Published in final edited form as:

J Head Trauma Rehabil. 2010 ; 25(3): 173–183. doi:10.1097/HTR.0b013e3181dc98ff.

Endurance Training and Cardiorespiratory Conditioning after Traumatic Brain Injury

Kurt A. Mossberg, PT, PhD¹, William E. Amonette, MA¹, and Brent E. Masel, MD²

¹ University of Texas Medical Branch, Galveston, TX

² Transitional Learning Center, Galveston, TX

Abstract

Objective—To examine the importance of cardiorespiratory conditioning after traumatic brain injury (TBI) and provide recommendations for patients recovering from TBI.

Method—Review of literature assessing the effectiveness of endurance training programs.

Main outcomes and results—A sedentary lifestyle and lack of endurance are common characteristics of individuals with TBI who have a reduction in peak aerobic capacity of 25-30% compared to healthy sedentary persons. Increased physical activity and exercise training improves cardiorespiratory fitness in many populations with physical and cognitive impairments. Therefore, increasing the endurance and cardiorespiratory fitness of persons with TBI would seem to have important health implications. However, review of the TBI literature reveals that there have been few well-designed, well-controlled studies of physiologic and psychological adaptations of fitness training. Also lacking are long-term follow-up studies of persons with TBI.

Conclusions—Assessing endurance capacity and cardiorespiratory fitness early in the TBI rehabilitation process merits consideration as a standard of care by professional rehabilitation societies. Also, providing effective, safe and accessible training modalities would seem to be an important consideration for persons with TBI, given the mobility impairments many possess. Long-term follow-up studies are needed to assess the effectiveness of cardiorespiratory training programs on overall morbidity and mortality.

Keywords

head injury; rehabilitation; oxygen consumption; disability; fitness

INTRODUCTION

In this manuscript, we review the literature that describes the importance of incorporating endurance training, when feasible, across the continuum of recovery from traumatic brain injury (TBI). Included are discussions of: (1) morbidity and mortality and how endurance training can have a positive impact; (2) expected responses and adaptations to cardiorespiratory fitness training and how these may be altered in patients with TBI; (3) a review of studies that have examined fitness levels and training programs aimed at improving physical and metabolic

Address all correspondence and reprint requests to: Kurt A. Mossberg, PT, PhD University of Texas Medical Branch 301 University Blvd. Galveston, TX 77555-1144 Tel: (409) 772-3069 Fax: (409) 747-1613 kmossber@utmb.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

work capacity, and (4) limitations affecting rehabilitation specialists and persons with TBI when cardiorespiratory conditioning programs are undertaken.

The impact of a sedentary lifestyle on healthy (or able bodied) persons has been studied extensively. The importance of conditioning and endurance training for the overall health and well-being of normal, healthy individuals in society has been well documented.¹⁻³ The benefits of increased physical activity levels on health have been shown in a variety of disease categories (for review see⁴). These include, but are not limited to, decreases in all-cause cardiovascular disease, decreased incidence of colon cancer, improved glucose tolerance (prevention of Type 2 diabetes mellitus), decreased incidence of osteoporosis, improved lipid profiles (decreased triglycerides, increase HDL-cholesterol), decrease incidence of depression, and decreased body weight.

Formal exercise programs and interventions would equate to increased physical activity levels. Increased physical activity levels might not equate to formal exercise interventions. Studies that report on the benefits of increased physical activity may include formal exercise interventions or may simply report results of subjects that had increased daily caloric expenditure above that seen in normal, sedentary individuals. Similarly, studies have reported on increased aerobic capacity, peak aerobic capacity and increased oxygen uptake. Aerobic capacity and peak oxygen uptake essentially describe the same thing, that being the capacity of the total oxygen delivery and utilization system of the body. Because this system includes the heart, lungs and skeletal muscle functional capacities, it is considered the gold standard for overall physical fitness or physical work capacity.⁵ Many of these terms are used interchangeably but what should be explicitly stated is whether someone is reporting maximal or submaximal capacities.

Health differences have been evaluated and discussed for patients who exercise post-stroke^{6, 7} and post-spinal cord injury.^{8, 9} It has also been suggested that vocational status is positively correlated with physical activity levels.^{10, 11} In addition, it has been reported that patients with other physical and cognitive disabilities have derived health benefits from increased physical activity.¹²⁻¹⁵ It is abundantly clear that increased physical activity in the form of cardiorespiratory fitness training improves health. The role of increased physical activity in prevention of secondary morbidity in healthy, non-disabled individuals necessitates more emphasis on physical activity as a preventative measure against chronic disease¹⁶ in patients recovering from TBI.

A large majority of persons with TBI are young and likely to survive into older age. For various reasons, many adopt a sedentary lifestyle.¹⁷⁻¹⁹ The possibility of a sedentary lifestyle has the potential for developing secondary health problems that will add further burden to an already strained health care system. Yet, for persons with TBI, little has been published about cardiorespiratory fitness and endurance training programs. Most physical therapy interventions after TBI focus on specific impairments such as spasticity, flexibility, muscle force production, balance, gait kinematics, and functional skills. However, based on clinical experience, there is a large group of individuals with TBI that have few, if any, physical impairments and the focus of rehabilitation for these individuals is on cognitive, behavioral and motivational impairments. Often overlooked is the need to improve physical work capacity and endurance, putatively aimed at reducing levels of fatigue, a common complaint in patients after TBI.²⁰

It is generally agreed that peak aerobic capacities of patient with TBI are on the order of 65-74% of normal.^{17, 21, 22} However, due to variations in measurement techniques, exercise modalities, and physical impairments associated with TBI, knowing the true magnitude of deficit is difficult. Normative values from which peak aerobic capacity estimates are derived have differed and most importantly, testing protocols for subjects with TBI have varied. It is well

known that peak oxygen consumption is higher when one is tested on a treadmill versus a bicycle ergometer.²³ Similarly, Hunter and coworkers found peak oxygen consumption (VO_2) was significantly higher on a treadmill than on a bicycle ergometer in individuals with TBI.²² Studies using cycle ergometry to measure peak VO_2 may underestimate the true metabolic capacity of patients with a TBI.

Becker and colleagues directly compared the physiologic responses to exercise of sedentary non-disabled individuals to patients with TBI.²⁴ However, 58% of the patients (11/19) with TBI had residual motor impairments. These investigators found pulmonary function at rest was reduced 25-40%. Other measures that included oxygen consumption as part of the assessment (ventilatory equivalent for oxygen and oxygen pulse) suggest that the total O_2 delivery system (aerobic capacity) is significantly reduced in persons recovering from TBI. To our knowledge, only one study has directly compared the aerobic capacities of patients with TBI who have few, if any, motor impairments with non-disabled individuals of similar age and gender using an identical graded exercise test.²⁵ The study confirmed that previous estimates of peak VO_2 of patients recovering from TBI are approximately 75% of a similar sedentary cohort. Other physiologic responses to exercise (e.g., heart rate (HR), pulmonary ventilation (V_E)) were similarly impaired. For peak VO_2 , the majority of patients with TBI were equal to or less than the 10th percentile of age- and gender-matched population normative data.

