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Improved Cardiorespiratory Fitness with Aerobic Exercise Training in Individuals with Traumatic Brain Injury

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Abstract

Objective—To examine cardiorespiratory fitness in individuals with traumatic brain injury (TBI), prior to and following participation in a supervised 12-week aerobic exercise training program.

Methods—Ten subjects with non-penetrating TBI (TBI severity: Mild, 50%; Moderate, 40%; Severe, 10%; Time since injury: 6.6 ± 6.8 years, mean $\pm$ SD) performed exercise training on a treadmill 3 times a week for 30 minutes at vigorous intensity (70 – 80 % of heart rate reserve). All subjects completed a cardiopulmonary exercise test with gas exchange measured and a questionnaire related to fatigue (Fatigue Severity Scale; FSS) at baseline and following exercise training.

Results—After training, increases ($p < 0.01$) in peak oxygen consumption (VO_2 ; $+3.1 \pm 2.4$ ml/min/kg), time to volitional fatigue ($+1.4 \pm 0.8$ min), and peak work rate (WR; $+59 \pm 43$ watts) were observed. At the anaerobic threshold, VO_2 ($+3.6 \pm 2.1$ ml/kg/min), treadmill time ($+1.8 \pm 1.1$ min) and WR ($+37 \pm 39$ watts) were higher ($p < 0.01$) following exercise training. Subjects also reported significantly lower ($p < 0.05$) FSS composite scores (-0.9 ± 1.3) following exercise training.

Conclusion—These findings suggest that individuals with TBI may benefit from participation in vigorous aerobic exercise training with improved cardiorespiratory fitness and diminished fatigue.

Keywords

VO_2 ; exercise tolerance; endurance training; physical activity; fatigue

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Conflicts of Interest:

All authors have no conflict of interest to declare.

INTRODUCTION

Approximately 1.7 million cases of traumatic brain injury (TBI) occur each year¹ affecting all age groups across the lifespan. Advances in medicine have allowed many individuals to survive their initial brain trauma, yet some of these individuals still suffer from long-term disabilities.^{2,3} Moreover, individuals with TBI may encounter injury-related, personal and/or environmental obstacles that lead to prolonged physical inactivity.⁴⁻⁷ Poor cardiorespiratory fitness ensues as a result of extended sedentary behavior,⁸ which further exacerbates physical activity intolerance to even low intensity activities of short duration. Physical inactivity is also associated with greater perceived fatigue severity,^{9,10} operationally defined as the degree to which fatigue is reported to interfere with physical and social functioning.¹¹

Peak oxygen consumption (VO_2), as measured during cardiopulmonary exercise testing (CPET), is well recognized as an overall index of cardiorespiratory health and fitness.^{12,13} Previous studies have indicated that peak VO_2 may be as much as 25% lower in individuals with TBI compared to sedentary but otherwise healthy adults.^{14,15} In addition, the anaerobic threshold (AT) which reflects exercise intolerance,¹⁶ has also been found to be substantially lower in individuals with TBI than in healthy cohorts without head injuries.¹⁷ Thus, individuals with TBI may become fatigued while participating in physical activities that are of relatively low energy demands. A vicious cycle may thereby be created in which these individuals avoid engaging in physical activity, further reducing their cardiorespiratory fitness and increasing their fatigability.¹⁸

Fatigue is a common complaint in those with TBI^{19,20} and may be related to a number of factors including poor cardiorespiratory fitness¹⁷, poor sleep quality²¹⁻²³ and depression.^{23,24} Aerobic exercise training is commonly used to improve overall cardiorespiratory fitness in the general population²⁵ including various disease groups.²⁶⁻³⁰ However, the use of aerobic exercise training in individuals with TBI has been limited to a small number of studies^{14,31-36} that have yielded mixed results. While some studies reported improvements in peak VO_2 ^{14,31,32} and power output^{33,36} in individuals with TBI following aerobic exercise training, these improvements were not supported by other studies.^{34,37}

A recent Cochrane systematic review concluded that there was insufficient evidence to support the effectiveness of aerobic exercise training for improving cardiorespiratory fitness in individuals with TBI.³⁷ Moreover, the disparity among previous studies on aerobic exercise and cardiorespiratory fitness in individuals with TBI has not been fully explained. Previous studies^{14,31-36} used various exercise modes with different training intensities, durations and frequencies. In some cases, exercise training was mainly conducted using a different mode of exercise than the testing session (i.e. specificity of training).^{14,31,34,36} Several studies also inferred cardiorespiratory fitness from indirect measures obtained during sub-maximal exercise tests.^{35,36} These issues could collectively result in inaccurate conclusions being drawn regarding the use of aerobic exercise training in individuals with TBI.

