

Exercise and Traumatic Brain Injury

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Disclosure

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Objectives

- ❖ Understand the impact of traumatic brain injury on human metabolic capacity and its effects on the physiologic response to exercise
- ❖ Understand the potential positive effects of aerobic training following TBI
- ❖ Understand the key components in the prescription of exercise following TBI

Statistics

- ❖ 1.7 million people sustain a traumatic brain injury every year in the United States
 - ❖ Approximately 5.3 million require assistance to complete activities of daily living
- ❖ Traumatic brain injury affects the whole body and multiple systems
 - ❖ Leads to neurological changes, physical, cognitive, sensory, and psychosocial impairment
- ❖ Majority of those affected are young and likely to survive into older age

Secondary Health Consequences

- ❖ **3 times more likely to die from a circulatory condition** (cardiovascular, cerebrovascular, thromboembolic disease) compared to the general population *Shavelle et al*
- ❖ **Reduction in life expectancy of 7 years** following a moderate to severe traumatic brain injury. Follow-up study on the same cohort revealed the greatest proportion of deaths resulted from circulatory conditions. *Harrison-Felix*
- ❖ **Increased risk for mood disorders:** Potential negative impact on functional recovery. May exacerbate cognitive and/or behavioral changes.

Bed Rest

Acute

- ❖ Negative affects on cardiopulmonary and musculoskeletal systems within 3 days; headache, restlessness, and sleep changes may develop after 3-6 days of bed rest; after a week, mood changes and vestibular sensitivity are common *Fortney*

Bed Rest, cont.

Prolonged

- ❖ Cardiovascular changes:
 - ❖ Postural hypotension
 - ❖ Loss of aerobic capacity
 - ❖ Reduction in cardiac output persists past one month
- ❖ Musculoskeletal:
 - ❖ Up to 40% loss of muscle strength: loss is more pronounced in the lower limbs versus upper limbs
 - ❖ Decrease in bone density
 - ❖ Shortening of soft tissues/contractures *Bell*
- ❖ Effects on respiratory system, balance, cognition, sleep, psychiatric function

Health Risks Associated with Sedentary Lifestyle

- ❖ 2008 Physical Activity Guidelines for Americans
 - ❖ Coronary heart disease
 - ❖ Hypertension
 - ❖ Ischemic stroke
 - ❖ Dyslipidemia
 - ❖ Osteoporosis
 - ❖ Obesity
 - ❖ Diabetes Type 2
 - ❖ Colon and breast cancer

