TBI AND EXERCISE: A REHABILITATIVE STRATEGY WITH UNTAPPED POTENTIAL

Lisa MK Chin, PhD
Objectives

1. Review the health-related benefits of regular physical activity
2. Describe cardiorespiratory fitness and aerobic exercise training
3. Examine aerobic exercise training on physical fatigue, sleep, mood, cognition and quality of life in TBI
4. Discuss the adaptations/mechanisms related to exercise training in TBI
5. Highlight the advantages/challenges to implementation of exercise programs in TBI
Brief Historical Perspective

• The Ancients
  ▫ “Eating alone will not keep a man well; he must also take exercise” – Herodicus, 400 BC

• The Middle Ages
  ▫ “...exercise was invented and used to clean the body when it was too full of harmful things.” – Mendez, 1553

• The Enlightenment
  ▫ “Let tailors be advised to take physical exercise at any rate on holidays....[so] to counteract the harm done by many days of sedentary life” – Ramazzini, 1713

*Physical Activity and Health: A Report of the Surgeon General, 1996*
Early Epidemiology Studies on Cardiovascular Disease and Physical Activity

Morris et al., *Lancet*, 1953; 262:1111-20
Published Studies To Date

- Cardiovascular Disease + Exercise
- Diabetes + Exercise
- Cancer + Exercise

Pubmed search on 10/11/2015
Health Benefits Associated With Regular Exercise

<table>
<thead>
<tr>
<th>Physical</th>
<th>Mental</th>
</tr>
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<tbody>
<tr>
<td>• Improved cardiovascular and respiratory function</td>
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<td>• Reduced risk for certain chronic diseases</td>
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<td>• Delayed all-cause mortality</td>
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Published Studies To Date

- Depression + Exercise
- Dementia + Exercise
- Brain Injury + Exercise

Pubmed search on 10/11/2015
# Health Benefits Associated With Regular Exercise

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<th>Physical</th>
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<tr>
<td>• Improved cardiovascular and respiratory function</td>
<td>• Improves and prevents anxiety and depressive disorders/symptoms</td>
</tr>
<tr>
<td>• Reduced risk factors for cardiovascular disease</td>
<td>• Protects against cognitive decline</td>
</tr>
<tr>
<td>• Reduced risk for certain chronic diseases</td>
<td>• Lowers risk of dementia</td>
</tr>
<tr>
<td>• Delayed all-cause mortality</td>
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</tbody>
</table>

Cardiorespiratory Fitness

- Important health outcome measure
  - An independent prognostic indicator of overall morbidity and mortality
  - Valid in wide range of individuals
- Measured during an exercise test
  - Peak $O_2$ uptake ($VO_2$), time to exhaustion, anaerobic threshold (AT)

From Blair et al., JAMA, 1996; 276:205-10
Cardiorespiratory Fitness

VO₂ (l/min)

0.0 1.0 2.0 3.0 4.0 5.0 6.0

0 60 120 180 240 300 360 420 480 540 600 660 720 780

20 45 70 95 120 145 170 195 220 245 270 295 320 345

WR (W)

Time (s)

Max WR

Absolute VO₂ peak

VO₂ peak

Max WR

WR (W)

Department of Rehabilitation Science
College of Health and Human Services
Cardiorespiratory Fitness

- **VO$_2$ (l/min)**
- **VCO$_2$**

**Anaerobic Threshold (AT)**

**Time (s)**

**WR (W)**
Cardiorespiratory Fitness and TBI

Data from Amonette & Mossberg, *J Head Trauma Rehabil*, 2013; 28: E13-20
Aerobic Exercise Training

- Involves rhythmic movement of large muscle groups for a sustained period of time
  - Walking, running, swimming, biking
- Improves the efficiency of the aerobic energy producing systems

Modified from Milani et al., *Circulation*, 2004; 110: e27-31
Aerobic Exercise Training

• FITT Principle for cardiorespiratory fitness
  ▪ **F**requency: Number of days per week
  ▪ **I**ntensity: How hard a person works to do this activity
  ▪ **T**ime: Length of time the activity is performed
  ▪ **T**ype: Mode of exercise