The anaerobic threshold (AT) during graded exercise testing is a point when the serum lactic acid levels begin to increase significantly, leading to muscle fatigue and shortness of breath. Along with lower peak aerobic work capacities, unpublished data from our laboratory suggests that the ATs of patients with TBI are exceptionally low during submaximal work. In fact, the data show that the AT may occur below the reported metabolic demands of yard mowing, sweeping, or laundry (Figure 1; metabolic equivalent data for common ADLs were reported by Crouter and colleagues.²⁶ A metabolic equivalent (MET) equals the resting oxygen consumption (approximately 3.5mL/min/kg body weight)). These and other findings in our laboratory point to the possibility that fatigue in persons with TBI may have a metabolic and physiologic component, at least partially. As studies become published on this issue, the rationale for initiating endurance training and aerobic exercises early in the rehabilitation process is likely to strengthen.

MEASUREMENT OF ENDURANCE CAPACITY

There are a variety of ways to assess mobility in the rehabilitation setting²⁷ as described elsewhere in this issue. This review focuses on endurance capacity and cardiorespiratory fitness. How to best assess the physiologic and metabolic aspects of mobility are important considerations. Understanding the acute responses and long term adaptations are keys to understanding whether an exercise intervention will have a positive (or negative) effect of overall health. The gold standard for measuring physical fitness is to measure peak VO_2 during a maximal graded exercise test in which the workload progressively increases. These tests are most often performed on treadmills or cycle ergometers or some other device in which workload can be increased incrementally. Protocols have been designed that are similar to standard cardiac stress tests that measure heart rate, blood pressure and electrocardiogram (ECG). Optimally, these tests should include the collection of expired gases so the subject's metabolic response can be assessed. In addition to peak oxygen uptake, the metabolic response provides additional information on carbon dioxide production (VCO_2) and pulmonary ventilation (V_E). Simple calculations with these variables allow one to estimate cardiac stroke volume and efficiency of breathing during exercise (see Table 1). Since all variables are measured continuously, submaximal responses can be monitored to provide an estimate of efficiency of movement (oxygen consumption per unit of work). Movement efficiency is

particularly important when one considers the high incidence of neuromusculoskeletal abnormalities in patients with TBI.

Because of balance and gait impairments that many patients with TBI demonstrate, the cycle ergometer, upright or recumbent, is commonly used for exercise testing. However, patients with TBI elicit higher peak VO_2 when being tested on a treadmill versus a bicycle ergometer²² due to localized muscle (quadriceps) fatigue. Using test-retest designs, both leg cycle ergometry¹⁷ and treadmill testing²⁸ have been shown to be reliable in patients recovering from TBI. Besides eliciting higher peak VO_2 , treadmill testing is recommended, when feasible and safe, because it is more functional. Body weight support harness systems can be used to provide an added level of security for the individual being tested.

Since testing of peak VO_2 requires expensive equipment and highly trained personnel, alternative *submaximal* methods of testing have been developed. One can estimate aerobic capacity using a timed walk or run test. First proposed by Cooper,²⁹ these tests have been used frequently in a variety of patient populations.^{30, 31} The most common is the six minute walk and is a measure of the total distance walked in 6 minutes with a minimal amount of turns or changes in direction. It is best combined with a measure of heart rate so an estimate of energy expenditure can be calculated (see Table 1). The test has been shown to be reliable in subjects with TBI.³² The modified 20 meter shuttle run³³, another variation of the walk / run test used to estimate peak oxygen consumption, was also one of the first to be evaluated for reliability in patients with TBI. Based on our clinical experience, we recommend the six minute walk combined with a measure of heart rate since it is the most feasible to perform for the majority of patients with TBI that have the capacity to ambulate with or without an assistive device.

NORMAL RESPONSES AND ADAPTATIONS TO EXERCISE

Acute Responses to Exercise

In healthy individuals, the cardiorespiratory, musculoskeletal and endocrine systems respond in a predictable way to increases in physical and metabolic work demands. Upon initiation of an exercise stress, heart rate and cardiac contractility increase due to the action of the sympathetic nervous system and release of epinephrine and norepinephrine.³⁴ This results in an increase in stroke volume and cardiac output. Pulmonary V_E also increases with rising physical work demands. Increased V_E and cardiac output accommodate delivery of saturated hemoglobin (oxygenated blood) to working skeletal muscle, resulting in increased oxygen consumption that fuels aerobic metabolism. Carbon dioxide is removed from the blood through pulmonary V_E and its production is also increased, depending upon the intensity of work.

Neurohormonal mechanisms mediate increased blood flow to active skeletal muscle through vasodilatation while decreased flow through inactive tissues occurs by means of vasoconstriction.³⁵ Blood flow to the brain is also affected by exercise. In a study of 13 healthy males performing exercise to exhaustion, it was found that mean blood flow velocity in the middle cerebral artery increased as did brain extraction of O_2 , glucose and lactate.³⁶

Heart rate and oxygen consumption increase linearly in relation to physical work demands.³⁷ Additionally, the ratio of CO_2 production to O_2 consumption, the respiratory exchange ratio (RER), exceeds 1.0 as the intensity of work increases and there is a significant increase in energy derived from anaerobic metabolism. At maximum work capacity, VO_2 reaches a plateau and the RER is near 1.15. Heart rate and V_E also peak at maximum work capacity, but RER continues to rise for several minutes after exercise is stopped.

Plasma levels of several hormones change depending on 1) the time from onset of exercise, 2) the intensity of exercise, 3) the total duration of exercise and 4) the recovery from exercise.

These include changes in epinephrine and norepinephrine, growth hormone (GH), adrenocorticotropin hormone, cortisol, prolactin, and β -endorphin.³⁸ In addition to testosterone, each of these hormones is responsible for regulating physiological processes necessary to complete or recover from the physical workload. Understanding the hormonal responses to exercise may be especially relevant for patients with TBI because of the increased prevalence of neurohormonal pathology at rest.³⁹ This will be discussed briefly in the next section.