Exercise Terminology

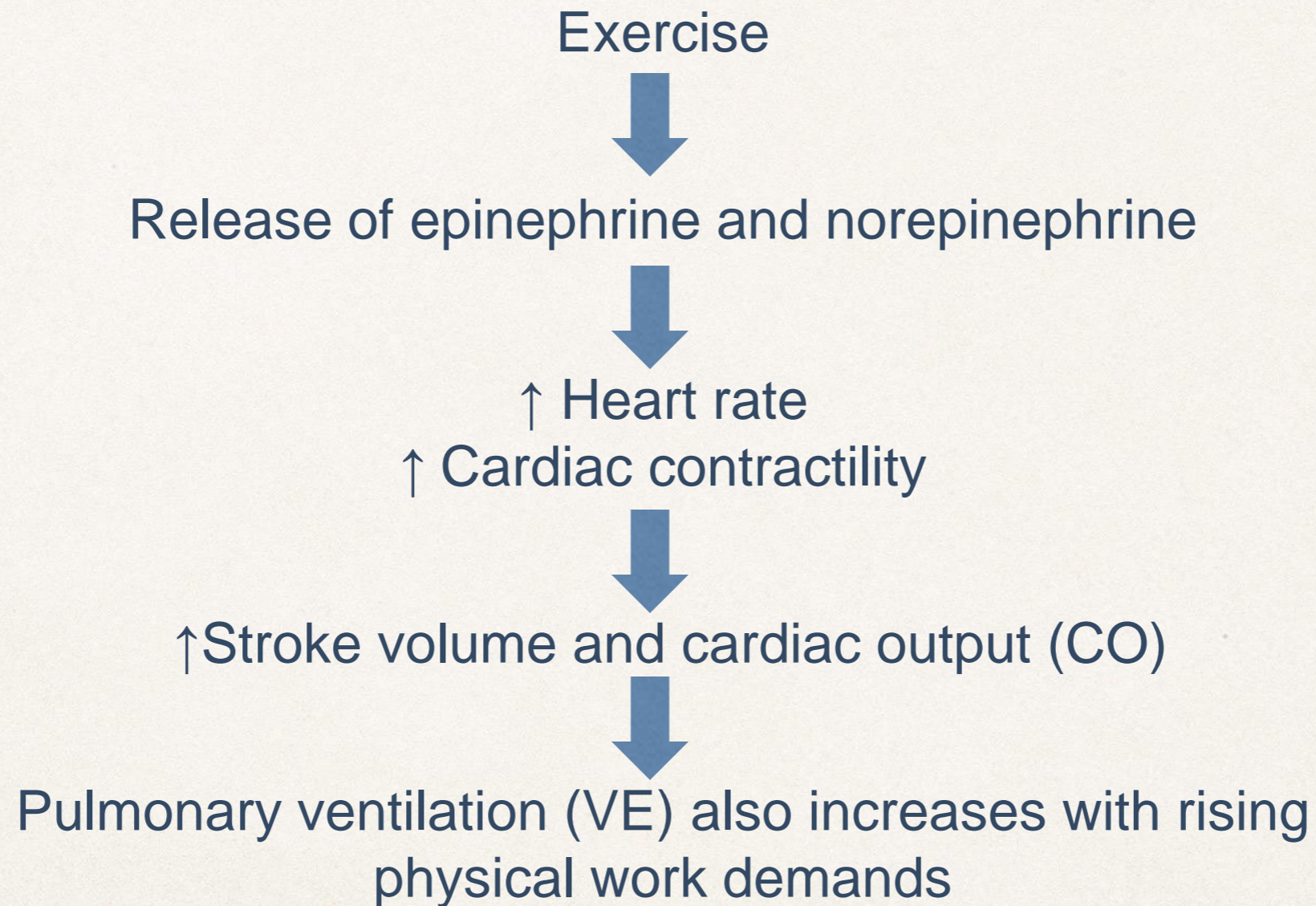
- ❖ Maximal oxygen consumption, maximal oxygen uptake, or maximal aerobic capacity, $\text{VO}_{2\text{max}}$ = maximum rate of oxygen consumption as measured through incremental exercise
 - ❖ Describes capacity of total oxygen delivery and utilization system of the body
 - ❖ Considered the gold standard for overall aerobic physical fitness or physical work capacity
 - ❖ Important determinant of a person's endurance capacity during prolonged, sub-maximal exercise
- ❖ Anaerobic threshold (AT)
 - ❖ Point in which the serum lactic acid levels begin to increase significantly, leading to muscle fatigue and shortness of breath

Graded Exercise Test with Progressive Workload

- ❖ Requires highly trained personnel and specialized equipment
- ❖ Ventilation, oxygen and carbon dioxide concentration of inhaled and exhaled gases are measured to assess metabolic response
- ❖ Alternative estimates of aerobic capacity *Mossberg*
 - ❖ Six minute walk: Total distance walked in 6 minutes with minimal turns or changes in direction
 - ❖ Modified 20-meter shuttle run

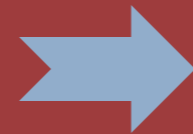


Acute Response to Exercise



Acute Response to Exercise, cont.