To address these current informational gaps, we performed a non-controlled pre-intervention trial that examined the effects of a supervised, 12-week, vigorous aerobic exercise training

program on cardiorespiratory fitness and fatigue severity in individuals with TBI. We hypothesized that after aerobic exercise training, individuals with TBI would show improvements in measures of cardiorespiratory fitness and decreases in self-reported fatigue severity.

METHODS

This study was approved by the respective Institutional Review Boards of the participating institutions (National Institutes of Health, NIH 11-CC-0088, Uniformed Services University of the Health Sciences, USUHS G192HI-H; George Mason University, GMU 7286) and registered on clinicaltrials.gov (NCT01294332) before subject enrollment. Written consent was obtained from all subjects prior to participation in the study.

Subjects

Individuals with TBI were recruited from the Washington, D.C. area and enrolled if they met the following inclusion criteria: had a non-penetrating TBI more than 6 months prior to enrollment; were non-smokers; were between the ages of 21 and 45 years of age; were free of known metabolic, respiratory or cardiovascular disease; and able to walk independently on the treadmill without assistance or requiring support. Subjects were also sedentary and not currently participating in any exercise programs as determined by a physician evaluation in which levels of physical activity and exercise regimen were reviewed. Subjects participating in regular exercise of 3 or more times a week at intensities greater than 4 metabolic equivalents (MET) were excluded. In addition, female subjects were not pregnant at the time of enrollment and were required to have monthly pregnancy screenings throughout the study.

A total of 12 subjects enrolled in this study. Participants were community dwelling and living independently in the community. Two of the original 12 subjects were withdrawn by study investigators, one due to pregnancy and the other due to non-compliance with the exercise training program. Ten subjects completed the protocol and were included in the data analyses.

Study Design

Prior to performing the exercise test, subjects completed the Fatigue Severity Scale¹¹ (FSS) to evaluate self-reported fatigue as defined by its perceived impact on physical and social functioning. Subsequently, a CPET for analysis of pulmonary gas exchange and cardiorespiratory function was performed using a modified Bruce treadmill protocol.³⁸ Subjects were allowed to lightly touch the handrails of the treadmill for balance, however they were discouraged from leaning or supporting their body weight during exercise. The CPET was terminated when the subject indicated she or he was unable to continue exercising despite strong verbal encouragement from the testing team. Attainment of peak exercise was confirmed by a respiratory exchange ratio (RER) greater than 1.10.¹²

Following baseline testing, subjects began a supervised aerobic exercise training program for 12 weeks. Each session consisted of aerobic exercise performed on a treadmill 3 times a week for 30 minutes, with an additional 5 to 10 minutes of warm-up and cool-down period

on the treadmill. The goal was to complete 30 minutes of continuous exercise at a target heart rate (HR) range that was individualized for each subject based on their peak HR achieved during the CPET. The target HR range was between 70 and 80% of the subjects' HR reserve (HRR) and calculated as follows:

$$70 \text{ and } 80\% \text{ HRR} = [0.7 \text{ and } 0.8 \times (\text{peak HR} - \text{resting HR})] + \text{resting HR}$$

Speed and/or grade were continually adjusted to maintain an intensity that elicited an exercising HR that was within the target HR range. If the session was interrupted or a subject requested a break, the exercise time would resume only after the subject had achieved the target HR range again. Heart rate, perceived exertion using the Borg Category-Ratio Scale³⁹ (0 to 10 rating) and treadmill speed and grade were recorded throughout the training sessions. From these recordings, a minute-by-minute log was generated providing averages for each session. These averages were then used to calculate each subjects' overall training HR, perceived exertion and work rate over the 12 week training period (Table 2). After completing the exercise training regimen, subjects repeated the FSS questionnaire and CPET assessments.

