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Rocky Mountain Regional Brain Injury System
Predictive Determinants of Outcome

- Type and severity of neurological injury
- Type and severity of bodily injuries
- Pre-injury characteristics (biological, social)
- Psychosocial co-morbidities
- Supports, treatment paradigms, environment
Neuropathology of Head Injuries
Gennarelli and Graham: 1998

TBI is a Process not an Event

Physiological Disruption  Structural Integrity
RECOVERY PATTERNS

- Not Random
- CHI-more specific
- Neurological and semi-predictable
- Correlates with clinical and diagnostics
Specific Types of Injuries

- Diffuse Injury
- Diffuse Axonal Injury
- Focal
- Multi-Focal/ Mixed
- Hypoxia--Ischemia
INJURY SEVERITY RELATES TO AXONAL FUNCTION

Physiologic ➔ ➔ ➔ Anatomic
Disruption
SPECTRUM OF DIFFUSE BRAIN INJURY

- Mild Concussion
- Classical Cerebral Concussion
- Diffuse Injury
- Diffuse White Matter Shearing

Increasing Disruption of Axonal Fibers
Diffuse Axonal Injury (DAI)

Clinical Indicators

Depth of unconsciousness (LOC)
Duration of disturbed consciousness (PTA)
Spectrum of Injury Severity
(Surrogate Clinical Tools)

- Glasgow Coma Scale (GCS) depth of unconsciousness
- Time to Follow Commands (TFC) duration of unconsciousness
- Post-traumatic amnesia (GOAT)
- Neuroimaging and other diagnostics
- Clinical exam
# GLASGOW COMA SCALE

<table>
<thead>
<tr>
<th><strong>Eye Opening</strong></th>
<th><strong>Verbal Response</strong></th>
<th><strong>Motor Response</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>4 = Spontaneously</td>
<td>5 = Oriented</td>
<td>6 = Follows Commands</td>
</tr>
<tr>
<td>3 = To Voice</td>
<td>4 = Confused</td>
<td>5 = Localizes to Pain</td>
</tr>
<tr>
<td>2 = To Pain</td>
<td>3 = Inappropriate Words</td>
<td>4 = Withdrawal to Pain</td>
</tr>
<tr>
<td>1 = None</td>
<td>2 = Incomprehensible Sounds</td>
<td>3 = Abnormal Flexion</td>
</tr>
<tr>
<td></td>
<td>1 = None</td>
<td>2 = Abnormal Extension</td>
</tr>
</tbody>
</table>
One year psychosocial outcome in head injury
Dikmen, 1999

N = 466

GLASGOW COMA SCORE

GCS 13-15
GCS 9-12
GCS 6-8
GCS 3-5

GOOD
MODERATE
SEVERE
VEG/DEAD
Cumulative Percent of Head-Injured Subjects Who Return to Work

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>% Returned to Work</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td>12 months</td>
</tr>
<tr>
<td><strong>Neurological Severity</strong></td>
<td></td>
</tr>
<tr>
<td><strong>GCS</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;8</td>
<td>26</td>
</tr>
<tr>
<td>9-12</td>
<td>56</td>
</tr>
<tr>
<td>13-15</td>
<td>80</td>
</tr>
</tbody>
</table>

Head-injury severity was assessed by the Glasgow Coma Scale (GCS) obtained in the emergency department and by time to follow commands. The GCS evaluates depth of coma by responsiveness in eye opening, motor and verbal modalities.

-Dikmen 1999
## Cumulative Percent of Head-Injured Subjects Who Return to Work

### % Returned to Work

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</table>

#### Demographics

**Time to Follow Commands**

**Neurological Severity**

**TFC**

<table>
<thead>
<tr>
<th>&lt;5 h</th>
<th>82</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-24 h</td>
<td>67</td>
</tr>
<tr>
<td>25 H-6 d</td>
<td>67</td>
</tr>
<tr>
<td>7-13 d</td>
<td>46</td>
</tr>
<tr>
<td>14-28 d</td>
<td>21</td>
</tr>
<tr>
<td>&gt;29 d</td>
<td>6</td>
</tr>
</tbody>
</table>

Time to follow commands was used as a measure to length of coma and was operationally defined as the duration of time between the injury and the patients’ regaining the ability to respond consistently to verbal commands as defined by the motor component of the GCS.