↑ VE and CO promotes the delivery of oxygenated blood to working skeletal muscle



↑ O₂ consumption to fuel aerobic metabolism

Vasoconstriction causes reduction of blood flow to inactive tissues

Vasodilatation causes increase in blood flow to active tissues

Chronic Response to Exercise

Lower resting heart rate

Lower heart rate at submaximal workloads

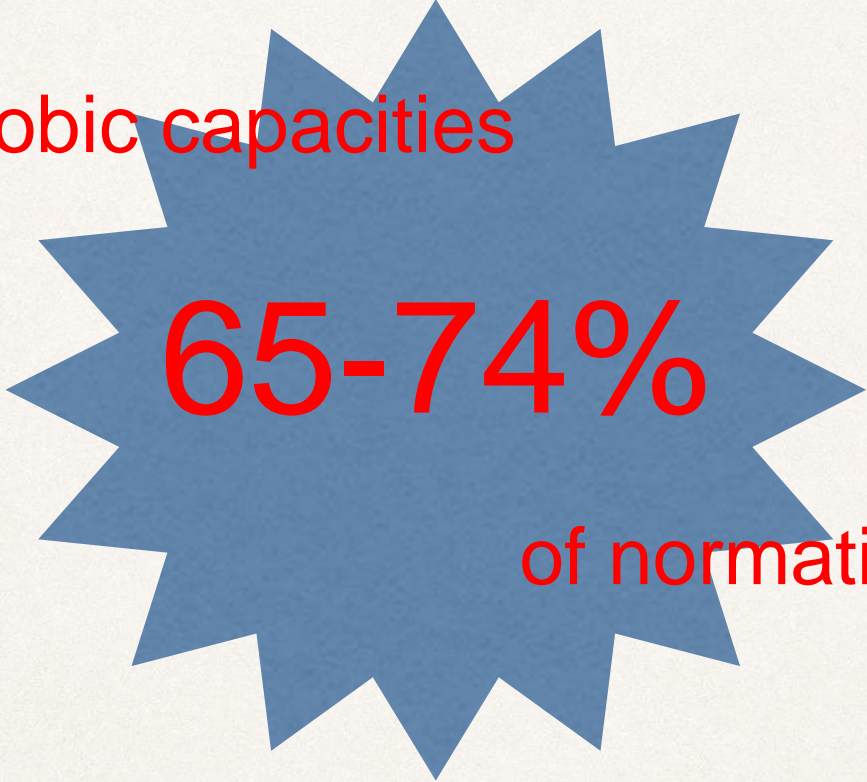
Enhanced O₂ delivery with improved extraction by muscles

Increased skeletal muscle capillary density

Increased epinephrine and norepinephrine response at maximal exercise

Exercise Capacity Following TBI

Peak aerobic capacities



65-74%

of normative values

Compared to non-injured, sedentary persons, $\dot{V}O_2$ reduced by
25-30%

Exercise Capacity Following TBI, cont.

- ❖ Becker *et al.*
 - ❖ Direct comparison of sedentary, non-injured subjects to patients with history of TBI (11/19 had residual motor deficits)
 - ❖ Pulmonary function at rest was reduced by 25-40%, reduction in total O₂ delivered
- ❖ Mossberg 2007:
 - ❖ Compared a convenience sample of 13 subjects with TBI (mild-severe) to 13 subjects without a TBI
 - ❖ Subjects were required to ambulate independently on a treadmill at a speed of 3.3 mph
 - ❖ Results:
 - ❖ Limitation in exercise cardiac output
 - ❖ Peak VO₂ was 75% of the sedentary cohort
 - ❖ Only 8/13 subjects with TBI reached 90% of age-predicted maximum heart rate
 - ❖ Reduced breathing efficiency
 - ❖ Impaired pulmonary ventilation with higher submaximal V_E/VO₂
- ❖ Anaerobic threshold of patients with TBI may be lower during submaximal work; may occur below the metabolic demand of common ADL's (mowing, sweeping, laundry).

Exercise Capacity in Mild TBI

147 Junior hockey players



14 Concussed



Athletes with concussion were divided two groups:

- MT--Those who missed playing time because of the injury (N 9)
- NMT--Those who did not miss play (N 5)

Gall *et al*

Exercise Capacity in Mild TBI, cont.