Chronic Adaptations Arising from Endurance Training

In healthy individuals undergoing long term training, adaptations occur biochemically and physiologically to increase physical and metabolic work capacity. These adaptations are also associated with improved health and reduced mortality.⁴⁰ Resting heart rate is lower as a result of endurance training.^{41, 42} Additionally, heart rate at submaximal workloads is decreased due to an increased stroke volume and elevated parasympathetic stimulation.⁴¹ An increase in stroke volume, and, subsequently, cardiac output, results in no change or a slight decrease in heart rate at maximal exercise. Peak V_E is also elevated after endurance training.⁴³ The entire O_2 delivery system is enhanced as a result of long term training. In addition to central adaptations, chronic exercise also induces peripheral adaptations that improve exercise capacity (e.g., an increase in skeletal muscle capillary density and increased arteriovenous oxygen differences (increased O_2 extraction by skeletal muscle)).³⁷

Chronic endurance training results in alterations of both resting levels of several hormones and their response to an acute bout of exercise. Epinephrine and norepinephrine are lower during submaximal work,⁴⁴ but respond to a greater degree at maximal exercise.⁴⁵ Along with increases in stroke volume, the decreased circulating levels of these hormones at submaximal exercise may partially explain the reduced heart rate observed in endurance trained individuals.⁴¹

Endocrine responses and adaptations to exercise may be of great importance considering that the incidence of hypopituitarism has been reported as 16 - 56% percent of patients with moderate to severe TBI.³⁹ In addition, GH and testosterone have both been found to be deficient in individuals with TBI. Recently, aerobic work capacities of patients with TBI who had normal serum GH were compared to patients with abnormally low GH.⁴⁶ The results indicated that patients with TBI who were GH sufficient demonstrated higher work capacities than patients who were GH deficient; however, the normal GH group still had an aerobic capacity that was 75% of healthy sedentary individuals. Endurance training may be of particular relevance for patients with TBI who also have hypopituitarism, since long-term training is expected to elicit changes in the hypothalamus-pituitary-adrenal and hypothalamus-pituitary-thyroid axes (for review see 47).

POTENTIAL IMPORTANCE OF ENDURANCE TRAINING FOR INDIVIDUALS RECOVERING FROM TBI

Many patients who suffer a TBI, especially those admitted to hospital with moderate to severe injuries, undergo a period of bed rest and immobility. The physiological effects of bed rest have been well documented^{48, 49} and have been addressed as they specifically relate to patients with TBI.¹⁸ Bed rest, depending on its duration, has significant negative consequences for all bodily systems, especially systems involved in oxygen delivery and utilization such as the cardiovascular, pulmonary and muscular systems. According to Bell¹⁸ there are many comorbidities that can result from bed rest and immobility and have negative consequences on the quality of life of individuals living with the sequelae of TBI and some of these will be addressed in the following sections.

Cardiovascular System

Pathology of the cardiovascular system is a major long-term consequence of a TBI. Shavelle and colleagues studied individuals with TBI surviving more than one year and found they were 3 times more likely to die of circulatory conditions, including cardiovascular, cerebrovascular and thromboembolic disease when compared to the general population.⁵⁰ In a 2004 study of mortality among 2,178 individuals with moderate to severe TBI who survived more than one year after injury, it was shown that individuals with TBI had a life expectancy reduction of 7 years and were twice as likely to die when compared to individuals in the general population of similar race, gender and age.⁵¹ A follow-up study published two years later on the same patient cohort revealed that the greatest proportion of deaths resulted from circulatory problems (2140 patients survived more than one year and there were 124 deaths during the follow-up period of the study). Although the number of circulatory deaths was not significantly different from the general population, it was 34% higher than expected.⁵² Using ICD-9 codes, these authors reported 33 circulatory related deaths that included ischemic heart disease (14), other heart disease (10), cerebrovascular disease (6), hypertensive disease (1), arterial embolism (1), and pulmonary embolism (1). They recommended that clinicians be cognizant of the importance of the prevention strategies to reduce the cardiovascular morbidity and mortality in patient with TBI.

Sleep

Poor sleep, and its sequelae, is common following a TBI. Objective polysomnographic abnormalities have been reported in as many as 47% of individuals with a TBI.⁵³ Although the effects of exercise on sleep in the TBI population have not been studied, moderate intensity exercise was found to raise self-reported sleep quality scores in older adults.⁵⁴ In a study on healthy army recruits, Shapiro and coworkers found that aerobic exercise improved sleep onset latency and sleep efficiency, as well as decreased wake time during sleep.⁵⁵

Fatigue

Fatigue is commonly reported by persons who have incurred a traumatic brain injury (TBI) and has been extensively reviewed previously.⁵⁶ Clearly, fatigue is a multidimensional phenomenon with cognitive, affective, subjective and physical components. Fatigue has been defined as “weariness or exhaustion from labor, exertion, or stress AND the temporary loss of power to respond that is induced in a sensory receptor or motor end organ by continued stimulation.”⁵⁷

The relationship of physical fitness to the subjective complaint of fatigue following a TBI has not been extensively studied. However, in other groups with disabilities in which the level of aerobic fitness is significantly reduced, a reduction in fatigue has been reported after endurance conditioning in patients with cancer^{58, 59} and multiple sclerosis.^{60, 61} Bateman and coworkers randomized 157 patients with acquired brain injury (ABI) (44 with TBI, 70 with CVA, and 43 with other closed head injuries) into groups of exercise training (n=78) or relaxation training (n=79).⁶² Fifty-five patients completed the prescribed exercise training that included a maximum of 30 minutes of cycle ergometry, three times a week for eight weeks at an intensity of 60-90% of age-predicted HR_{max} . Although there was improvement in cardiovascular fitness, this did not extend to a significant improvement in responses to a fatigue questionnaire.⁶³ Unfortunately, it is unclear from the report how many patients with the differing types of brain injuries completed the training. Obviously, there is a marked need for further study of the relationship of fatigue to cardiovascular fitness in chronic TBI.

Psychiatric Conditions

Psychiatric and psychological conditions after a TBI are well documented, with survivors at increased risk for generalized anxiety disorders, aggressive behaviors and depression.⁶⁴ Research in uninjured populations suggests that aerobic exercise may improve mental health. A large study of healthy American adults showed that regular aerobic exercise was associated with a decreased incidence of depression and anxiety disorders.⁶⁵ In a study on 156 volunteers with major depression, Babyak and coworkers compared the effects of aerobic exercise to medication. They found that aerobic exercise significantly reduced the levels of depression at the end of the four month treatment phase. At 10 months, the exercise group also had significantly lower relapse rates than the medication group.⁶⁶ In a study of over 3200 adults from Finland, regular aerobic exercise was associated with reduced depression, anger, cynical distrust and stress.⁶⁷ Moreover, it has been suggested that exercise training improves mood and emotion in patients with TBI.⁶⁸ The results of this study, while retrospective, provides evidence for designing prospective, randomized controlled trials.