-Dikmen 1999
Acute Signs of Traumatic Brain Injury

- Normal Consciousness
- Injury
- Retrograde Amnesia
- Loss of Consciousness
- Posttraumatic Confusion-Amnesia
Outcome probability at one year post injury in a group of patients admitted to inpatient rehabilitation with moderate to severe traumatic brain injury classified by duration of posttraumatic amnesia (PTA). Outcomes are categorized by the Glasgow Outcome Scale (veg., vegetative state; sev. Severe disability's mod. Moderate disability; good, good recovery).

-Levin et al, dikmen et al, Katz alexander
SPECTRUM OF DIFFUSE BRAIN INJURY

- Mild Concussion
- Classical Cerebral Concussion
- Diffuse Injury
- Diffuse White Matter Shearing

Increasing Disruption of Axonal Fibers
MILD TBI

Predictors of Outcome – Risk Factors

- Medical
- Psychological Processes
- Environmental
DIFFUSE INJURY

LOC > 24 Hours

Generalized Damage to Axonal Structure

or

Brain White Matter
EIGHT STAGES OF COGNITIVE RECOVERY FOR HEAD TRAUMA

- Level I - Coma
- Level II - Generalized Response
- Level III - Localized Response
- Level IV - Confused/Agitated
- Level V - Confused/Inappropriate/Non-agitated
- Level VI - Confused/Appropriate
- Level VII - Automatic/Appropriate
- Level VIII - Purposeful/Appropriate
Case 1

DAI
GCS 4
TFC 4 weeks
PTA 3 months?
Severe DAI Syndromes (Differential)

- Vegetative State (disconnection bs, wm, th, ctx)
- Minimal Responsive State (white matter)
- Akinetic Mutism (supplemental motor area)
- Locked-Out Syndrome (thalamic)
- Locked-In and Locked In Plus (brainstem)
Hypoxia - Ischemia

Border zone ischemia (shock, circulatory insufficiency)

Cerebral artery zones
Anterior  Middle  Posterior

Infarction

Border zone between artery zones

Infarction
Hypoxic and/or Ischemic Patterns

- Hippocampal cells (amnestic)
- Purkinge cerebellar cells (dystaxic)
- Basal Ganglia (parkinsonian spectrum)
- Watershed or “Borderzones” (dyspraxia, visual perceptual, motor planning, tactile auditory and visual defensiveness)
- Mixed Pattern (movement disorders, myoclonus)
THE NEUROBIOLOGY OF INJURY

- Neurodiagnostic advances
- Development of novel and innovative therapies
NEUROIMAGING ADVANCES
Expanded Understanding of Injury Relationships

- **Anatomy**
  - CT
  - MRI
  - MRA
HEMATOMAS

- Extradural
- Subdural
- Intracerebral
NEUROIMAGING ADVANCES
Expanded Understanding of Injury Relationships

- Anatomy
  - CT
  - MRI
  - MRA

- Physiology – Advanced MRI techniques
  - SPECT
  - PET
  - EEG
  - Brain Mapping techniques
MRI in 2001+: Evaluating brain physiology

- **Goal:** Improve diagnostic sensitivity / specificity.

- **Tests:**
  - Diffusion imaging: evaluates water motion.
  - Spectroscopy: studies tissue metabolism.
  - Functional MR: evaluates brain function.
MR diffusion imaging

Normal                     Abnormal
Tensor & fMRI - Fusion

Combined fMRI Expressive Speech Map with MR Tractography from Diffusion Tensor Imaging

**fMRI**
- Gradient-echo epiRT
- 26 cm FOV, 128x128
- TE/TR=50/4000ms, 90°
- 65 phases

**Diffusion Tensor Imaging**
- Six direction encoding, $b = 1576$ s/mm$^2$
- SE-EPI, 24 cm FOV, 128x128

*Image Courtesy of M.D. Anderson Cancer Center*
TRACTOGRAPHY

arc. fasciculus

unc. fasciculus
NEUROIMAGING ADVANCES
Expanded Understanding of Injury Relationships