• Recommendations for the general population:
  ▪ 5 days/week of moderate intensity for 30 minutes, or 3 days/week of vigorous intensity for 25 minutes, or combination
Aerobic Exercise Training

- **Relative Intensity**

<table>
<thead>
<tr>
<th>Intensity</th>
<th>%Heart Rate Reserve</th>
<th>%Heart Rate Max</th>
<th>% VO$_2$max</th>
<th>Perceived Exertion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Light</td>
<td>&lt; 30</td>
<td>&lt; 57</td>
<td>&lt; 37</td>
<td>0.5 – 1</td>
</tr>
<tr>
<td>Light</td>
<td>30 – 39</td>
<td>57 – 63</td>
<td>37 – 45</td>
<td>2 – 3</td>
</tr>
<tr>
<td>Moderate</td>
<td>40 – 59</td>
<td>64 – 76</td>
<td>46 – 63</td>
<td>4 – 6</td>
</tr>
<tr>
<td>Vigorous</td>
<td>60 – 89</td>
<td>77 – 95</td>
<td>64 – 90</td>
<td>7 – 8</td>
</tr>
<tr>
<td>Near maximal</td>
<td>≥ 90</td>
<td>≥ 96</td>
<td>≥ 91</td>
<td>9 – 10</td>
</tr>
</tbody>
</table>

TBI and Chronic Conditions

- Among TBI survivors:
  - 75% report significant levels of fatigue \(\text{Cantor et al., JHTR, 2008}\)
  - 30 – 70% experience sleep problem \(\text{Ouellet et al., JHTR, 2006}\)
  - 49% have major depressive disorder \(\text{Bombardier et al., JAMA, 2010}\)
  - 65% of moderate/severe TBI and 20% of mild TBI have cognitive problems \(\text{Rabinowitz & Levin, 2014; Barker-Collo et al., Brain Inj, 2015}\)
TBI and Chronic Diseases

- TBI linked to increases in:
  - Post traumatic stress disorder
  - Parkinson’s Disease
  - Alzheimer’s Disease
  - Dementia
  - Epilepsy
  - Stroke

Burke et al., *Neurology*, 2013;81:33-39
Ferguson et al., *Epilepsia*, 2010;51:891-8
Gardner et al., *Ann Neurol*, 2015;77:987-995
Gardner et al., *JAMA Neurol*, 2014;71:1490-1497
Bazarian et al., *J Head Trauma Rehabil*, 2009;24:439-51
Exploring the Literature

- Self-report account of exercise in the recovery from a TBI
  - Suffered a severe TBI in final year of medical school
  - Discovered “early morning exercise” improved his symptoms
  - Obtained medical degree 5 years after the accident
  - Attributed his recovery to his physical fitness

- Followed-up with case studies on treating severe TBI with a “vigorous early morning exercise” routine

Programme development

The role of and possibilities for physical conditioning programmes in the rehabilitation of traumatically brain-injured persons

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‡Centre de Réadaptation pour Traumatisés Crâniens de Cénac and Service de Neurochirurgie, Hôpital Pellegrin, Bordeaux, France
§Centre de Réadaptation pour Traumatisés Crâniens de Cénac, Cénac, France

(Received 8 August 1989; accepted 6 September 1989)

The development of rehabilitation programmes for traumatically brain-injured persons is a complex and multidisciplinary effort. One aspect of such programmes is the development of physical work capacity via exercise or physical conditioning. This paper reviews literature dealing with the physical work capacity following traumatic brain injury and its responses to training. The incorporation of physical activity into a specific rehabilitation programme is described and the possible roles of exercise in the rehabilitation programme are discussed.
Fitness training for cardiorespiratory conditioning after traumatic brain injury (Review)

Hassett L, Moseley AM, Tate R, Harmer AR

Fitness training to improve fitness after traumatic brain injury

Traumatic brain injury is the leading cause of long-term disability in children and young adults. Reduced fitness is a common problem after traumatic brain injury. Clinically, fitness training is used to address this problem.

