015. JAMA Neurol; 72 (5): 530-538

Significantly less CBF in supplementary motor area in the concussion group 24 h after injury.

Wang, Y et al. 2015. Journal of Neurotrauma; 32: 1-10

Less CBF diffuse cortical & subcortical regions 8 days after injury.

Purpose

Cerebral Blood Flow (CBF) Regulation

Functional Outcome
Transcranial Doppler Ultrasound


Vascular Territories
Study Population

Student Athletes (NCAA Division I & Rec Sports)
Both men and women
Sports related concussion
No concussion for the past year

Research Design

Cross-sectional → Healthy Controls
Longitudinal → Concussion

Laboratory Visits ~ 3 hour

- Health History
- SCAT-3
- PHQ-9
- Insomnia Severity Index
- Trails A & B
- Balance
- Cerebral Blood Flow Regulation:
  - Central Autoregulation during sitting and oscillatory squatting
  - Central vasoreactivity to CO2
- Neurovascular Coupling with N-Back Test
- 40 Test
- Blood biomarkers

Cerebrovascular Research Lab
Time Domain

Frequency Domain

Transfer Function Analysis

Blood Pressure  Cerebral blood flow

Gain  Cerebral autoregulation

Results
At Rest

<table>
<thead>
<tr>
<th>Normalized LF Gain (%/mm Hg)</th>
<th>Control</th>
<th>Day 3</th>
<th>Day 21</th>
<th>Day 30</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
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<td>1.0</td>
<td>1.5</td>
<td>2.0</td>
<td>1.0</td>
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<tr>
<td>Cerebral Autoregulation</td>
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</table>

During Squatting

<table>
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<tr>
<th>Normalized LF Gain (%/mm Hg)</th>
<th>Control</th>
<th>Day 3</th>
<th>Day 21</th>
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Cerebral Vasoreactivity

Cerebral Vasoreactivity to CO₂

Results

Headache Associated with Low CVR
Neurovascular Coupling

Rest 2-Back

0.03

0.01

0.003

*
Summary

Symptom recovery precede physiological recovery
Persistent perturbation may contribute to prolonged recovery or leave an athlete vulnerable
TCD may be useful vascular biomarker for tracking physiological recovery after concussion.

Thank You

BIBLIOGRAPHY