- **Anatomy**
  - CT
  - MRI
  - MRA

- **Physiology – Advanced MRI techniques**
  - SPECT
  - PET
  - EEG
  - Brain Mapping techniques

- **Functional**
  - QMRI
  - FMRI
Figure 3. Functional Magnetic Resonance Imaging Showing Effects of Attention on the Neural Correlates of Working Memory.
PREDICTOR RESEARCH

- Advanced Neuro-imaging
- Gender
- Biologic markers – APOE$_4$
DIFFUSE VS. FOCAL INJURIES (emerging or isolated)
Focal

- Neuroanatomically specific
- Cortical Contusions
- Frequently Frontal and/or Temporal
- GCS,TFC (brief ) and disproportionate to PTA
- Physical, Cognitive and Neurobehavioral characteristics
COUP

CONTRE-COUP
Case 2

Fall
Orbitofrontal
Bi temporal
Mesial contusion Axial
T2 weighted
BG - basal ganglia
OF - orbital frontal cortex
PTO - parieto-temporo-occipital
RF - reticular formation
SF - superior frontal cortex
T - thalamus
W - Wernicke’s area
CAUSE OF DISABILITY

- MENTAL > PHYSICAL
Common Neuro-Medical Sequelae

- Hydrocephalus
- Seizures
- Spasticity/dystonia
- Posttraumatic Movement Disorders
- Heterotopic Ossification
- Communicative, cognitive and behavioral disturbances
Ventricular Shunting

- Hydrocephalus vs. Atrophy
- Risk Benefit Ratio (complications/outcome)
- Timing
- Type of Shunt Valve (programmable)
- Rehabilitation Synergy (therapy/medications)
- Long term management
SEIZURES

- Risk/benefit considerations
- Provide “functional” control without side-effects.
NEW ANTI-EPILEPTIC DRUGS

- Levaracitam
- Lamotrigine
- Felbamate
- Tiagabine
- Topiramate
- Vigabatrin
- Others…….
REFRACTIVE CONSIDERATIONS

- Electrophysiologic and Imaging Workup
- Surgical Options
- Vagus Nerve Stimulators
- Genetic Research – “Inherited Epilepsies”
The NCP System: Implanted Components
TYPES OF SURGERY

- Temporal lobectomy
- Extratemporal resections
- Corpus callosotomy
- Stereotaxic procedures
- Hemispherectomy
MOTOR
NEG. MOTOR
SPEECH
OTHER HIGHER CORTICAL
EPISTHALERAL SENSORY
= MAX. STIM. (mA)
SPASTICITY

- Dantrolene Sodium
- Lioresal
- Diazepam
- Tizanidine
- Clonidine
- Klonopin
SPASTICITY – ADJUNCTIVE PROCEDURES

- Local and Regional Anesthetic Blocks *
- Phenol Neurolysis *
- Botox Type A Injection Therapy *

* Coupled with Rehabilitative Techniques
 SPASTICITY – ADJUNCTIVE PROCEDURES

- Intrathecal Lioresal Pump
- Central Neurosurgical Intervention
- Functional Orthopedic Interventions
Intrathecal Baclofen (ITB) Therapy: Before and After Treatment
POSTTRAUMATIC MOVEMENT DISORDERS

- Akinetic or Hypokinetic – Parkinsonian
- Hyperkinetic
  - Tremors
  - Ataxia
  - Myoclonus
  - Dyskinesias
  - Dystonias
NEUROPHYSIOLOGIC CORRELATES OF MOVEMENT DICTATE “RATIONAL” TREATMENT

- AEDs
- Anti-Anxiety
- Parkinsonian Meds
POSTTRAUMATIC MOVEMENT DISORDERS

- Parkinson’s research
- Essential Tremor Research

Deep Brain Thalamic Stimulator
TREMOR

Deep Brain

Thalamic Stimulator
HETEROTOPIC OSSIFICATION

- Non-Steroidal Anti-Inflammatories
- Diphosphonates (Didronel)
- Radiation Therapy
- Surgical Excision
COGNITIVE-BEHAVIORAL DISTURBANCES