Cognition

Numerous studies have shown that a brain injury may well be a risk factor for the development of Alzheimer's disease (for review see⁶⁹). In a large study of veterans from World War II, Plassman and colleagues found that any history of head injury more than doubled the risk of developing AD and increased the chances of developing non-Alzheimer's dementia.⁷⁰ Even individuals with no known cognitive impairment after their TBI, have an increased risk of an earlier onset of dementia due to AD.⁷¹ The Institute of Medicine (IOM), in their report on the Gulf War and Health, concluded that "... there is sufficient evidence of an association between moderate and severe TBI and dementia of the Alzheimer's type."⁶⁴ As one ages, there is an increased risk of dementia and it has been shown that the greater the distance elderly men walk in a day, the lower the risk of dementia.⁷² The relationship between levels of aerobic fitness and cognition in older adults is well established. Aerobic fitness training may also be associated with decreased brain tissue loss in aging adults.⁷³ Increased physical activity is associated with decreased risks of dementia, AD and cognitive impairment in the elderly.⁷⁴ Neurodegenerative disease such as Alzheimer's and Parkinson's is accelerated after TBI⁶⁴ and exercise has been shown to have several positive benefits that may delay the onset of age related decline in brain function in other patient populations (for review see⁷⁵). The effects of exercise training on neuropsychological status are detailed elsewhere by Lojovich in this issue.

Animal Studies Related to Importance of Aerobic Exercise for Patients with TBI

More recently, we have begun to gain insight into the protective effects of exercise on brain function primarily from studies of various animal models. Animal studies offer the advantage of being able to study the cellular and molecular events taking place in the brain as a result of exercise. Aerobic exercise, along with cognitive stimulation, dietary restriction and certain phytochemicals, has been shown to contribute to neuroprotection in animals by stimulating production of brain derived neurotrophic factor (BDNF), glia cell line-derived neurotrophic factor (GDNF) and other stress response proteins (for reviews see ⁷⁶⁻⁷⁷). BDNF is a protein that acts to support existing neurons and encourage growth and differentiation of new neurons and synapses (neurogenesis) in the central and peripheral nervous system.⁷⁸⁻⁷⁹ It is active in the cortex, hippocampus and basal forebrain - areas which are vital for memory, learning and higher cognitive functions including long term memory.⁸⁰⁻⁸¹ Exposure to the stress hormone, corticosterone, decreases expression of BDNF in rats and may lead to eventual atrophy of the hippocampus.⁸² On the other hand, voluntary exercise performed by rats strongly increases expression of BDNF in the brain and may protect against this atrophy and promote brain vascularization, neurogenesis and functional changes in the neuronal structure. In addition, exercise has also been shown to reduce the negative effects of a high fat diet on BDNF in rats.

⁸³ Elucidating the neurobiochemical mechanisms operating in the human, especially after TBI, is possible with the development of new imaging modalities and biomarkers.

EFFECTIVENESS OF ENDURANCE TRAINING IN PATIENTS WITH TBI

Few studies have evaluated the efficacy of endurance training and the resultant adaptations in patients who only had a TBI. The majority have focused on patients recovering from stroke (for review see 84). Almost two decades ago, the role of physical conditioning in persons with TBI was addressed.⁸⁵ These authors review previous work and argue that the reduced physical work capacity common in patients with TBI can be improved with training and should be considered a necessary component of rehabilitation programs. Moreover, a relationship between aerobic training, improved endurance capacity and successful return to employment has been proposed.²¹ Given the degree of cognitive, behavioral, and motor impairments that affect the TBI population, increasing aerobic fitness may be challenging. However, several investigators have demonstrated success at improving physical endurance and / or metabolic capacity in patients with a TBI.

Hunter and colleagues demonstrated that a combined steady state endurance training and strength training program improved aerobic capacity from 74% to 85% of predicted values for age and gender.²² In a post-acute residential treatment setting, patients 1 year post TBI (n=9), CVA (n=2) and TBI + CVA (n=1) completed a total of 25 minutes at 60-80% of age-predicted maximal heart rate, 2-3 days per week. Following three months of training, significant improvements were observed in peak VO_2 and peak power output. Similarly, we have unpublished preliminary data showing that patients one year after moderate to severe injury (but recovered having only minimal gait impairment) improved their peak VO_2 more than 30% after an average of 15 weeks of properly supervised training. Also evident in this cohort were significant improvements in breathing efficiency.

Routine physical therapy and specific aerobic training can improve submaximal ambulatory efficiency in patients with a brain injury.⁸⁶ In a study by Mossberg et al, forty patients in the post acute phase of recovery received one hour of physical therapy three times a week, including individualized training of gross motor skills, flexibility, strength, and endurance. On average, 15-20 minutes of the therapy session was devoted to moderate intensity aerobic exercise 2-3 times per week. Peak VO_2 was measured before and after the intervention. Test data after intervention showed that VO_2 , at any given workload, was lower after the therapy intervention suggesting improved movement efficiency. However, no significant differences were evident in peak VO_2 . A lack of change in peak VO_2 may have been due to the fact that the study cohort of patients was unsupervised during the aerobic fitness program, possibly resulting in inadequate exercise durations and intensities necessary to improve peak aerobic capacity. Table 2 provides guidelines / recommendations for a proper exercise prescription with the goal of increasing cardiorespiratory fitness and endurance.³

In one of the better designed studies of fitness training in patients with brain injuries, the previously cited study by Bateman and coworkers⁶² randomized 157 patients with acquired brain injury (ABI) into an exercise training group or relaxation training group. Fifty-five patients completed the prescribed exercise training and sixty-three patients completed the relaxation training consisting of breathing exercises, progressive muscle relaxation techniques, and visualization exercises for the same frequency and duration. Before and after the intervention, peak aerobic capacity was estimated using a multi-stage submaximal cycle ergometry test in which submaximal heart rate and work were measured. Disability and dependency were measured using the Barthel Index, the Functional Independence Measure (FIM), and the Nottingham Extended Activities of Daily Living Index (NEADLI). Additionally, functional changes were measured using the Berg Balance Scale and 10-meter

walk time. Post-test measurements showed that subjects engaging in exercise training improved peak work output on the cycle ergometer compared to the relaxation control group. However, no significant differences were observed in the disability dependency scales, balance scores, or walk velocities between groups. This may have occurred because many of these assessment tools have ceiling effects and may not be appropriate predictors of return to higher levels of mobility. Again, it is unclear from the report how many patients with the differing types of brain injuries completed the training. More importantly, actual changes in peak aerobic capacity were not assessed.

Circuit Training

Circuit training is an exercise program that combines resistance exercise with aerobic exercise. It may be particularly useful because the variety of exercises performed. Based on clinical experience with many different patient populations, this type of training could ameliorate the monotony of exercise with a single modality and provide an effective alternative for patients who are difficult to motivate and easily bored with one type of exercise (e.g., training only on treadmill or cycle ergometry). In one of the first studies involving exercise and TBI, Jankowski and Sullivan performed a case-series analysis investigating the effects of circuit training on oxidative capacities of patients with a TBI.²¹ Fourteen sedentary adult subjects who previously suffered a TBI completed the sixteen-week protocol. The subjects completed an array of tests that included peak VO_2 and metabolic efficiency in walking. After the sixteen-week program, the subjects exhibited greater aerobic capacities but showed no change in oxygen costs (i.e., efficiency) of walking.