❖ Gall *et al.*

- ❖ Exercise protocol within 72 hours of being asymptomatic at rest, test repeated 5 days after initial exercise assessment
- ❖ Exercise included a 10 minute, low-moderate intensity steady state exercise bout, followed by a high intensity bout. The high intensity bouts were repeated until the athlete could no longer maintain the workload.
- ❖ Results
 - ❖ On average MT started exercise at 6.7 days, NMT group at 2.0 days
 - ❖ No significant difference in the (1) number of exercise bouts or in the (2) blood lactate levels at rest or post-exercise between concussed and matched controls
 - ❖ The MT group had a higher rise in heart rate and a higher heart rate during low-moderate exercise compared to matched controls. Increased heart rate was still present in the second exercise test 12 days post-injury.

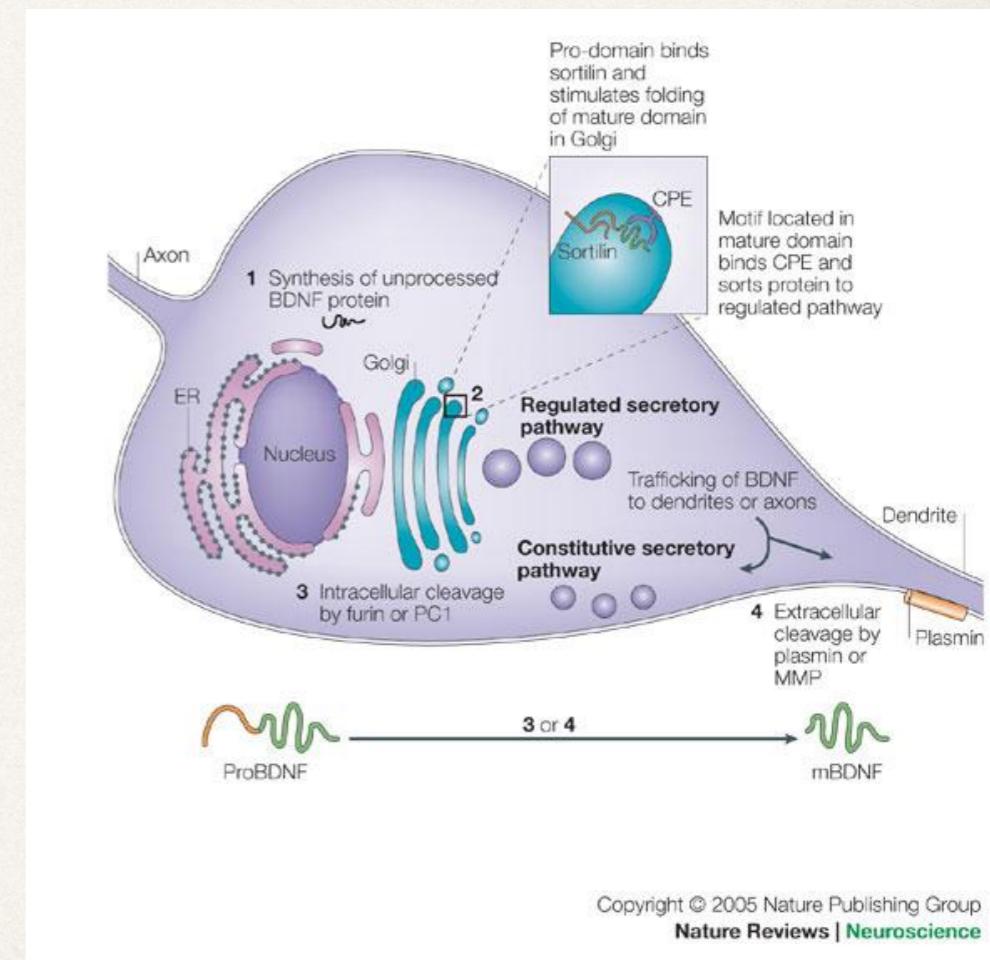
Related Changes Following mTBI

- ❖ Goldstein: Altered autonomic regulation is due to changes in the autonomic centers in the brain and/or an uncoupling of connections between the central ANS and the heart after TBI
- ❖ Leddy: Cerebral autoregulation and cerebral blood flow is altered after concussion