Six studies, incorporating 303 people with traumatic brain injuries, were included in this review. The people were mostly male, in their mid thirties, and had sustained severe brain injuries. No studies were found that included children. Three of the six studies assessed change in fitness after fitness training. The results were mixed with one study showing an improvement in fitness and the other two studies showing no significant improvement. Four of the six studies had no drop-outs from the fitness training group and no adverse events were reported in any study.

There is insufficient evidence to draw any clear conclusions as to the effects of fitness training on fitness. Whilst it appears to be a safe and accepted intervention for people with traumatic brain injury, further well-designed studies are required to make any definite conclusions.

Hassett et al., Cochrane Database Syst Rev, 2008
Exploring the Literature

• TBI and exercise studies

![Bar chart showing the number of articles in different categories from 1985-1990 to 2011-2015. The categories are Reviews, Animal Studies, and Human Studies.]

Pubmed search on 10/11/2015
# TBI and Aerobic Exercise Studies

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Design</th>
<th>n</th>
<th>Type</th>
<th>Length</th>
<th>Frequency per week</th>
<th>Aerobic Duration</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chin et al.</td>
<td>2014</td>
<td>Pre-Post</td>
<td>10</td>
<td>Treadmill</td>
<td>12 weeks</td>
<td>3</td>
<td>30 mins</td>
<td>Vigorous</td>
</tr>
<tr>
<td>Hoffman et al.</td>
<td>2010</td>
<td>RCT</td>
<td>76</td>
<td>Choice† &amp; home</td>
<td>10 weeks</td>
<td>5</td>
<td>30 mins</td>
<td>Moderate</td>
</tr>
<tr>
<td>Driver et al.</td>
<td>2009</td>
<td>RCT</td>
<td>16</td>
<td>Aquatic</td>
<td>8 weeks</td>
<td>3</td>
<td>60 mins</td>
<td>Moderate</td>
</tr>
<tr>
<td>Gordon et al.</td>
<td>1998</td>
<td>Retrospective</td>
<td>240</td>
<td>Jog, swim or bike</td>
<td>≥ 6 mths</td>
<td>≥ 3</td>
<td>≥ 30 mins</td>
<td>-</td>
</tr>
<tr>
<td>Jankowski et al.</td>
<td>1990</td>
<td>Pre-Post</td>
<td>14</td>
<td>Circuit†</td>
<td>16 weeks</td>
<td>3</td>
<td>Up to 45 mins</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

† Treadmill, stair-stepper, rowing, cycle, track
‡ Stair climbing, rope skipping, jogging and cycling
Exercise: TBI and Fatigue

- Better cardiorespiratory fitness

Chin et al., J Head Trauma Rehabil, 2014
Exercise: TBI and Fatigue

- Better cardiorespiratory fitness

*Chin et al., J Head Trauma Rehabil, 2014*
Exercise: TBI and Fatigue

- Improved fatigability

Jankowski et al., Arch Phys Med Rehabil, 1990;71:500-4
Exercise: TBI and Fatigue

- Improved fatigability and self-reported fatigue severity

*17% drop in fatigability

*20% decrease in fatigue

Jankowski et al., Arch Phys Med Rehabil, 1990;71:500-4
Chin et al., J Head Trauma Rehabil, 2014
Exercise: TBI and Sleep

- Better sleep quality

Chin et al., unpublished findings
Exercise: TBI and Mood Changes

- Improvement in mood after 8 weeks of training

From Driver and Ede, Brain Injury, 2009; 23:203-12
Exercise: TBI and Mood Changes

- Improved mood after 4 weeks

- Improved mood after a single bout

Weinstein et al., Psychosom Med, 2015
Exercise: TBI and Cognition

- Less cognitive symptoms

*From Gordon et al., J Head Trauma Rehabil, 1998;13:58-67*
Exercise: TBI and Cognition

- Improved processing speed, executive functioning and overall cognition

\[ \text{Chin et al., Arch Phys Med Rehabil, 2015; 96:754-9} \]
Exercise: TBI and Cognition