In a second study, Bhambhani and coworkers found circuit training to be effective in improving cardiorespiratory fitness of patients with TBI.⁸⁷ The exercise protocol combined intermittent upper and lower body high resistance, short duration exercise (e.g., weight lifting) with low resistance, longer duration aerobic exercise (e.g., cycle ergometry, treadmill walking, and upper body ergometry). During each exercise session, subjects were encouraged to maintain a heart rate at or above 60% of their heart rate reserve. Testing was performed at baseline, 6 and 12 weeks after training. No significant differences were observed in any of the measurements at the mid-point evaluation. However, after 12 weeks, significant improvements were evident in peak power output, peak VO and V_E .⁸⁷ These data suggest that circuit training may be an effective technique for improving aerobic capacity in patients with a TBI.

Novel Exercise Interventions for Improvements of Physical Work Capacity in Persons with a TBI

Along with traditional physical therapy and exercise modalities, some unique exercise interventions have shown promise toward improving the work capacities of patients with a brain injury. Driver and colleagues compared joint flexibility, muscle strength, muscle endurance and work capacities of patients before and after an aquatics training program.⁸⁸ Sixteen patients were randomly assigned to an experimental exercise group or a control group. The experimental group completed 24 exercise sessions over an eight-week period in which they participated in strength, endurance, flexibility and aerobic exercises in a pool at 50-70% of their heart rate reserve. Subjects assigned to the control group completed a vocational rehabilitation program in which subjects performed reading and writing exercises. The aquatics group showed improvements in strength, body composition, and cycle ergometry peak wattage and time compared to the control group.

Virtual reality training is a novel exercise modality receiving more attention in a variety of patient populations. It may be particularly beneficial for patients with TBI, again because of the potential motivational challenges they experience. Virtual reality training offers a variety of experiences that may encourage increased movement and, if performed at sufficient

intensities, may have the potential to increase cardiorespiratory fitness.⁸⁹ One can easily imagine virtual reality systems specifically designed to improve endurance and cardiorespiratory capacity.

Body weight support treadmill training (BWSTT) is another unique exercise intervention that could potentially improve cardiorespiratory fitness. This is a useful modality, especially for patients with severe gait impairments. It was recently reported that two patients with TBI who engaged in a high intensity BWSTT program increased their aerobic capacity by an average of 20%. The subjects trained for 11 and 15 weeks at work rates approximating 60-75% of age-predicted maximal heart rate.⁹⁰ Both subjects engaged in 2-3 sessions a week and ambulated at speeds and inclines that progressively increased as gait kinematics and endurance improved. Although more research is needed, these data lend support to the use of BWSTT in patients with a TBI because exercise efficiency and overall metabolic and mechanical work capacity may improve.

FUTURE DIRECTIONS / CONCLUSIONS

Overall, these data show that patients with a TBI can increase peak aerobic capacity with a properly designed and supervised endurance training program. We strongly recommend that the guidelines outlined in Table 2 be followed as closely as feasible. The results of previous studies in subjects with TBI clearly indicate that significant changes in aerobic capacity and cardiorespiratory fitness will only occur if there is a reasonable approximation of the intensity, frequency and duration guidelines.^{21, 22, 86, 87, 90, 91}

The degree to which aerobic exercise improvements translate to changes in functional capabilities is not well established. Traditional physical therapy is effective in improving mechanical efficiency but may need to include vigorous endurance training or circuit training to increase maximal aerobic capacity. Both aquatic rehabilitation and BWSTT are promising interventions for the improvement of metabolic work capacity; however, more data are needed to validate current research. Unfortunately, the TBI literature on this issue is sparse and too few studies investigating the long-term impact of endurance training have been done using well controlled, randomized designs.

Although exercise is a useful tool to improve overall health and well being, an important issue to consider is when to initiate high level endurance training in the recovery/rehabilitation process. If implemented too early it could have detrimental effects; this has been demonstrated in animal models of TBI.^{92, 93} These studies have shown that an exercise intervention initiated more acutely after injury may compromise neuroplasticity. An additional caveat is that the majority of the animal studies that have examined the effects of exercise after experimental TBI involved only animals who exercised voluntarily on either running wheels or treadmills. This is particularly relevant for human studies in patients recovering from TBI. Major questions remain on how best to translate results of animal studies to humans. When in the continuum of care is it appropriate and not detrimental to long term outcomes to initiate a cardiorespiratory fitness program? What are the best methods to motivate a patient with TBI to exercise and what degree of commitment on the part of the patient is necessary for a successful outcome? Should educational activities on the benefits of physical activity be a component of the standard of care and when in the continuum of care would these activities have the greatest impact? Collaborations between physical therapists/exercise physiologists and clinical neuropsychologists will be necessary in future studies to answer some of these questions.

One of the key assumptions underlying brain injury rehabilitation is the concept that neural plasticity is beneficial to functional recovery. The term 'plasticity' was first used by William James in 1890 while describing a key feature of human behavior – the ability to change in a meaningful way (i.e., "behavioral plasticity").⁹⁴ The term 'plasticity' now includes molecular,

cellular, structural and systemic changes that will ultimately impact behavioral plasticity. Based on animal studies and investigations in other human populations, we believe there is enough evidence to warrant studies that can answer the question whether chronic exercise can induce plasticity in patients with TBI and consequently bring about improved physiologic and behavioral outcomes.

Lastly, patients with mild TBI are often not referred to physical therapy because they are identified as having only subtle physical impairments. Even those with more severe injuries initially, who appear to have fully recovered physically from a clinical standpoint, may have compromised endurance and aerobic capacities. They may also have impairments in agility, dynamic balance and coordination.⁹⁵ These subtle difficulties could easily prevent one from participating in high level mobility type activities. In addition, individuals with little physical impairment may have barriers to participation because of cognitive, behavioral and executive impairments. These individuals do not typically receive the proper supervision and education necessary to begin and continue a cardiorespiratory fitness program. Educating patients on the long term health benefits of cardiorespiratory conditioning, especially as it relates to an individual recovering from a TBI, should be an integral part of the rehabilitation process.

Acknowledgments

This work was partially supported by the National Institutes of Health R01 HD046570 to Dr. Mossberg. The authors thank Paula Skinkis for editorial assistance.

