Neuroplasticity and Prognosis Following Traumatic Brain Injury

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Disclosure Statement

No financial or non financial interests to disclose
Objectives

- Discuss the role of neuroplasticity in recovery following a traumatic brain injury
- Identify factors that influence prognosis following a traumatic brain injury
- Discuss the role of the interdisciplinary team in educating patients and their families on the recovery process following a traumatic brain injury
Traumatic Brain Injury

• A TBI is caused by a sudden bump, blow or jolt to the head or penetrating head injury that disrupts the normal function of the brain

CDC
Traumatic Brain Injury

- TBI impairs:
  - Movement
  - Balance
  - Sensation (including vision and hearing)
  - Emotional functioning
  - Behavior
  - Cognition
  - Sleep
  - Bowel and bladder
  - Speech
Long-term Impact of TBI

• Results in long-term disability
  – Unemployment
  – Changes in family dynamics
  – Social Isolation
  – Physical disability
  – Secondary health issues
Avenues for improving brain function after injury:

1. Limit severity of the initial injury to minimize loss of function.
2. Reorganize the brain to restore and compensate for function that has already been compromised or lost.

Kleim and Jones, 2008
Neuroplasticity

- The capacity for neurons to structurally and functionally adapt in order to reorganize neural circuits

Warraich and Kleim, 2010; Kleim, 2011; Kleim and Jones, 2008
Neuroplasticity

• Basis for learning and improving function after a brain injury

• Processes are modulated by behavior and environment
  – Behavior- personal factors on behalf of the patient
  – Environment- enriched by therapists treating the patient

Warraich and Kleim, 2010; Kleim, 2011; Kleim and Jones, 2008
## Recovery or Compensation

<table>
<thead>
<tr>
<th></th>
<th>Recovery</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neural</strong></td>
<td>Restoring function in neural tissue that was initially lost due to injury or disease</td>
<td>Residual neural tissue takes over a function lost due to injury or disease.</td>
</tr>
<tr>
<td><strong>Behavioral: Motor</strong></td>
<td>Restoring the ability to perform movement or a task in the same manner as it was performed prior to injury or disease.</td>
<td>Performing movement or a task in a manner different from how it was performed prior to injury or disease.</td>
</tr>
</tbody>
</table>

Kleim, 2011
Motor Learning

A set of processes associated with practice or experience leading to relatively permanent changes in the capability for motor skill.

Schmidt, 1991
Motor Learning

• Performance:
  – *temporary* change in movement pattern

• Learning:
  – *permanent* change in movement pattern
Short-term changes
Long-term changes

Motor Learning

Short-term changes
Long-term changes

Neuroplasticity

Adapted from Shumway-Cook and Wollacott, 2001
Principles of Neuroplasticity
Principle 1: Use it or lose it

- Neuronal circuits not actively engaged in task performance for an extended period of time begin to degrade or there is a reallocation of cortical territory.

Kleim and Jones 2008
Use it or lose it

Kleim, 2011
Development of Learned Non-use

INJURY-STROKE

Unsuccessful Motor Attempts

Punishment (pain, failure) → Behavior Suppression → Masked Ability

Compensatory Behavior Pattern

Positive Reinforcement

Less effective behavior strengthened

Learned Nonuse

Figure adapted from Taub et al., 1994
Principle 2: Use it and improve it

• Training that drives a specific brain function can lead to an enhancement of that function

Kleim and Jones, 2008
Use it and improve it

No motor rehab

Motor rehab

Kleim, 2011
Use it and improve it

Task

Sequence A: 4, 1, 3, 2, 4

Sequence B: 4, 2, 3, 1, 4

Karni et al, 1995
Use it and improve it

Karni et al, 1995
Principle 3: Specificity

• The nature of the training experience dictates the nature of the plasticity

• Clinical implication: practice the skill that needs to be relearned.
Specificity

Karni et al, 1995
Principles 4 & 5: Repetition and Intensity Matter

• Induction of plasticity requires sufficient repetition and training intensity

• Clinical implication: increase repetitions of practice. Be careful of fatigue.