- Minimal Responsive
- Agitated – Aggressive
- Initiation and Communication
- Memory and Cognition
- Mood
NEUROTRANSMITTER IMBALANCES

- Acute
- Subacute
- Chronic
Neuropharmacology
MEMORY AND COGNITIVE DISORDERS

- Acetylcholine Enhancers (Alzheimer's Meds)
- Vitamins (Lecithin, Phosphatidylcholine)
- Nootropes (Piracetam, Pramiracetam)
MOOD DISORDERS

- Tricyclic Antidepressants
- Novel Antidepressants
- Mood Stabilizers – AEDs (VPA, CBZ)
- Lithium
- Anxiolytics
- Neuroleptics
NEUROFUNCTIONAL FUTURE CONSIDERATIONS

- HBO – acute vs. chronic
- Neural transplantation research
- Gene therapy
HYPERBARIC OXYGEN THERAPY (HBO)

- Carbon Monoxide
- Hypoxic – ischemic encephalopathy
- Traumatic focal and/or diffuse axonal injury
NEURAL TRANSPLANTATION

- Parkinson’s and Huntington’s research
- Embryonic neural tissue grafting
  - replacement of damaged nerve cells
  - re-establishment of neural pathways
  - release of specific neurotransmitters
  - production of factors which promote neural growth
Stroke Rescue

Can cells injected into the brain reverse paralysis?

By KATHLEEN FACKELMANN
HOLISTIC APPROACHES

Evidence Based Guidelines?
HOLISTIC APPROACHES

- Herbs
- Vitamins
- Diet
- Sport Supplements
- Procedures, i.e., acupuncture, therapeutic touch techniques, CST, etc.
Pharmacological Modulation of Plasticity in the Human Motor Cortex

Neurorehab and Neural Repair 20(2) 2006
AGING CONSIDERATIONS

- Normal Aging
- Dementia – Alzheimer’s
- Psychosocial dilemmas
Age-related changes in brain perfusion of normal subjects detected by $^{99m}$Tc-HMPAO SPECT
Effect of Estrogen on Brain Activation Patterns in Postmenopausal Women During Working Memory Tasks

Shaywitz, MD, et al.
JAMA, April 7, 1999
Figure 2. Functional Magnetic Resonance Imaging Showing Effect of Estrogen on the Verbal Storage Component of Verbal Working Memory

Estrogen was associated with increased activation of the anterior, frontal lobe regions (superior [regions 2 and 4] and middle [region 5] frontal gyri) bilaterally. Of the posterior regions, estrogen was associated with increased activation of the inferior parietal lobule bilaterally (regions 1 and 3); and the superior (region 6) and middle (region 7) occipital gyri on the right. Sites with decreased activation on estrogen included regions around the inferior parietal lobule, as indicated by letter a, the left precentral sulcus, as indicated by letter b, and the right superior temporal gyrus, as indicated by letter c. Letters under each image correspond to the following positions on the z-axis of the Talairach atlas: A indicates 50; B, 40; C, 32; D, 24; and E, 12.
DETERMINANTS OF OUTCOME

- Pre-injury Personality Characteristics
- Type and Severity Neurologic Injury
- Support System Available
‘It is not only the kind of injury that matters, but also the kind of head.’

Sir Charles Symonds, 1937
LIFE ADAPTATION

Quality of Life and Outcome Considerations
WIT MODEL

Whatever It Takes:
A Model for Community-Based Services

Willer, B., Corrigan, J.D., Brain Injury
8:7 1994, 647-659
“To be all within one’s abilities”

- Relationships
- Productivity
- Socialization
Pathways and Planning Outcome Oriented Treatment.

“I Skate to where the puck will be”
-Wayne Gretsky
AWARENESS AND ACCESS

- Surveillance research
- TBI Model Systems 5 → 17 centers
- TBI Act 1995
  - Federal Initiatives
  - State Demonstration Grants
  - NIH Guidelines
- Information and dissemination
  - World Wide Web - Internet