REFERENCES

1. Paffenbarger R, Hyde R, Wing A, Hsieh C. Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med* 1986;314:605–613. [PubMed: 3945246]
2. Pate R, Pratt M, Blair S, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA* 1995;273(5):402–407. [PubMed: 7823386]
3. Haskell W, Lee I, Pate R, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007;116(9):1081–1093. [PubMed: 17671237]
4. Chakravarthy, M.; Booth, F. Exercise. Hanley & Belfus; Philadelphia: 2003.
5. McArdle, W.; Katch, F.; Katch, V. Exercise Physiology: Energy, Nutrition, and Human Performance. 5 ed.. Lippincott Williams & Wilkins; Philadelphia, PA: 2001.
6. Macko R, Ivey F, Forrester L, et al. Treadmill exercise rehabilitation improves ambulatory function and cardiovascular fitness in patients with chronic stroke: A randomized, controlled trial. *Stroke* 2005;36(10):2206–2211. [PubMed: 16151035]
7. Stuart M, Chard S, Roettger S. Exercise for chronic stroke survivors: a policy perspective. *J Rehabil Res Dev* 2008;45(2):329–335. [PubMed: 18566950]
8. Cowell L, Squires W, Raven P. Benefits of aerobic exercise for the paraplegic: a brief review. *Med Sci Sports Exerc* 1986;18(5):501–508. [PubMed: 3534507]
9. Jacobs P, Nash M. Exercise recommendations for individuals with spinal cord injury. *Sports Med* 2004;34(11):727–751. [PubMed: 15456347]
10. Curtis K, McClanahan S, Hall K, Dillon D, Brown K. Health, vocational, and functional status in spinal cord injured athletes and nonathletes. *Arch Phys Med Rehabil* 1986;67:862–865. [PubMed: 3800613]
11. Noreau, Shephard R. Return to work after spinal cord injury: the potential contribution of physical fitness. *Paraplegia* 1992;30(8):563–572. [PubMed: 1522998]
12. Pitetti K, Rimmer J, Fernhall B. Physical fitness and adults with mental retardation. An overview of current research and future directions. *Sports Med* 1993;16(1):23–56. [PubMed: 8356375]
13. Santiago M, Coyle C, WB K. Aerobic exercise effect on individuals with physical disabilities. *Arch Phys Med Rehabil* 1993;74(11):1192–1198. [PubMed: 8239961]

14. Heath, G.; Fentem, P. Physical activity among persons with disabilities -- A public health perspective.. In: Holloszy, J., editor. Exercise and Sport Sciences Reviews. Vol. 25. Williams and Wilkins; Baltimore: 1997. p. 195-234.
15. Cooper R, Quatrano L, Axelson P, et al. Research on physical activity and health among people with disabilities: a consensus statement. J Rehabil Res Dev 1999;36(2):142–154. [PubMed: 10661530]
16. Booth F, Gordon S. Advocacy is needed to promote research into diseases of physical inactivity. Exerc Sport Sci Rev 2000;28(4):145–147. [PubMed: 11064846]
17. Bhambhani Y, Rowland G, Farag M. Reliability of peak cardiorespiratory responses in patients with moderate to severe traumatic brain injury. Arch Phys Med Rehabil 2003;84(11):1629–1636. [PubMed: 14639562]
18. Bell, K. Complications associated with immobility after TBI.. In: Zasler, N.; Katz, D.; Zafonte, R., editors. Brain Injury Medicine. Demos Medical Publishing; New York: 2007. p. 605-614.
19. Sullivan, K. Therapy interventions for mobility impairments and motor skill acquisition after TBI.. In: Zasler, N.; Katz, D.; Zafonte, R., editors. Brain Injury Medicine. Demos Medical Publishing; New York: 2007. p. 929-946.
20. Bushnik T, Englander J, Wright J. Patterns of fatigue and its correlates over the first 2 years after traumatic brain injury. J Head Trauma Rehabil 2008;23(1):25–32. [PubMed: 18219232]
21. Jankowski L, Sullivan S. Aerobic and neuromuscular training: Effect on the capacity, efficiency, and fatigability of patients with traumatic brain injuries. Arch Phys Med Rehabil 1990;71:500–504. [PubMed: 2350220]
22. Hunter M, Tomberlin J, Kirkikis C, Kuna S. Progressive exercise testing in closed head-injured subjects: Comparison of exercise apparatus in assessment of a physical conditioning program. Phys Ther 1990;70(6):363–371. [PubMed: 2345780]
23. Hermansen L, Saltin B. Oxygen uptake during maximal treadmill and bicycle exercise. J Appl Physiol 1969;26(1):31–37. [PubMed: 5762873]
24. Becker E, Bar-Or O, Mendelson L, Najenson T. Pulmonary functions and responses to exercise of patients following cranio cerebral injury. Scand J Rehabil Med 1978;10:47–50. [PubMed: 675182]
25. Mossberg K, Ayala D, Baker T, Heard J, Masel B. Aerobic capacity after traumatic brain injury: comparison with a nondisabled cohort. Arch Phys Med Rehabil 2007;88(3):315–320. [PubMed: 17321823]
26. Crouter S, Clowers K, Bassett D. A novel method for using accelerometer data to predict energy expenditure.[see comment]. J Appl Physiol 2006;100(4):1324–1331. [PubMed: 16322367]
27. Bussmann J, Stam H. Techniques for measurement and assessment of mobility in rehabilitation: a theoretical approach. Clin Rehabil 1998;12(6):455–464. [PubMed: 9869249]
28. Mossberg K, Greene B. Reliability of graded exercise testing after traumatic brain injury: submaximal and peak responses. Am J Phys Med Rehabil 2005;84(7):492–500. [PubMed: 15973085]
29. Cooper K. A means of assessing maximal oxygen intake: correlation between field and treadmill testing. JAMA 1968;203(3):135–138.
30. Butland R, Pang J, Gross E, Woodcock A, Geddes D. Two-, six-, and 12-minute walking tests in respiratory disease. Brit Med J 1982;284:1607–1608. [PubMed: 6805625]
31. Guyatt G, Sullivan M, Thompson P, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. Can Med Assoc J 1985;132(8):919–923. [PubMed: 3978515]
32. Mossberg K. Reliability of a timed walk test in persons with acquired brain injury. Am J Phys Med Rehabil 2003;82(5):385–390. [PubMed: 12704280]
33. Vitale A, Jankowski L, Sullivan S. Reliability of a walk/run test to estimate aerobic capacity in a brain-injured population. Brain Injury 1997;11(1):67–76. [PubMed: 9012553]
34. Mazzeo R. Catecholamine responses to acute and chronic exercise. Med Sci Sports Exerc 1991;23(7):839–845. [PubMed: 1681408]
35. Segal, S.; Bearden, S. Organization and control of circulation to skeletal muscle.. In: Tipton, C., editor. ACSM's Advanced Exercise Physiology. Lippincott Williams & Wilkins; Philadelphia: 2006. p. 343-356.
36. Gonzalez-Alonso J, Dalsgaard M, Osada T, et al. Brain and central haemodynamics and oxygenation during maximal exercise in humans. J Physiol 2004;557(Pt 1):331–342. [PubMed: 15004212]