Data Collection and Outcome Measures

Pulmonary gas exchange was measured using a computerized metabolic cart with automated gas analyzers (CardiO2 Ultima, MedGraphics Corp, St. Paul, Minnesota). Subjects wore a fitted face mask with an attached pneumotachometer that interfaced with the main system. Prior to testing, flow calibrations were performed using a 3-L syringe and the gas analyzers were calibrated to precision-analyzed gas mixtures. Gas exchange variables were measured continuously during the exercise test and included O₂ consumption (VO₂), CO₂ output (VCO₂), minute ventilation (VE), ventilatory equivalent for O₂ (VE/VO₂), ventilatory equivalent for CO₂ (VE/VCO₂), end-tidal partial pressure of O₂ (PETCO₂), end-tidal partial pressure of CO₂ (PETCO₂) and RER (ratio of VCO₂ to VO₂). A 12-lead electrocardiogram was also used to monitor subjects' HR throughout the CPET.

The outcome measures of interest pertain to the VO₂ values, work rate and treadmill time, at both peak exercise and at the anaerobic threshold (AT). VO₂ at peak exercise represents the overall cardiorespiratory fitness of the subject, while VO₂ at the AT is a measure of fatigability as it directly relates to endurance performance.^{40–42} Peak VO₂ was determined as an average of the final 15 seconds of VO₂ values of the exercise test. The AT was identified by visual inspection of multiple gas exchange variables⁴³ and described as the VO₂ at which the following were observed to occur simultaneously: 1) VCO₂ increased out of proportion to the increase of VO₂, 2) VE increased out of proportion to the increase of VO₂, 3) VE/VO₂ began to rise with no systematic increase in VE/VCO₂, and 4) PETO₂ began to rise with a plateau in PETCO₂. The treadmill time and work rate associated with peak exercise and AT were also determined.

The Fatigue Severity Scale (FSS)¹¹ was used to measure subjects' perception of fatigue and its impact on their physical and social functioning over the past week. Nine measurement items were rated on a 7-point Likert scale with higher values indicating greater levels of perceived fatigue. The FSS composite score was calculated as an average of all 9 measurement items.^{44,45} While the FSS was originally developed for detecting fatigue in

patients with multiple sclerosis and systemic lupus erythematosus,¹¹ it has also been shown to distinguish between fatigue experienced by individuals with brain injury and healthy controls.^{46,47} A score equal to or greater than 4 was used as a cut-off indicating severe fatigue. Previous studies have demonstrated that a score ≥ 4 reliably differentiated fatigue in various clinical populations compared to controls.^{11,48} Several studies in individuals with TBI have also reported using a cut-off score of 4.^{23,49–51} The FSS questionnaire was always completed prior to performing the CPET.

Statistical Analysis

Data were analyzed using SPSS version 21.0 (IBM Corp., Armonk, NY). The cardiorespiratory fitness measures and FSS questionnaire composite scores were compared using a paired sample t-test, while a Wilcoxon sign ranked test was used to analyze the FSS individual measurement items. Significance was set at $p < 0.05$ (one-tailed). The analyses met the assumptions for one-tailed significance in that 1) previous work has indicated that aerobic exercise training improves cardiorespiratory fitness and fatigue severity in the general population without biological plausibility for it resulting in a decrement in patients with TBI, and 2) the directional hypotheses were determined a priori. Data are presented as mean $\pm$ one standard deviation (SD).

RESULTS

A description of the subjects that participated in this study is provided in Table 1. On average, subjects were 32.9 ± 6.5 years of age, with a body mass index of 23.8 ± 4.4 kg/m². Four of the 10 subjects were male, and the average time since injury was 6.6 ± 6.8 years. Injury severity was classified by VA/DoD Clinical Practice Guidelines^{52,53} and was mild in 50% of the subjects, moderate in 40%, and severe in 10%. The cause of injury was primarily due to falls (7 subjects), followed by motor vehicle accidents (2 subjects) and pedestrian-motor vehicle accident (1 subject).