- Significant relationship between gains in measures of cardiorespiratory fitness and cognitive function

Modified from Chin et al., Arch Phys Med Rehabil, 2015; 96:754-9
Exercise: TBI and Quality of Life

• Better perceived quality of life

"How satisfied are you with..."
1. The health of your body
2. Your ability to think and remember
3. How happy you are
4. How much you see your family and friends
5. The help you get from family and friends
6. Your contribution to the community
7. Your activities outside work
8. How your income meets your needs
9. How respected you are by others
10. The meaning and purpose of life
11. With working/not working/retirement

Patrick et al., J Gen Intern Med, 1988;3:218-23
Hoffman et al., PM&R, 2010;10:911-9
Exercise: TBI and Quality of Life

- Better perceived health status

* From Gordon et al., J Head Trauma Rehabil, 1998;13:58-67
Summary of TBI & Exercise Studies

• Support in the literature that aerobic exercise is beneficial in persons with TBI
  ▫ Both physical and mental benefits

• Benefits obtained with aerobic exercise recommendations for the general population
  ▫ Different aerobic activities and intensities

• Caveats
  ▫ Safe and feasible?
  ▫ Adherence?
  ▫ When to start exercise?
Mechanisms For Exercise on Brain Function

- Brain blood flow (meet metabolic needs, remove waste products)
- Neurotrophic factors (supports growth, survival and maintenance of neurons)
- Neurotransmitters (allows signaling between neuron by neurotransmission)
- Growth factors (stimulates cell growth and proliferation)
- Angiogenesis (growth of new blood vessels)
- Neurogenesis (birth of new neurons)
- Synaptogenesis (formation of synapses between neurons)
- Neuroprotection (preservation of neurons)

Lojovich, J Head Trauma Rehabil, 2010;25:184-92
Mechanisms Underlying Exercise in TBI

• Vascular Integrity

TBI
- Impaired/absent cerebral autoregulation
- Impaired cerebrovascular reactivity

Exercise
- ↑ regional cerebral blood flow
- ↑ brain VEGF
- Upregulated endothelial NO synthesis

Outcome
- Vascular growth
- Neuroplasticity

Archer et al., *Acta Neurol Scand*, 2012; 125:293-302
Mechanisms Underlying Exercise in TBI

- Anti-apoptosis

TBI
- Neuronal cell death
- ↑ pro-apoptotic protein
- ↓ anti-apoptotic proteins

Exercise
- ↑ BDNF
- ↑ IGF-1
- ↑ VEGF
- ↑ GH
- Stem cell proliferation
- Activation of anti-apoptotic pathways

Outcome
- ↓ cell death
- Neurogenesis
- Synaptogenesis
- Angiogenesis

Archer et al., Acta Neurol Scand, 2012; 125:293-302
Mechanisms Underlying Exercise in TBI

- Neuronal Protection
  - Neurogenic reserve
  - Enhanced cerebrovascular integrity
  - Production of neuroprotective proteins

Exercise → TBI → Outcome

- Cell death
- Cerebral inflammation
- Impaired cerebrovascular autoregulation/reactivity
- Resistant to inflammatory damage
- Protects against TBI-induced toxicity

Archer et al., *Acta Neurol Scand*, 2012; 125:293-302
Advantages/Challenges to Implementation of Exercise Programs in TBI

<table>
<thead>
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<th>Advantages</th>
<th>Challenges</th>
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<tr>
<td>• Wide range of health related benefits</td>
<td>• Physical challenges</td>
</tr>
<tr>
<td>• Easily implemented</td>
<td>▫ Alternatives like BWST</td>
</tr>
<tr>
<td>▫ Community settings</td>
<td>• Cognitive impairments</td>
</tr>
<tr>
<td>• Cost effective</td>
<td>▫ Supportive devices</td>
</tr>
<tr>
<td>• Sustainable</td>
<td>• Adherence</td>
</tr>
<tr>
<td>▫ Infrastructure present</td>
<td>▫ Group exercises, social participation</td>
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Thank you!

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