37. Thompson, W., editor. ACSM's Guidelines for Exercise Testing and Prescription. 8 ed.. Wolters Kluwer / Lippincott Williams & Wilkins; Philadelphia: 2010.
38. de Vries W, Bernards N, de Rooij M, Koppeschaar H. Dynamic exercise discloses different time-related responses in stress hormones. *Psychosom Med* 2000;62(6):866–872. [PubMed: 11139007]
39. Lieberman S, Oberoi A, Gilkison C, Masel B, Urban R. Prevalence of neuroendocrine dysfunction in patients recovering from traumatic brain injury. *J Clin Endocrinol Metab* 2001;86(6):2752–2756. [PubMed: 11397882]
40. Colditz G. Economic costs of obesity and inactivity. *Med Sci Sports Exerc* 1999;31(11 Suppl):S663–s667. [PubMed: 10593542]
41. Carter J, Banister E, Blaber A. Effect of endurance exercise on autonomic control of heart rate. *Sports Med* 2003;33(1):33–46. [PubMed: 12477376]
42. Winsley R, Battersby G, Cockle H. Heart rate variability assessment of overreaching in active and sedentary females. *Int J Sports Med* 2005;26(9):768–773. [PubMed: 16237623]
43. Norton K, Squires B, Norton L, Craig N, McGrath P, Olds T. Exercise stimulus increases ventilation from maximal to supramaximal intensity. *Eur J Appl Physiol Occup Physiol* 1995;70(2):115–125. [PubMed: 7768233]
44. Winder W, Hickson R, Hagberg J, Ehsani A, McLane J. Training-induced changes in hormonal and metabolic responses to submaximal exercise. *J Appl Physiol* 1979;46(4):766–771. [PubMed: 457555]
45. de Diego Acosta A, Garcia J, Fernandez-Pastor V, Peran S, Ruiz M, Guirado F. Influence of fitness on the integrated neuroendocrine response to aerobic exercise until exhaustion. *J Physiol Biochem* 2001;57(4):313–320. [PubMed: 12005034]
46. Mossberg K, Masel B, Gilkison C, Urban R. Aerobic capacity and growth hormone deficiency after traumatic brain injury. *J Clin Endocrinol Metab* 2008;93(7):2581–2587. [PubMed: 18413421]
47. Mastorakos G, Pavlatou M. Exercise as a stress model and the interplay between the hypothalamus-pituitary-adrenal and the hypothalamus-pituitary-thyroid axes. *Horm Metab Res* 2005;37(9):577–584. [PubMed: 16175498]
48. Harrison T. Abuse of rest as a therapeutic measure for patients with cardiovascular disease. *JAMA* 1944;125(16):1075–1077.
49. Greenleaf J, Kozlowski S, Terjung R. Physiological consequences of reduced activity during bed rest. *Exercise and Sport Sciences Reviews* 1982;10:84–119. [PubMed: 6749519]
50. Shavelle R, Strauss D, Whyte J, Day S, Yu Y. Long-term causes of death after traumatic brain injury. *Am J Phys Med Rehabil* 2001;80(7):510–516. [PubMed: 11421519]
51. Harrison-Felix C, Whiteneck G, DeVivo M, Hammond F, Jha A. Mortality following rehabilitation in the Traumatic Brain Injury Model Systems of Care.[see comment]. *Neurorehabil* 2004;19(1):45–54.
52. Harrison-Felix C, Whiteneck G, Devivo M, Hammond F, Jha A. Causes of death following 1 year postinjury among individuals with traumatic brain injury. *J Head Trauma Rehabil* 2006;21(1):22–33. [PubMed: 16456389]
53. Masel B, Scheibel R, Kimbark T, Kuna S. Excessive daytime sleepiness in adults with brain injuries. *Arch Phys Med Rehabil* 2001;82(11):1526–1532. [PubMed: 11689971]
54. King A, Oman R, Brassington G, Bliwise D, Haskell W. Moderate-intensity exercise and self-rated quality of sleep in older adults. A randomized controlled trial.[see comment]. *JAMA* 1997;277(1):32–37. [PubMed: 8980207]
55. Shapiro C, Warren P, Trinder J, et al. Fitness facilitates sleep. *Eur J Appl Physiol* 1984;53(1):1–4.
56. Gordon W. Post-TBI fatigue. *J Head Trauma Rehabil* 2008;23(1):2.
57. Merriam-Webster. Fatigue. [January 18, 2010]. last update Available at: <http://www.merriam-webster.com/dictionary/fatigue>. 2010
58. Dimeo F, Stieglitz R, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. *Cancer* 1999;85(10):2273–2277. [PubMed: 10326708]
59. McTiernan A. Physical activity after cancer: physiologic outcomes. *Cancer Investigation* 2004;22(1):68–81. [PubMed: 15069764]

60. Petajan J, Gappmaier E, White A. Impact of aerobic training on fitness and quality of life in multiple sclerosis. *Ann Neurol* 1996;39:432–441. [PubMed: 8619521]
61. Mostert S, Kesselring J. Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. *Mult Scler* 2002;8(2):161–168. [PubMed: 11990874]
62. Bateman A, Culpan F, Pickering A, Powell J, Scott O, Greenwood R. The effect of aerobic training on rehabilitation outcomes after recent severe brain injury: a randomized controlled evaluation. *Arch Phys Med Rehabil* 2001;82(2):174–182. [PubMed: 11239307]
63. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. *J Psychosom Res* 1993;37(2):147–153. [PubMed: 8463991]
64. IOM. Gulf War and Health: Volume 7: Long-Term Consequences of Traumatic Brain Injury. Vol. 7. The National Academies Press; Washington, DC: 2009.
65. Goodwin R. Association between physical activity and mental disorders among adults in the United States. *Prev Med* 2003;36(6):698–703. [PubMed: 12744913]
66. Babyak M, Blumenthal J, Herman S, et al. Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months. *Psychosom Med* 2000;62(5):633–638. [PubMed: 11020092]
67. Hassmen P, Koivula N, Uutela A. Physical exercise and psychological well-being: a population study in Finland. *Prev Med* 2000;30(1):17–25. [PubMed: 10642456]
68. Gordon W, Sliwinski M, Echo J, McLoughlin M, Sheerer M, Meili T. The benefits of exercise in individuals with traumatic brain injury: a retrospective study. *J Head Trauma Rehabil* 1998;13(4):58–67. [PubMed: 9651240]
69. Jellinger K. Head injury and dementia. *Curr Opin Neurol* 2004;17(6):719–723.
70. Plassman B, Havlik R, Steffens D, et al. Documented head injury in early adulthood and risk of Alzheimer's disease and other dementias. *Neurology* 2000;55(8):1158–1166. [PubMed: 11071494]
71. Schofield P, Tang M, Marder K, et al. Alzheimer's disease after remote head injury: an incidence study. *J Neurol Neurosurg Psychiatry* 1997;62(2):119–124. [PubMed: 9048710]
72. Abbott R, White L, Ross G, Masaki K, Curb J, Petrovitch H. Walking and dementia in physically capable elderly men. *JAMA* Sep;2004 292(12):1447–1453. [PubMed: 15383515]
73. Colcombe S, Erickson K, Raz N, et al. Aerobic fitness reduces brain tissue loss in aging humans. *J Gerontol* 2003;58A(2):176–180.
74. Lautenschlager N, Cox K, Flicker L, et al. Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: A randomized trial. *JAMA* 2008;300(9):1027–1037. [PubMed: 18768414]
75. Kiraly M, Kiraly S. The effect of exercise on hippocampal integrity: review of recent research. *Int J Psychiat Med* 2005;35(1):75–89.
76. Kleim J, Jones T, Schallert T. Motor enrichment and the induction of plasticity before or after brain injury. *Neurochemical Res* 2003;28(11):1757–1769.
77. Mattson M, Magnus T. Ageing and neuronal vulnerability. *Nat Rev Neurosci* 2006;7(4):278–294. [PubMed: 16552414]
78. Acheson A, Conover J, Fandl J, et al. A BDNF autocrine loop in adult sensory neurons prevents cell death.[see comment]. *Nature* 1995;374(6521):450–453. [PubMed: 7700353]
79. Huang E, Reichardt L. Neurotrophins: roles in neuronal development and function. *Annu Rev Neurosci* 2001;24:677–736. [PubMed: 11520916]
80. Yamada K, Nabeshima T. Brain-derived neurotrophic factor/TrkB signaling in memory processes. *J Pharmacol Sci* 2003;91(4):267–270. [PubMed: 12719654]
81. Zigova T, Pencea V, Wiegand S, Luskin M. Intraventricular administration of BDNF increases the number of newly generated neurons in the adult olfactory bulb. *Mol Cell Neurosci* 1998;11(4):234–245. [PubMed: 9675054]
82. Warner-Schmidt J, Duman R. Hippocampal neurogenesis: opposing effects of stress and antidepressant treatment. *Hippocampus* 2006;16(3):239–249. [PubMed: 16425236]
83. Molteni R, Wu A, Vaynman S, Ying Z, Barnard R, Gomez-Pinilla F. Exercise reverses the harmful effects of consumption of a high-fat diet on synaptic and behavioral plasticity associated to the action of brain-derived neurotrophic factor. *Neuroscience* 2004;123(2):429–440. [PubMed: 14698750]