Kleim and Jones, 2008
Repetition

Upper Extremity \( n=27 \)

<table>
<thead>
<tr>
<th>Task</th>
<th>Mean Reps/Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Exercise</td>
<td>26.44</td>
</tr>
<tr>
<td>Passive Exercise</td>
<td>11.93</td>
</tr>
<tr>
<td>Functional</td>
<td>22.33</td>
</tr>
<tr>
<td>Sensory</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>60.85</td>
</tr>
</tbody>
</table>

Lower Extremity \( n=28 \)

<table>
<thead>
<tr>
<th>Task</th>
<th>Mean Reps/Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Exercise</td>
<td>77.79</td>
</tr>
<tr>
<td>Passive Exercise</td>
<td>1.46</td>
</tr>
<tr>
<td>Functional</td>
<td>0.14</td>
</tr>
<tr>
<td>Sensory</td>
<td>0.21</td>
</tr>
<tr>
<td>Total</td>
<td>79.61</td>
</tr>
</tbody>
</table>

Kimberley et al, 2010
Principle 6: Time matters

• Different forms of plasticity occur at different times during training

• Clinical implication: consider the acuity of the patient

Kleim and Jones 2008
TBI- Primary Injury

**Focal Injury**
- Intracerebral hemorrhage
- Focal contusion
- Epidural Hematoma
- Subdural Hematoma
- Focal ischemia

**Diffuse Injury**
- Diffuse Axonal Injury
- Subarachnoid hemorrhage
- Hypoxia
- Hypotension
- Elevated ICP
- Hydrocephalus
- Metabolic abnormalities
- Infection

Dombovy, 2011
TBI– Secondary Injury

- Excitotoxicity
- Mitochondria dysfunction
- Oxidative Stress
- Inflammation
- Edema
Extracranial Factors Influencing Secondary Brain Injury

- Alcohol or drug intoxication
- Anemia
- Hypercapnia
- Hypoglycemia
- Hyponatremia
- Hypotension
- Hypoxemia
- Malnutrition
- Systemic infection
- Vascular Disease

Dombovy, 2011
Experience-dependent Plasticity or Spontaneous Recovery

- **Mechanism for spontaneous recovery is reversal** of acute physiologic changes due to injury
  - edema
  - brain metabolism
  - learned non-use
  - abnormal brain metabolism
  - inflammation
  - neural excitability
  - diaschisis
Timing of rehabilitation

**Acute**
- Time period: up to 1 month post injury
- Rehab environment: acute care hospital to acute inpatient rehab hospital
- Injury: Primary and Secondary Injury Evolving
- Recovery: Spontaneous / Experience

**Sub-acute**
- Time period: 1 - 6 month post injury
- Rehab environment: acute inpatient rehabilitation, outpatient clinic, community programs
- Injury: Primary and Secondary Injury Evolving
- Recovery: Spontaneous / Experience

**Chronic**
- Time period: > 6 months post injury
- Rehab environment: outpatient clinic, community programs
- Injury: Primary and Secondary Injury Completed
- Recovery: Experience

Bader et al., 2006; StrokEngine, Sullivan, 2007
Early vs Late Treatment

Leon-Carrion et al, 2013

n=58; severe TBI
Principle 7: Salience matters

• The training experience must be important

• Clinical implication: consider the individual’s goals

Kleim and Jones, 2008
Principle 8: Age matters

- Training-induced plasticity occurs more readily in younger brains
- However, the aging brain has the capacity for neuroplastic changes.