A summary of the exercise training sessions for all subjects is provided in Table 2. There was a high rate of adherence for the training sessions ($92.5 \pm 4.2\%$) with subjects averaging $1,005 \pm 38$ minutes of total aerobic exercise time over the course of 12 weeks. The average training HR of 155 ± 7 beats/minute was equivalent to $78 \pm 2\%$ of subjects' HRR, which lies at the upper end of the established target HR range of 70 to 80 % HRR. The percent of total time subjects spent within or above the target HR range was $98.7 \pm 2.1\%$. Subjects began the first week of exercise at a power output equivalent to $27 \pm 9\%$ of the peak work rate achieved on the baseline CPET. By the end of the training period, subjects were at $47 \pm 9\%$ of their baseline peak work rate. The reported perceived exertion during exercise using the Borg Category-Ratio scale was 4.3 ± 1.4 , which transforms to a rating of 14.3 ± 2.3 on the original Borg Rating of Perceived Exertion scale (6 – 20 scale),⁵⁴ and was consistent with a vigorous exercise intensity.²⁵

Results of the CPET obtained before and after aerobic exercise training are summarized in Table 3. All subjects demonstrated sufficient effort during the CPET¹³ and peak VO₂ appeared to approach a physiological maximum as evidenced by an average RER of >1.3 at both pre- and post-training CPET. After training, a significant increase ($p < 0.01$) in peak

VO₂ of $9 \pm 7\%$ was observed. Subjects were able to exercise significantly longer ($p < 0.01$) on the treadmill and at a significantly higher ($p < 0.01$) peak work rate (WR) compared to baseline. At the anaerobic threshold, VO₂, WR and time at which AT occurred were also greater ($p < 0.01$) after training over baseline. Expressed as a percent of peak VO₂, the AT was higher ($p < 0.01$) following training compared to baseline ($56.5 \pm 5.9\%$ vs. $51.1 \pm 6.5\%$). No difference was found in peak HR attained during the pre- and post-training CPET. The findings from the CPET are also described in Figure 1 where the pre- and post-training responses for a representative subject are shown. There were no serious adverse events during the CPET or aerobic exercise training sessions. Several subjects experienced minor and reversible self-limiting musculoskeletal issues such as muscle soreness and mild medial tibial stress syndrome (shin splints). Musculoskeletal injuries are among the probable risks associated with exercise⁸ and have a prevalence rate of approximately 15% in sedentary individuals.⁵⁵

The pre- and post- training FSS composite score for each subject is shown in Figure 2, with median scores for the individual FSS measurement items in Figure 3. A significantly lower FSS composite score was observed following aerobic exercise training (4.1 ± 2.1 vs. 3.2 ± 1.9 ; $p = 0.029$; Figure 2). At baseline, only 4 of the 10 subjects had composite scores ≥ 4 (Figure 2). This would indicate that for most of the subjects, fatigue was not severe enough to interfere with their physical and social functioning. However, examination of the 9 individual items on the FSS at baseline revealed median scores ≥ 4 on 6 items that mainly corresponded to physical functioning (Figure 3). At least half of the subjects regarded fatigue to be severe with respect to those 6 measurement items. After training, only one of the FSS items had a median score ≥ 4 , and fatigue was reported to be less severe ($p < 0.05$) relative to 4 of the 9 FSS items (Figure 3).

DISCUSSION

Individuals with TBI were shown to gain cardiorespiratory benefits from a supervised vigorous aerobic exercise training program. Significant improvements were observed in overall cardiorespiratory fitness, as indicated by increases in peak VO₂, work rate and time to volitional exhaustion. The anaerobic threshold offers a physiological index of fatigability, and the increased VO₂, work rate and exercise time at the anaerobic threshold indicates that fatigability was significantly reduced after aerobic exercise training in these individuals with TBI. Consistent with the improvements in CPET performance, subjects also reported significant reductions in fatigue severity following exercise training. Post-training decreases in 4 of the 9 FSS items suggested that the aerobic exercise training regimen may have been effective at reversing self-reported, activity-related fatigue in these subjects. Overall, the results of this study indicated that these individuals with TBI benefited significantly from participation in vigorous aerobic exercise training.