84. Ivey F, Hafer-Macko C, Macko R. Exercise training for cardiometabolic adaptation after stroke. *J Cardiopulm Rehabil Prevent* 2008;28(1):2–11.
85. Sullivan S, Richer E, Laurent F. The role and possibilities for physical conditioning programmes in the rehabilitation of traumatically brain-injured persons. *Brain Injury* 1990;4(4):407–414. [PubMed: 2252972]
86. Mossberg K, Kuna S, Masel B. Ambulatory efficiency in persons with acquired brain injury after a rehabilitation intervention {erratum appears in *Brain Injury* 17(3):266, 2003}. *Brain Injury* 2002;16(9):789–797. [PubMed: 12217204]
87. Bhambhani Y, Rowland G, Farag M. Effects of circuit training on body composition and peak cardiorespiratory responses in patients with moderate to severe traumatic brain injury. *Arch Phys Med Rehabil* 2005;86(2):268–276. [PubMed: 15706553]
88. Driver S, O'Connor J, Lox C, Rees K. Evaluation of an aquatics programme on fitness parameters of individuals with a brain injury. *Brain Injur* 2004;18(9):847–859.
89. Greal M, Heffernan D. The rehabilitation of brain injured children: the case for including physical exercise and virtual reality. *Pediatric Rehabil* 2000;4(2):41–49.
90. Mossberg K, Orlander E, Norcross J. Cardiorespiratory capacity after weight-supported treadmill training in patients with traumatic brain injury. *Phys Ther* 2008;88(1):77–87. [PubMed: 17940106]
91. Greal M, Johnson D, Rushton S. Improving cognitive function after brain injury: The use of exercise and virtual reality. *Arch Phys Med Rehabil* 1999;80(6):661–667. [PubMed: 10378492]
92. Griesbach G, Gomez-Pinilla F, Hovda D. The upregulation of plasticity-related proteins following TBI is disrupted with acute voluntary exercise. *Brain Res* 2004;2:154–162. [PubMed: 15246851]
93. Griesbach G, Hovda D, Molteni R, Wu A, Gomez-Pinilla F. Voluntary exercise following traumatic brain injury: brain-derived neurotrophic factor upregulation and recovery of function. *Neuroscience* 2004;125(1):129–139. [PubMed: 15051152]
94. Cotman C, Berchtold N. Exercise: a behavioral intervention to enhance brain health and plasticity. *Trends Neurosci* 2002;25(6):295–301. [PubMed: 12086747]
95. Rinne M, Pasanen M, Vartiainen M, Lehto T, Sarajuuri J, Alaranta H. Motor performance in physically well-recovered men with traumatic brain injury. *J Rehabil Med* 2006;38(4):224–229. [PubMed: 16801204]

Figure 1.

Functional significance of the anaerobic threshold (AT) as measured using ventilatory threshold and peak exercise capacities of patients with a traumatic brain injury. Data indicate that many common ADL's are supra threshold activities for patients with a TBI.

Table 1

Variables calculated from collected values during the maximal physiologic and metabolic graded exercise test and the submaximal 6 minute walk.

Variable	Collected data
Cardiac stroke volume (estimated strength of left ventricular pump)	$SV \text{ (mL O}_2 \cdot \text{beat}^{-1}) = VO_2 \text{ (mL} \cdot \text{min}^{-1}) \cdot \text{HR (beats} \cdot \text{min}^{-1})^{-1}$
Ventilatory equivalent for oxygen (efficiency of breathing)	$V_{Eq}O_2 = V_E \text{ (L} \cdot \text{min}^{-1}) \cdot VO_2 \text{ (L} \cdot \text{min}^{-1})^{-1}$
Ventilatory equivalent for carbon dioxide (efficiency of breathing)	$V_{Eq}CO_2 = V_E \text{ (L} \cdot \text{min}^{-1}) \cdot VCO_2 \text{ (L} \cdot \text{min}^{-1})^{-1}$
Respiratory exchange ratio (magnitude of anaerobic metabolism)	$RER = VCO_2 \text{ (L} \cdot \text{min}^{-1}) \cdot VO_2 \text{ (L} \cdot \text{min}^{-1})^{-1}$
Physiologic cost index (estimated energy expenditure from submaximal 6 minute walk)	$PCI \text{ (beats} \cdot \text{meter}^{-1}) = \text{HR (beats} \cdot \text{min}^{-1}) \cdot \text{velocity (meters} \cdot \text{min}^{-1})^{-1}$

Table 2

Guidelines for cardiorespiratory and endurance training (adapted from American College of Sports Medicine and the American Heart Association³).

Parameter	Recommendation
Type of exercise *	low resistance, rhythmic, dynamic (e.g., walking, jogging, running, cycling, elliptical)
Intensity *	60 – 90% of age-predicted maximal HR (~210 – age)
Duration *	20 – 40 minutes per session (depending on level of fitness and readiness for training)
Frequency	3 – 4 times per week

* See text for more detailed explanation of variability or adjustment necessary depending on the functional mobility of the individual.