Imaging and Recovery of Function Recovery After Brain Injury

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Background

- Weakness and difficulty controlling muscles is common after a brain injury
  - Traumatic Brain Injury
  - Non-traumatic brain injury/Stroke
“Will he/she ever do ____ again?”

- Prediction of recovery is one of the most commonly asked question after any brain injury.
- The ability to predict some outcomes after brain injury in a broad sense is good.
GCS
- Lower scores associated with worse outcomes
- No threshold values

Length of Coma
- Longer duration associated with worse outcomes
- Threshold values:
  - Severe disability unlikely when less than 2 weeks
  - Good recovery unlikely when greater than 4 weeks

PTA
- Longer duration associated with worse outcomes
- Threshold values:
  - Severe disability unlikely when less than 2 months
  - Good recovery unlikely when greater than 3 months

Age
- Older age associated with worse outcomes
- Threshold values:
  - Good recovery unlikely when older than 65 years old
Glasgow Outcome Scale (GOS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Death</td>
</tr>
<tr>
<td>2</td>
<td>Vegetative State</td>
</tr>
<tr>
<td>3</td>
<td>Severe Disability</td>
</tr>
<tr>
<td>4</td>
<td>Moderate Disability</td>
</tr>
<tr>
<td>5</td>
<td>Low Disability</td>
</tr>
</tbody>
</table>

- Severe damage with prolonged state of unresponsiveness and a lack of higher mental functions
- Severe injury with permanent need for help with daily living
- No need for assistance in everyday life, employment is possible but may require special equipment.
- Light damage with minor neurological and psychological deficits.

- Broad categories with limited sensitivity
- Not an accurate indicator of specific functional abilities
# Glasgow Outcome Scale - Extended (GOSE)

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<th>Score</th>
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<tr>
<td>1</td>
<td>Death</td>
</tr>
<tr>
<td>2</td>
<td>Vegetative State</td>
</tr>
<tr>
<td>3</td>
<td>Low Severe Disability</td>
</tr>
<tr>
<td>4</td>
<td>Upper Severe Disability</td>
</tr>
<tr>
<td>5</td>
<td>Low Moderate Disability</td>
</tr>
<tr>
<td>6</td>
<td>Upper Moderate Disability</td>
</tr>
<tr>
<td>7</td>
<td>Low Good Recovery</td>
</tr>
<tr>
<td>8</td>
<td>Upper Good Recovery</td>
</tr>
</tbody>
</table>

## Outcome Details

- **Death**: --
- **Vegetative State**: Severe damage with prolonged state of unresponsiveness and a lack of higher mental functions.
- **Low Severe Disability**: Patient who is dependent for daily support for mental or physical disability, usually a combination of both. If the patient can be left alone for more than 8h at home it is upper level of SD, if not then it is low level of SD.
- **Upper Severe Disability**: Patients have some disability such as aphasia, hemiparesis or epilepsy and/or deficits of memory or personality but are able to look after themselves. They are independent at home but dependent outside. If they are able to return to work even with special arrangement it is upper level of MD, if not then it is low level of MD.
- **Low Moderate Disability**: Patients have some disability such as aphasia, hemiparesis or epilepsy and/or deficits of memory or personality but are able to look after themselves. They are independent at home but dependent outside. If they are able to return to work even with special arrangement it is upper level of MD, if not then it is low level of MD.
- **Upper Moderate Disability**: Resumption of normal life with the capacity to work even if pre-injury status has not been achieved. Some patients have minor neurological or psychological deficits. If these deficits are not disabling then it is upper level of GR, if disabling then it is lower level of GR.
Background

- Very specific areas of recovery (hand function, leg function) is more difficult to predict

- In a recent survey, only 37% of brain injury physicians felt comfortable about prognosis after a brain injury

Decisions regarding therapy, discharge destination, long term prognosis, and optimal allocation of resources are being made earlier now than ever before.
Background

These early decisions can significantly impact the long term outcome for a patient.
So...

- How do we do a **better** and **more specific** job at predicting functional recovery after a brain injury?
What’s inside?
What’s inside?

▶ Specifically: which areas in the brain are responsible for which functions?
Phrenology

- The brain is composed of multiple, distinct, innate faculties.
- Because they are distinct, each faculty must have a separate seat or "organ" in the brain.
- The size of an organ, other things being equal, is a measure of its power.
- The shape of the brain is determined by the development of the various organs.
- As the skull takes its shape from the brain, the surface of the skull can be read as an accurate index of psychological aptitudes and tendencies.
Phrenology
Phrenology
Head Measurements Help To Identify Criminals

A device long used by hat stores, to measure the size and shape of a customer's head, now helps police of Norwalk, Conn., to identify criminals. According to sponsors of the new method, who use it in conjunction with fingerprinting, no two men have heads of exactly the same shape. Therefore, the perforated contour patterns produced by the device will afford a check on a suspect's identity, and may prove particularly valuable if he has attempted to alter his fingerprints by chemical or surgical means. Since he cannot change the contour of his skull, this would remain as a telltale clue to his identity.