Only a few studies have examined cardiorespiratory fitness and aerobic exercise training in individuals with TBI.⁵⁶ Differences in exercise training methods and outcome variables make direct comparisons of these studies with the present study somewhat difficult. Several studies inferred cardiorespiratory fitness from changes in work rate during a peak³³ or sub-maximal^{35,36} exercise test. Conversely, among the 4 studies that directly measured peak

VO₂, aerobic exercise was only a component of circuit exercise training in these studies.^{14,31,32,34} The mode of exercise training varied greatly among prior studies and included multiple combined modes,^{14,31,32,34} cycling,^{33,35} and aquatic³⁶ exercise. A wide range of training intensities have also been used such as low intensity,³⁴ 50 – 70% HRR,^{32,36} 60 – 80% predicted maximal HR,^{14,33,35} and 70% estimated maximal VO₂.³¹ Previous studies have used aerobic training frequencies of 2 sessions,³⁴ 3 sessions^{31–33,35,36} and 5 sessions¹⁴ per week, and duration of aerobic exercise of 15–30 minutes,^{14,32–35} 45 minutes³¹ and 60 minutes.³⁶ Training programs have been conducted over 8 weeks,^{33,36} 12 weeks,^{14,32,33,35} and 16 weeks.^{31,34} The present study used the highest intensity of exercise among all the studies (vigorous at 70 – 80% HRR²⁵), sustained for 30 minutes, 3 times a week, which is consistent with published guidelines for frequency, duration and intensity of aerobic exercise for improved cardiorespiratory fitness in the general population.²⁵

Despite methodological differences among the previous studies, 5 of the 7 studies reported an improvement in cardiorespiratory fitness.^{14,31–33,36} Although the findings of Mossberg et al³⁴ were inconsistent with these reports, it was acknowledged that the exercise training performed by the subjects in that study may not have been of sufficient intensity to produce an aerobic training adaptation. Bateman et al³⁵ showed a significant increase in work rate during sub-maximal exercise testing in their training group that consisted of patients with various causes of brain injury. However, a sub-analysis of only the patients with TBI (28% of all patients) failed to reflect the overall improvement.³⁷ The reported total time of participation in aerobic exercise for all subjects in the Bateman³⁵ study was 552 minutes over 12 weeks with 56% of the time spent within or above the training target heart rate. Compared to the present study, this was 42 – 45% less exercise time performed at a lighter intensity over the same time period. These studies suggest that improvements in cardiorespiratory fitness are possible in individuals with TBI when exercise is of sufficient intensity and duration⁵⁶ to induce an aerobic effect. Results of the current study suggest that exercise of higher intensity may be more effective for improving cardiorespiratory fitness in individuals with TBI, particularly when sustained at the intended target heart rate range for a given period of time.

The improvements in cardiorespiratory fitness in the present study suggest that individuals with TBI adapt similarly to exercise training as those in the general population. Endurance training has been widely shown to improve peak VO₂ across age groups^{57–59} and various disease states.^{26–30} Subjects in this study demonstrated an average increase in peak VO₂ of 9% which is on par with the general population for this frequency, duration and intensity of exercise (9 to 12%).⁵⁸ An increase in the anaerobic threshold is also generally observed with aerobic exercise training⁶⁰ and is an established marker of decreased fatigability and improved endurance capacity. Expressed as an increase in relative VO₂, the improvement in the anaerobic threshold was 21 ± 14 % over baseline following training. The effect size for an increase in absolute VO₂ was 1.5, which was similar to that reported by Londeree⁶⁰ in a meta-analysis for endurance training in healthy individuals at comparable exercise intensities to the present study (weighted mean effect size of 1.6).

Training-induced increases in peak WR and WR at the anaerobic threshold may be associated with improved physical activity tolerance, and increased capacity to sustain

activities at a given work rate with less fatigue. One MET is equal to a VO_2 of 3.5 ml/kg/min. In this study, subjects demonstrated an approximate 1 MET improvement in both peak VO_2 and anaerobic threshold. An improvement in cardiorespiratory capacity of just 1 MET increases the threshold for the onset of activity-induced fatigue from that associated with lower energy demands, such as vacuuming, to significantly higher energy demands such as brisk walking at 3.5 mph.⁶¹ A 1-MET improvement has also been associated with a 12% improvement in survival in adult males.⁶²

The FSS composite score decreased by 16% and was lower than the cut-off score of 4 suggesting subjects as a group were no longer reporting severe fatigue following exercise training. Six of the 9 FSS measurement items had median scores ≤ 4 , indicating that specific aspects of fatigue primarily with respect to physical functioning were perceived to be disruptive at baseline. After training, only one of these items indicated that fatigue was problematic relative to the aspect measured. These data suggest that in individuals with TBI, aerobic exercise training reduced select aspects of fatigue, thereby improving their ability to function physically and socially.

All subjects in the current study were able to tolerate the exercise training regimen as demonstrated by the high rate of adherence and sustained vigorous exercise intensity (Table 2). Even though the training intensity was determined relative to subjects' individual capacities, their higher level of cardiorespiratory fitness and lack of gait or mobility impairments may have facilitated the overall capacity to sustain the vigorous training regimen. It remains unknown if individuals with lower cardiorespiratory fitness levels and mobility deficits would be able to sustain an equally demanding regimen, even if it were prescribed according to their individual capacities. In this study, the two least physically fit subjects (baseline peak $\text{VO}_2 < 30$ ml/min/kg) were indeed able to maintain exercise at the upper range of the target HR. Individuals with lower levels of fitness are reported to gain as much improvement from low intensity exercise as from higher intensity exercise.⁶³ However, high exercise intensity has the advantage of being associated with overall lower mortality rates⁶⁴ and lower risk of cardiovascular disease.⁶⁵ While the objective in this study was 30 minutes of continuous exercise at target heart rate, it has been previously shown that intermittent exercise (i.e. three exercise bouts of 10 minutes performed within a day at the same intensity) resulted in similar cardiorespiratory fitness benefits as a continuous exercise training protocol.⁶⁶ This may be an attractive alternative for individuals that are severely deconditioned as shorter bouts of exercise may be perceived as less overwhelming and physically easier to complete.⁶⁷

A limitation of the current study is that the subjects were able to walk unassisted on the treadmill and may not have been as deconditioned as the typical patient with TBI. Thus, our results might understate the potential impact of this intervention. Previous studies reported that peak VO_2 in individuals with TBI was approximately 75% of sedentary normal controls.^{14,15} Subjects in the current study had a peak VO_2 that was $101 \pm 7\%$ of their predicted level (for sedentary populations based on height, weight, age and gender⁴³), and would not be considered to have poor or impaired cardiorespiratory fitness. In general, gains in peak VO_2 are inversely related to pre-training fitness levels and this relationship is independent of training intensity, frequency and duration.⁵⁸ While the current study showed

a significant improvement in cardiorespiratory fitness in ambulatory individuals with TBI of normal baseline cardiorespiratory fitness, it is possible that even greater gains may occur in individuals whose cardiorespiratory fitness is poor at baseline. However, it is unknown how these results will extend to individuals with gait impairments or those that are unable to walk independently on the treadmill.

Another potential limitation of this study is the non-randomized design and the lack of a control arm. This would have more specific implications for measuring changes in self-reported fatigue. However, subjects were considered to be past the acute phase of their injury, so spontaneous changes in cardiovascular status were unlikely. Although this study had a small sample size, these findings demonstrate the strong effect of a well-executed supervised aerobic exercise training program in individuals with TBI. Subjects enrolled in this study were adults between 21 and 45 years of age with a broad range of time post-injury, ranging from 6 months to 17 years. Therefore, results from this study cannot be extended to older adults and adolescents, or those in the acute or sub-acute phase of recovery.

CONCLUSION

This study described improvements in cardiorespiratory fitness and fatigability based on actual pulmonary gas exchange and treadmill performance measures, following aerobic exercise training in individuals with TBI. The training regimen was of vigorous intensity and conformed to established guidelines for training in the general population. A similar mode of exercise training and testing was used. The subjects in this study demonstrated improvements in cardiorespiratory fitness similar to those expected in the general population. Improvements in cardiorespiratory fitness were also concomitant with reduced self-reported fatigue severity. Regular participation in supervised aerobic exercise training was found to be feasible, without serious adverse events, and of potential benefit for individuals who have TBI.

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Figure 1.

Results of the cardiopulmonary exercise test (CPET) for a representative subject. Data points are shown pre (○) and post (●) aerobic exercise training. The main findings were that the post test showed greater peak VO_2 , higher peak work rate (WR), extended time to volitional exhaustion, increased VO_2 at the anaerobic threshold (AT), and greater WR and time at AT compared to the pre test.

Figure 2.

The FSS composite score for each subject at pre- and post-aerobic exercise training () with average scores shown (mean $\pm$ SD; ■). * Significantly ($p < 0.05$) different from pre-training.

Figure 3. Median scores to the 9 measurement items on the Fatigue Severity Scale (FSS) Questionnaire. Scores 4 indicates “Severe fatigue” and is demarcated as a dashed line. Mean ($\pm$ SD) at pre- and post-aerobic exercise training is shown with p-values.

Table 1

Subject Characteristics

Subject	Gender	Age (years)	TBI Severity	Cause of Injury	Time Since Injury (years)
1	Male	34	Severe	MVA	17.2
2	Female	32	Moderate	Fall	2.1
3	Male	30	Mild	Fall	3.7
4	Male	35	Moderate	Fall	1.0
5	Female	42	Moderate	Fall	1.1
6	Female	29	Moderate	Fall	13.8
7	Female	34	Mild	MVA	9.9
8	Male	23	Mild	Fall	16.0*
9	Female	44	Mild	Fall	1.1
10	Female	26	Mild	Pedestrian-MVA	0.6

Abbreviations: MVA, motor-vehicle accident.

Note: TBI severity as defined by VA/DoD Clinical Practice Guidelines^{52,53}.

* Participant met the inclusion criteria, however had multiple head injuries that were between 4 months and 16 years prior to enrollment. All injuries were mild in severity and sports-related. Index injury used is listed here.

Table 2

Summary of the Aerobic Exercise Training Sessions

Subject	# of Sessions	Training HR Range, (beats/min)		Average Training HR, (beats/min)	% HRR	Week 1 WR, (W)	Highest WR in final 2 weeks, (W)	Average Perceived Exertion
		70% HRR	80% HRR					
1	33	150	161	160	79	34	207	7.6
2	34	147	158	158	80	74	104	4.0
3	32	144	156	152	77	134	231	2.7
4	33	139	149	148	79	145	226	4.4
5	35	142	154	154	80	67	118	3.0
6	34	157	166	161	74	62	133	4.4
7	32	143	153	150	77	82	133	3.0
8	36	140	150	144	74	124	186	5.4
9	33	148	159	158	79	82	115	4.2
10	31	155	167	166	79	46	69	4.2
Mean	33	147	157	155	78	85	152	4.3
SD	2	6	6	7	2	37	56	1.4

Abbreviations: HR, heart rate; HRR, heart rate reserve; WR, work rate.

Note: Perceived Exertion using Borg's Category Ratio Scale (0 to 10 scale).

Table 3

Results of the Cardiopulmonary Exercise Test (CPET) Performed Pre- and Post-Aerobic Exercise Training

CPET Variables	Pre	Post		p-value
Peak Exercise Measures				
Treadmill Time (min)	16.4 (1.9)	17.8 (2.4)	+1.4 (0.8)	< 0.001
VO ₂ (ml/kg/min)	37.1 (8.2)	40.2 (8.1)	+3.1 (2.4)	0.002
WR (W)	324 (90)	383 (104)	+59 (48)	0.002
HR (beats/min)	177 (7)	176 (11)	-1 (9)	0.369
RER	1.35 (0.1)	1.35 (0.1)	0 (0.1)	0.448
Sub-maximal Exercise Measures (at the anaerobic threshold)				
Treadmill Time (min)	9.3 (1.5)	11.0 (1.5)	+1.8 (1.1)	< 0.001
VO ₂ (ml/kg/min)	18.9 (4.1)	22.5 (3.5)	+3.6 (2.1)	< 0.001
WR (W)	123 (28)	160 (41)	+37 (39)	0.007

Abbreviations: VO₂, oxygen consumption; WR, work rate; HR, heart rate; RER, respiratory exchange ratio