Kleim and Jones, 2008
Age of Person with TBI

Rates of TBI-related Hospitalizations by Age Group — United States, 2001–2010

CDC
Principle 9: Transference

• Plasticity in response to one training experience can enhance the acquisition of similar behaviors

• Clinical implication: practice of one skill may transfer into the improvement of another skill

Kleim and Jones, 2008
Principle 10: Interference

- Plasticity in response to one experience can interfere with acquisition of other behaviors

- Clinical implication: compensatory strategies may impede skill acquisition.

Kleim and Jones, 2008
Agents that Promote Neuroplasticity

• Sleep

• Exercise
  • ↑BDNF
  • ↓Oxidative stress
  • ↓Cytokines

• Medication
  • Neuroprotection
  • Attention
  • Arousal

(Warriach and Kleim, 2010; Siengsukon and Boyd, 2009; Griesbach, 2010)
Neuroprotective Medication

- Statins
- Erythropoietin
- Minocycline
- Dexanabinol
- Magnesium
- Adenosine

- Progesterone***
- Cyclosporin
- NMDA receptor antagonists
- Citicholine
- Thyrotropin releasing hormone
- Co Enzyme Q 10
- SSRI’s
Prognosis

- Identifies milestones
  - Threshold values
- May help inform patients and families of what the future may hold
- May help guide decisions
Factors Influencing Prognosis

Glasgow Coma Scale (GCS)

- **Lower** scores are associated with **worse** outcomes

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The Glasgow Coma Scale assesses motor, verbal and eye opening response using the following criteria:

<table>
<thead>
<tr>
<th>Domain</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>Does not open eyes</td>
<td>Opens eyes in response to painful stimuli</td>
<td>Opens eyes in response to voice</td>
<td>Opens eyes spontaneously</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Verbal</td>
<td>Makes no sounds</td>
<td>Incomprehensible sounds</td>
<td>Utters inappropriate words</td>
<td>Confused, disoriented</td>
<td>Oriented, converses normally</td>
<td>N/A</td>
</tr>
<tr>
<td>Motor</td>
<td>Makes no movements</td>
<td>Extension to painful stimuli</td>
<td>Abnormal flexion to painful stimuli</td>
<td>Flexion / Withdrawal to painful stimuli</td>
<td>Localizes painful stimuli</td>
<td>Obeys commands</td>
</tr>
</tbody>
</table>

**Standard Cut Scores:**
- $> 13 = \text{Minor brain injury}$
- $9 - 12 = \text{Moderate brain injury}$
- $\leq 8 = \text{Severe brain injury}$

Kothari, 2007; Rehabmeasures.org
Factors Influencing Prognosis

Length of Coma

- **Longer** duration associated with **worse** outcomes
- Threshold values
  - Severe disability unlikely when less than two weeks
  - Good recovery unlikely when greater than four weeks

Kothari, 2007
Factors Influencing Prognosis

Post-traumatic Amnesia (PTA)

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

Kothari, 2007
Factors Influencing Prognosis

Age

- **Older age** associated with **worse** outcomes
- Threshold values
  - Good recovery unlikely when greater than 65 years

Kothari, 2007
Factors Influencing Prognosis

Neuroimaging

• Certain features associated with worse outcomes
  - Depth of lesion correlated with worse outcomes
  - SAH, cisternal effacement, midline shift, EDH or SDH correlated with worse outcomes

• Threshold values
  • Good recovery unlikely when bilateral brainstem lesions present on early MRI

Kothari, 2007
Conclusion

• After a brain injury, there is a capacity for recovery through neuroplasticity
• Certain factors may influence prognosis
• The rehabilitation team can help educate patients on the recovery process
References

• Dean CM, Channon EF, Hall JM. Sitting training early after stroke improves sitting ability and quality and carries over to standing up but not to walking: a randomised controlled trial. Australian Journal of Physiotherapy. 2007;53:97-102.
• Shumway-Cook A and Woollacott MH. Motor control: Theory and practical applications; 2nd ed. 2001; Lippincott Williams & Wilkins, Philadelphia, PA.
Thank you!