No, he's not being measured for a new hat. The device records the head shape, as seen at right.
Phrenology
Brodmann’s Classification

Brodmann’s cytotechtonic map (1909):
- Lateral surface
- Medial surface
Brodmann’s Classification
Brodmann’s Classification
Homunculus
Homunculus

Homunculus
Diaschisis

One part of the brain is dependent on other areas of the brain that are physically far away.

Computed Tomography (CT)
Computed Tomography (CT)
Computed Tomography (CT)
Magnetic Resonance Imaging (MRI)
Magnetic Resonance Imaging (MRI)
Magnetic Resonance Imaging (MRI)
With these images, people became good at predicting function in general
<table>
<thead>
<tr>
<th>STUDY</th>
<th>POPULATION/AGE (RANGE [MEAN])</th>
<th>NUMBER</th>
<th>OUTCOME</th>
<th>PREDICTOR</th>
<th>FINDINGS ASSOCIATED WITH WORSE OUTCOME</th>
<th>STATISTICS</th>
<th>&quot;THRESHOLD&quot; VALUES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopes, 2009 (56)</td>
<td>Moderate and severe; acute</td>
<td>100</td>
<td>GOS (6 months)</td>
<td>CT (admission); MRI (15 days status post trauma)</td>
<td>Univariate; CT findings and DAI on MRI; multivariate: DAI in brainstem</td>
<td>Univariate and multivariate</td>
<td>None</td>
</tr>
<tr>
<td>Jacobs, 2010 (57)</td>
<td>Moderate and severe; acute</td>
<td>679</td>
<td>GOSE (6 months)</td>
<td>CT (admission)</td>
<td>Univariate: any cisternal compression and/or absence; multivariate: compressed and/or absent ambient cisterns and/or fourth ventricle</td>
<td>Univariate and multivariate</td>
<td>None</td>
</tr>
<tr>
<td>Nelson, 2010 (58)</td>
<td>Moderate and severe; acute</td>
<td>363</td>
<td>GOS (12 months)</td>
<td>CT (admission)</td>
<td>Midline shift; SAH/IVH, and cisternal compression</td>
<td>Univariate and multivariate</td>
<td>None</td>
</tr>
<tr>
<td>Skandsen, 2010 (59)</td>
<td>Moderate and severe; acute</td>
<td>100</td>
<td>GOSE (12 months)</td>
<td>MRI (4 weeks)</td>
<td>DAI; brainstem involvement</td>
<td>Univariate</td>
<td>No one without DAI had severe disability (CI 0%-10%)</td>
</tr>
<tr>
<td>Jacobs, 2011 (60)</td>
<td>Moderate and severe; acute</td>
<td>568</td>
<td>GOSE (6 months)</td>
<td>CT</td>
<td>Lesion burden; SDH; hemorrhagic contusion</td>
<td>Univariate and multivariate</td>
<td>None</td>
</tr>
<tr>
<td>Skandsen, 2011 (61)</td>
<td>Moderate and severe; acute</td>
<td>100</td>
<td>GOSE (12 months)</td>
<td>MRI (4 weeks)</td>
<td>Blateral brainstem injury</td>
<td>Univariate and multivariate</td>
<td>Only 7% of patients with bilateral brainstem injury had a good recovery (CI 0%-34%)</td>
</tr>
<tr>
<td>Yeomans, 2011 (62)</td>
<td>Moderate and severe; acute</td>
<td>1,276</td>
<td>GOSE (12 months)</td>
<td>CT (admission)</td>
<td>Marshall CT classification; SAH</td>
<td>Multivariate</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; CT, computed tomography; DAI, diffuse axonal injury; EDH, epidural hematoma; GCS, Glasgow Outcome Scale; GOSE, Glasgow Outcome Scale Extended; GSW, gunshot wound; ICU, intensive care unit; IVH, intraventricular hemorrhage; MRI, magnetic resonance imaging; SAH, subarachnoid hemorrhage; SDH, subdural hematoma.
DTI – Diffusion Tensor Imaging
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DTI – Diffusion Tensor Imaging
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>N</th>
<th>TBI severity</th>
<th>DTI analyses method</th>
<th>DTI metric(s)</th>
<th>Clinical outcome measures</th>
<th>Significant relationships with clinical outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>Levin</td>
<td>37</td>
<td>Mild/Moderate</td>
<td>Fiber tracking</td>
<td>FA</td>
<td>Total Post-concussion Symptoms Score and Total Post-Traumatic Stress Disorder Symptoms Score</td>
<td>Negatively correlated with whole CC.</td>
</tr>
<tr>
<td>2011</td>
<td>Newcombe</td>
<td>68</td>
<td>Mixed</td>
<td>ROI</td>
<td>ADC</td>
<td>Glasgow Outcome Scale</td>
<td>Unfavorable outcomes were associated with higher ADC values of the supratentorial white matter, anterior CC, posterior CC, ventral midbrain, dorsal midbrain, pons, thalamus, and cerebellar peduncles.</td>
</tr>
<tr>
<td>2011</td>
<td>Palacios</td>
<td>15</td>
<td>Severe</td>
<td>Skeletorized Voxel Based Analyses</td>
<td>FA</td>
<td>Post-Traumatic Amnesia</td>
<td>Duration of Post-Traumatic Amnesia was correlated with lower FA of the corpus callosum, SLF, ILF, IFOF, uncinate fasciculus, cingulum, fornix and anterior thalamic radiation.</td>
</tr>
<tr>
<td>2008</td>
<td>Sidaros</td>
<td>30</td>
<td>Severe</td>
<td>ROI</td>
<td>FA</td>
<td>Glasgow Outcome Scale (Favorable vs Non-favorable)</td>
<td>The FA was significantly lower in non-favorable outcome group in the cerebral peduncle.</td>
</tr>
<tr>
<td>2011</td>
<td>Marquez de Plata</td>
<td>30</td>
<td>Not reported</td>
<td>Tractography</td>
<td>FA</td>
<td>Glasgow Outcome Scale-Extended</td>
<td>Positively correlated with whole CC, genu of CC, right ILF, and right IFOF.</td>
</tr>
</tbody>
</table>

IFOF: Inferior Fronto-Occipital Fasciculus; ILF: Inferior Longitudinal Fasciculus; SFL: Superior Longitudinal Fasciculus.
Functional MRI
fMRI

Nicola Filippini et al.
PNAS
2009;106:7209-7214
Functional MRI
fMRI
So…

- How do we better predict function after a brain injury?
How do we better predict function after a brain injury?

- Neuroimaging as it relates to function is an area currently under broad investigation
How do we better predict function after a brain injury?

- The identification of neuroimaging techniques that correlate with current and future function would provide clinicians with tools to better and more quickly create individualized treatment plans that maximize patient outcomes.


How do we better predict function after a brain injury?

A detailed understanding of network structure and function could provide a clear rationale for intervention.
How do we better predict function after a brain injury?

Drugs might be selected on the basis of their actions on network function.


How do we better predict function after a brain injury?

For example, dopaminergic agents have been proposed as cognitive enhancers that might improve many of the impairments commonly observed after TBI.


How do we better predict function after a brain injury?

- Only modest improvement has been observed using methylphenidate (ritalin) in treating impairments of processing speed and attention after TBI.

- However, a personalized approach might be required to select patients who have appropriate dysfunction and will be likely to respond well.


How do we better predict function after a brain injury?

- Information about post-injury structure and function in individual patients will provide important information that could be used to guide a network-based approach to treatment and drug selection.


How do we better predict function after a brain injury?

- Certain findings on fMRI were found to correlate with lower extremity motor recovery as measured by walking.

(Jayaram et al 2012), (Lindenberg et al 2010).
How do we better predict function after a brain injury?

- A significant relationship between fMRI-related findings and hand function was found and felt to be strong enough to establish fMRI-derived measures as valid structural surrogates of motor impairment after non-traumatic brain injury.

(Jayaram et al 2012), (Lindenberg et al 2010).
What is happening at MCW?

- Collaborative effort between at MCW and Marquette University

(Kalinosky et al 2013)
Many of the previous studies focused on manually selected regions of interest and do not take into account damage or loss of connections to other areas of the brain.

Recently, studies have found to significantly correlate with upper extremity function as measured by the Fugl-Meyer (FM) in controls and subjects with chronic brain injury impairments (Kalinosky et al 2013).
What is happening at MCW?

- No study has looked at the change that occurs between the acute injury and after several months of recovery.
Study Aims

- To evaluate the relationship between the fMRI findings and standardized clinical measures of function in focal brain injury recovery, including:
  - Modified Ashworth Scale
  - Fugl-Meyer Score (upper and lower extremity)
  - Berg Balance Assessment
  - Wolf Motor Assessment
  - Short Form-36 (SF36) of the Medical Outcomes Study (MOS) in acute stroke subjects.
Study Methods

- Patients <6 weeks from non traumatic brain injury with motor weakness
- Functional MRI (fMRI) will then be performed
- Functional testing and fMRI repeated at 4-6 months post-injury
Study Aims

- Information gained as a result of this study will help to better understand the relationship between neuroimaging and function
Study Aims

- Our hope is that this will allow clinicians to maximize their ability to select appropriate rehabilitation interventions that will minimize a brain injury survivors’ disability.
Thank You!