Animal Studies: Molecular Markers

- ❖ Brain-derived neurotrophic factor (BDNF):
 - ❖ Key growth factor that facilitates long-term potentiation; likely plays a role in the positive effects of exercise
 - ❖ Promotes neuroplasticity and neurogenesis in the central and peripheral nervous system
- ❖ BDNF and its downstream effectors on synaptic plasticity increase after physical activity
- ❖ Exposure to cortisol decreases the expression of BDNF in rats



Griesbach's Rats

Voluntary
exercise
after 2
weeks

- Up regulation of BDNF, CREB, Synapsin I
- Significant improvement in cognitive performance

Voluntary
exercise
before two
weeks

- More pronounced learning and memory deficits

Fluid-percussion injury (concussive injury model)

Benefits of Regular Physical Activity

Adults and Older Adults

Strong evidence

- Lower risk of early death
- Lower risk of coronary heart disease
- Lower risk of stroke
- Lower risk of high blood pressure
- Lower risk of adverse blood lipid profile
- Lower risk of type 2 diabetes
- Lower risk of metabolic syndrome
- Lower risk of colon cancer
- Lower risk of breast cancer
- Prevention of weight gain
- Weight loss, particularly when combined with reduced calorie intake
- Improved cardiorespiratory and muscular fitness
- Prevention of falls
- Reduced depression
- Better cognitive function (for older adults)

Moderate to strong evidence

- Better functional health (for older adults)
- Reduced abdominal obesity

Moderate evidence

- Lower risk of hip fracture
- Lower risk of lung cancer
- Lower risk of endometrial cancer
- Weight maintenance after weight loss
- Increased bone density
- Improved sleep quality

2008 Physical Activity Guidelines for Americans

Guidelines

- ❖ Duration

- ❖ Intensity

- ❖ Moderate intensity= 3.0 to 5.9 MET's (metabolic equivalents) or 5-6/10 relative intensity (0 is level of effort to sit and 10 is maximal effort)

- ❖ Vigorous intensity = 6.0 MET's or more or 7-8/10

- ❖ Frequency



The American Heart Association Recommendations for Physical Activity in Adults

At least 30 minutes of moderate-intensity aerobic activity **At least 5 days** per week for a total of **150 minutes**

OR

At least 25 minutes of vigorous aerobic activity **At least 3 days** per week for a total of **75 minutes**

or a combination of the two

AND

Moderate to **HIGH INTENSITY** muscle-strengthening activity **At least 2 days** per week for additional health benefits

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Learn more at heart.org/ActivityRecommendations.

Guidelines, cont.

Key Guidelines for Adults

- All adults should avoid inactivity. Some physical activity is better than none, and adults who participate in any amount of physical activity gain some health benefits.
- For substantial health benefits, adults should do at least 150 minutes (2 hours and 30 minutes) a week of moderate-intensity, or 75 minutes (1 hour and 15 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. Aerobic activity should be performed in episodes of at least 10 minutes, and preferably, it should be spread throughout the week.
- For additional and more extensive health benefits, adults should increase their aerobic physical activity to 300 minutes (5 hours) a week of moderate-intensity, or 150 minutes a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity activity. Additional health benefits are gained by engaging in physical activity beyond this amount.
- Adults should also do muscle-strengthening activities that are moderate or high intensity and involve all major muscle groups on 2 or more days a week, as these activities provide additional health benefits.

Mild TBI/Concussion

Considerations: Timing

- ❖ Period of rest: “cornerstone of concussion management” in sports related injuries
 - ❖ **Neurometabolic crisis**
 - ❖ Increased energy demand may hinder restorative processes
 - ❖ **Increased risk of repeat concussion**
 - ❖ Most likely to occur within 7 days of initial injury regardless of the presence or absence of symptoms
 - ❖ **Temporal window of vulnerability**
 - ❖ Second overlapping injury results in greater level of traumatic axonal injury and increased cognitive and behavioral deficits if it occurs before metabolic homeostasis has been restored
- ❖ **Blunting of expected exercise-induced increase in BDNF** when concussed rats engaged in exercise 1-2 weeks post-injury
- ❖ Inactivity can exacerbate or prolong recovery from many health conditions associated with TBI including vestibular disorders, affective disorders, post-traumatic stress disorder, chronic fatigue and pain disorders . *Silverberg*

Considerations for mTBI/Concussion: Timing, cont.

Kozlowski et al

Group with persistent post-
concussive symptoms
N 34



Sedentary, non-injured
control group
N 22



Exercise until exhaustion, inability to maintain speed, onset or exacerbation of symptoms, or reaching maximal allowable test capability (21 minutes)

Kozlowski Study, cont.

Median exercise time was
40% of control group



Reached almost 75%
of their age-predicted
maximal heart rate

Patients with persistent post-concussive symptoms have decreased tolerance to exercise compared to controls but they are able to safely participate in graded, low-level exercise even if symptomatic after 6 weeks.

Additional Considerations with mTBI

Cohort of 95 student athletes were retrospectively assigned to groups based on self-reported activity level *Majerski*

- ❖ Moderate levels of cognitive and physical exertion (school and light jogging) over a month following injury had better neuropsychological outcomes
- ❖ Minimal (no school or exercise activity) and high levels (school and participation in sports games) had worse visual memory and reaction time

Recommendations for Activity; Silverberg and Iverson

TABLE 2 *Recommendations for activity resumption following MTBI*

1. Bed rest exceeding 3 days is not recommended. (Strength of recommendation = D)
2. Gradual resumption of preinjury activities should begin as soon as tolerated. (Strength of recommendation = B)
3. For contact sports and other activities with a high MTBI exposure risk, a delay of at least 1 week will help reduce the risk of overlapping injuries. (Strength of recommendation = B)
4. The medium- and long-term risks of exertion sufficient to exacerbate symptoms are unknown. In theory, during the acute recovery period (eg, first 2 weeks postinjury), heavy exertion that elicits significant symptoms could be harmful. We simply do not know. In response to symptom exacerbations, patients should therefore be advised to temporarily reduce their physical and cognitive demands and resume their graduated return to activity at a slower pace. (Strength of recommendation = I)
5. After 1 month, supervised exercise should be considered as part of the treatment plan for individuals who remain symptomatic. (Strength of recommendation = C)

Considerations with TBI: Acute

- ❖ Jackson *et al.*: Randomized control study
 - ❖ 55 out of 90 subjects completed 24 sessions
 - ❖ Cycled up to 30 minutes 3 times per week over 12 weeks
 - ❖ 44 subjects were able to train for an average of at least 20 minutes per session
 - ❖ 18 subjects trained at >60% HR max
 - ❖ Some may take longer to achieve adequate intensity of aerobic exercise but are capable of participating

Considerations with TBI: Subacute, Chronic

- ❖ Jankowski and Sullivan: Case-series analysis of 14 sedentary patients with TBI who completed a 16 week resistance with aerobic exercise protocol
 - ❖ Increased aerobic capacity without change in oxygen cost or efficiency of walking
- ❖ Circuit training: Improved cardiorespiratory fitness after 6 weeks of training with improved peak power output, peak VO₂ *Bhambhani*
 - ❖ No change in body weight or percent body fat without controlling caloric intake
- ❖ Circuit training: Single-center observational study *Hassett*
 - ❖ The low intensity, long duration circuit class therapy provided sufficient exercise dosage for a fitness training effect for 62% of people with severe TBI

Considerations for TBI: Subacute, Chronic

Bateman: Randomized 157 subjects with severe acquired brain injury into exercise and relaxation training group

- ❖ Exercise group had improved peak work output on cycle ergometer
- ❖ No difference in disability dependency scales, balance scores or walking velocity

Aquatics: 24 exercise sessions over 8 weeks including aerobic exercises in pool at 50-70% of heart rate reserve *Driver*

- ❖ Improved strength, body composition, cycle ergometry peak wattage and time compared to control

Considerations for TBI: Subacute, Chronic

- ❖ Physical Therapy: One hour of physical therapy three times per week including individualized training of gross motor skills, flexibility, strength, endurance with 15-20 minutes devoted to moderate-intensity aerobic exercise 2-3 times per week *Mossberg*
 - ❖ Peak VO_2 at any given workload was lower after therapy intervention-
→ improved movement efficiency, but no significant difference in peak VO_2



Cochrane Review: Fitness Training to Improve Fitness after Traumatic Brain Injury 2009

- ❖ Six studies: Varied outcome measures
 - ❖ 3/6 randomized controlled studies indirectly assessed change in cardiorespiratory fitness after fitness training using peak power output obtained during cycle ergometry. One study showed improved cardiorespiratory fitness, the other two showed no significant improvement
 - ❖ 4/6 studies did not have any drop-outs; no adverse events reported in all studies
- ❖ Insufficient evidence about the effects of fitness training on cardiorespiratory fitness. Appears to be safe and accepted.

Barriers to Participation



- ❖ General Population

- ❖ Archives of Internal Medicine: Barriers to Weight Loss and Increased Physical Activity *Manson*

- ❖ Lack of perceived benefits, lack of time, lack of innovation, lack of support

- ❖ Lack of access, lack of education, lack of healthy food or physical education in schools

- ❖ Driver attempted to look at barriers to participation in physical activity: 28 outpatients with mild to severe TBI completed a questionnaire before discharge from a comprehensive outpatient program

- ❖ Those in action and maintenance “stage of change” completed more physical activity per week ($p < .001$) than pre-contemplators or contemplators

- ❖ Reavenall and Blake: Determinants of physical activity

- ❖ Multicenter cross-sectional questionnaire

- ❖ Self-efficacy for exercise was the only persistent factor that predicted significant exercise behavior

What The Research Tells Us

- ❖ Timing: Too early can compromise neuroplasticity and may place person at increased risk for permanent sequelae; too late risks development of chronic health consequences
- ❖ Rx: Exercise programs should be individualized to meet the patient's needs
 - ❖ Intensity, frequency, duration may be below recommended doses initially
 - ❖ Traditional physical therapy usually focuses on ROM, balance, function, spasticity
 - ❖ Most patients would benefit from starting with a supervised program that includes graduated, high level, sustained aerobic activity with eventual transition to a gym or independent exercise program

Pearls, Emeralds, and Diamonds

- ❖ All patients who have sustained a traumatic brain injury are at risk for a sedentary lifestyle and secondary health consequences
- ❖ Some physical activity is better than no physical activity
- ❖ More studies are needed to understand when it is safe to initiate exercise and if there exists an ideal path to increasing activity to meet the recommended daily dosage
- ❖ We need to understand the barriers to developing meaningful health promotion programs in order to improve the sustainability of each individual's lifetime participation



Appendix: Additional Terminology

- ❖ **Peak oxygen consumption ($\dot{V}O_2$):** Highest attained oxygen uptake; often used interchangeably with $\dot{V}O_{2\max}$ although each has its own criteria
- ❖ **Pulmonary minute ventilation (V_E):** Volume of air inspired or expired per minute.
- ❖ **Anaerobic threshold (AT):** Point in which the serum lactic acid levels begin to increase significantly, leading to muscle fatigue and shortness of breath

Appendix, cont.

- ❖ To accompany “Table 2 Recommendations for Activity Resumption Following MTBI”

TABLE 1 *Evidence ratings for practice recommendations*

| Evidence Rating | Description |
|------------------------|---|
| A | <p>A strong recommendation that the clinicians provide the intervention to eligible patients.</p> <p><i>Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.</i></p> |
| B | <p>A recommendation that clinicians provide (the service) to eligible patients.</p> <p><i>At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.</i></p> |
| C | <p>No recommendation for or against the routine provision of the intervention is made.</p> <p><i>At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.</i></p> |
| D | <p>Recommendation is made against routinely providing the intervention to patients.</p> <p><i>At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.</i></p> |
| I | <p>The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention.</p> <p><i>Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</i></p> |

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