RE-SCULPTING THE BRAIN AFTER INJURY: NEW EVIDENCE FROM NEUROIMAGING

DR. NAZNIN VIRJI-BABUL, P.T. PHD
DEPT. OF PHYSICAL THERAPY
DJAVAD MOWAFAGHIAN CENTRE FOR BRAIN HEALTH
UBC
PHINEAS GAGE: HISTORY’S MOST FAMOUS BRAIN INJURY SURVIVOR
QUESTIONS:
(1) What are the structural and functional imaging signatures of concussion?
(2) How do these signatures change with recovery/intervention?
White matter abnormalities

Adolescents (14-17yo) seen 18-61 days post sport-related mTBI

Virji-Babul et al., 2013
Changes in the genu of corpus callosum, anterior and posterior internal capsule and anterior corona radiata

Borich et al, 2013 J Neurotrauma
DTI STUDIES IN MTBI: ANTERIOR REGIONS MORE INVOLVED

Anisotropy Abnormalities and ROI Spatialities

Eierud et al, 2014
HOW DO STRUCTURAL CHANGES CORRESPOND TO FUNCTIONAL CHANGES IN THE BRAIN?
FUNCTIONAL IMAGING: TWO GENERAL APPROACHES

1. TASK BASED

2. RESTING STATE

Figure 5a: Brain at rest
SPONTANEOUS FLUCTUATIONS IN BOLD SIGNAL: FUNCTIONAL NETWORKS

DEFAULT MODE NETWORK (MONITORING INTERNAL ENVIRONMENT, SOCIAL COGNITION)

CENTRAL EXECUTIVE NETWORK (WORKING MEMORY, DECISION MAKING)

Seeley et al, 2007
RESTING STATE NETWORKS IN ADOLESCENTS:

Controls

DMN

Concussed

Executive function

Borich et al, J Neurotrauma, 2014
Concussed > Controls

A

R L

PCC

B

FP

C

FO
RESTING STATE EEG:

54 adolescent subjects
- 33 healthy soccer players
- 21 athletes with acute concussion
  (soccer or ice hockey)

64-channel EEG recording

5 minutes of eyes-closed rest

GRAPH THEORY: THE BRAIN AS A NETWORK

Courtesy S Achard
GRAPH THEORY: THE BRAIN AS A NETWORK

Global metrics: measurement of the structural property regarding to the whole graph.

Local metrics: measurement of the structural properties of each single node.
NO DIFFERENCE IN OVERALL TOPOLOGY OF FUNCTIONAL BRAIN NETWORKS (GLOBAL METRICS)

Control Adolescent  Concorded Adolescent

CONCUSSED GROUP: HIGHER VALUES IN DLPFC HUB

![Bar charts showing comparisons between controls and concussed groups in terms of Betweenness and Degree metrics. The graphs display higher values for the concussed group compared to the controls.]
DLPFC IN CONCUSSION: HUB OVERLOAD?

Stam, Nature Reviews Neuroscience, 2014
HOW DO EEG SIGNALS CHANGE OVER TIME?
NO CHANGE IN CONNECTIVITY IN CENTRAL, PARIETAL AND TEMPORAL REGIONS
Relationship between Symptoms and Frontal Connectivity

Porter, Munjal and Virji-Babul, In Preparation
MULTI-MODAL NEUROIMAGING IN ADULTS WITH MILD TO MODERATE TBI

Funded by: Eaton Education Group

Collaborators:
I. Torres, W. Panenka (Neuropsychiatry, UBC)
F. Beg, K. Popuri, D. Lu (SFU, Image Analysis Lab)
A. MacKay, B. Russell Schulz, I. Vavasour, J. Zhang (MRI Research Centre, UBC)
MRI:

Philips Achieva 3T scanner:
1) Anatomical 3D T1 scan
2) Diffusion tensor imaging: 60 Direction HARDI
3) Resting state fMRI (8 minutes)
4) Myelin water imaging: GRASE 48-echo, TE=8ms,

NEUROPSYCHOLOGY:

- NIH Toolbox Cognitive Battery.
- Phonemic Verbal Fluency (PVF) Language and executive retrieval
- Rey Auditory Verbal Learning Test (RAVLT) – Verbal List Learning and Memory
- Neurobehavioural symptom inventory (BSI-18)
- Satisfaction with life scale (SWLS)
- Alcohol, Smoking, and Substance Use Involvement Screening Test (ASSIST)
- Mini-international neuropsychiatric interview (MINI)
- Glasgow outcome scale- extended
- Patient Health Questionnaire-15
- Test of Memory Malingering (TOMM) – Test Compliance and Effort

Resting state EEG
PILOT STUDY

<table>
<thead>
<tr>
<th>Participants</th>
<th>12 adults with mild to moderate TBI (6 participated in MRI; 12 participated in EEG)</th>
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<tbody>
<tr>
<td>Age Range</td>
<td>18 – 51 years of age</td>
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<tr>
<td>MOI</td>
<td>Multiple concussions, MVA</td>
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<tr>
<td>Length of time since initial injury</td>
<td>6 months – 28 years</td>
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</tbody>
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| NIH TOOLBOX Scores (Age adjusted) | 84-153 (TBI group)  
                        | 129-153 (Control group) }
BASELINE COGNITIVE SCORES: NIH TOOLBOX

Fluid Cognition

Crystallized cognition
Axonal Injury

Forces applied to the brain cause axons to twist and tear; Brain cell death occurs
WHY STUDY MYELIN IN TBI?

• Animal models of TBI: stretch injury results in damage to myelin sheath

• Changes to central myelin and oligodendrocytes may continue over months following TBI (Maxwell, 2013)

• Injury to central myelin may contribute to continued axonal degeneration following TBI
Healthy Controls

TBI subjects

18 year old male  36 year old male  51 year old female
GLOBAL WHITE MATTER REDUCED IN TBI GROUP

MWF significantly lower in TBI (0.0886) compared to age and gender matched healthy controls (0.121); p=0.0024
MWF IN CORPUS CALLOSUM AND CORTICOSPINAL TRACT IS REDUCED IN TBI GROUP
DECREASE IN MWF CORRELATED WITH DECREASE IN CRYSTALLIZED AND FLUID COGNITION

NIH TB Oral Reading Recognition

Oral Reading Recognition Score vs. White Matter

R = .7
p = .03

NIH TB Picture Sequence Memory

Picture Sequence Memory Score vs. White Matter

R = .85
p = .01
INCREASED FUNCTIONAL CONNECTIVITY (EEG) CORRELATED WITH LOWER SCORES ON WORKING MEMORY

Increased global connectivity in TBI

Working memory vs clustering coefficient

R = .8
P = .001
3 MONTHS POST INTERVENTION: SMALL BUT SIGNIFICANT CHANGE IN FLUID COGNITION

Baseline and 3 months post-intervention:
Fluid cognition

Baseline and 3 months post-intervention:
Crystallized cognition
MWF IN RELATION TO AGE AND EDUCATION

Global White Matter vs. Age

Global White Matter vs. Years of Education

Legend:
- Control
- TBI
- TBIControl

Visit:
- Month3
- Month6
- PRE
• Increase connectivity associated with decreased crystallized and fluid cognition

TOO MUCH CONNECTIVITY IS BAD!
SUMMARY:

- Small but significant change in fluid cognition over 6 months
- Changes in EEG (functional connectivity) over 3 months
- So far no change in group average values for myelin
3 MONTHS POST-INTERVENTION: EEG MEASURES CLOSER TO CONTROL VALUES
COGNITIVE MEASURES

Fluid
Crystallized
Executive Frontal
Composite Scores

* TBI
* 3 Months
Control
3 MONTHS POST ARROWSMITH PROGRAM
EEG:

F10 Betweenness

F10 Hub Value
TIME POINT 1: BASELINE
CAN COGNITIVE THERAPY CHANGE THE BRAIN AFTER TBI?
POTENTIAL BIOMARKERS OF ACUTE AND CHRONIC TBI:

Changes in brain structure:
- Axonal injury: DTI – non specific
- Reduced myelin in whole brain and specific white matter tracts (MWF)
- MWF correlated with cognitive function

Changes in brain function:
- EEG: Increase in high frequency oscillations/decrease in low frequency oscillations in frontal regions
- EEG: Increase in functional connectivity in frontal regions

Reorganization over time (MWF& EEG)?
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STUDENTS: