Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2015;96:754-9

BRIEF REPORT

# Improved Cognitive Performance Following Aerobic Exercise Training in People With Traumatic Brain Injury

Lisa M. Chin, PhD,[a,b] Randall Eugene Keyser, PhD,[a,b] John Dsurney, PhD,[b,c] Leighton Chan, MD, MPH[b,c]

*From the [a]Department of Rehabilitation Science, George Mason University, Fairfax, VA; [b]Rehabilitation Medicine Department, National Institutes of Health, Clinical Center, Bethesda, MD; and [c]Center for Neuroscience and Regenerative Medicine, Bethesda, MD.*

**Abstract**

**Objective:** To examine cognitive function in individuals with traumatic brain injury (TBI) prior to and after participation in an aerobic exercise training program.

**Design:** Pre-post intervention study.

**Setting:** Medical research center.

**Participants:** Volunteer sample of individuals (N=7) (age, 33.3±7.9y) with chronic nonpenetrating TBI (injury severity: 3=mild, 4=moderate; time since most current injury: 4.0±5.5y) who were ambulatory.

**Intervention:** Twelve weeks of supervised vigorous aerobic exercise training performed 3 times a week for 30 minutes on a treadmill.

**Main Outcome Measures:** Cognitive function was assessed using the Trail Making Test Part A (TMT-A), Trail Making Test Part B (TMT-B), and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Sleep quality and depression were measured with the Pittsburgh Sleep Quality Index (PSQI) and Beck Depression Inventory, version 2 (BDI-II). Indices of cardiorespiratory fitness were used to examine the relation between improvements in cognitive function and cardiorespiratory fitness.

**Results:** After training, improvements in cognitive function were observed with greater scores on the TMT-A (10.3±6.8; $P$=.007), TMT-B (9.6±7.0; $P$=.011), and RBANS total scale (13.3±9.3; $P$=.009). No changes were observed in measures of the PSQI and BDI-II. The magnitude of cognitive improvements was also strongly related to the gains in cardiorespiratory fitness.

**Conclusions:** These findings suggest that vigorous aerobic exercise training may improve specific aspects of cognitive function in individuals with TBI and cardiorespiratory fitness gains may be a determinant of these improvements.

Archives of Physical Medicine and Rehabilitation 2015;96:754-9



Cognitive impairments among individuals who have sustained a traumatic brain injury (TBI) can have profound effects on quality of life,[1] psychosocial outcomes,[2] family functioning,[3] and employment status.[4,5] More than 50% of patients report cognitive problems several years after a major head injury,[6] and long-term cognitive dysfunction may persist even in patients with mild TBI.[7]

In recent years, aerobic exercise has gained attention for its neuroprotective effects and has been studied as an intervention in healthy older adults[8,9] and in those with cognitive impairments[10-12] and other neurologic disorders.[13] Aerobic exercise is associated with various physiological adaptations that have positive effects on cortical function, including angiogenesis and neurogenesis.[14] Evidence from animal studies suggests that cognitive deficits associated with TBI can be improved after exercise.[15-19] In rodents with experimentally induced TBI, better performance on the Morris water maze[15-18] and step-down avoidance task[19] was observed in animals that were exercised compared to being sedentary. This suggests that both learning and memory improve with exercise. The expression of the brain-derived neurotrophic factor was also found to be increased in the hippocampus,[15] which is an area associated with memory and learning.[20]

Supported by the Center for Neuroscience and Regenerative Medicine (grant no. G192HI-H) and the National Institutes of Health Clinical Center (rehabilitation medicine department intramural funds).

Disclosures: none.

0003-9993/14/$36 - see front matter © 2015 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2014.11.009

Despite encouraging findings in animal models, exercise has not been widely studied in individuals with TBI. To our knowledge, only a few prior studies have examined cognitive changes in patients with TBI after exercise training. These studies have found cognitive performance to either improve[21,22] or remain unchanged.[23] However, exercise per se was not the primary focus of the intervention, and vastly different components of exercise were used in these studies. This included exercise in a virtual environment,[21] at home with an audiotape,[23] or captured by self-reported exercise habits.[22] The varied exercise interventions used by previous studies make comparison and interpretation of the findings problematic.

We have previously demonstrated that individuals with chronic nonpenetrating TBI were able to perform vigorous aerobic exercise training and obtain cardiorespiratory fitness benefits with attenuated self-reported fatigue.[24] In the current study, a consecutive subset of these subjects performed neuropsychological testing prior to and after a vigorous 12-week aerobic exercise program. It was hypothesized that cognitive function would be improved in individuals with TBI after aerobic exercise training.

# Methods

Written consent was obtained from all subjects prior to study participation. This study was approved by the institutional review boards of all participating institutions and registered on the clinicaltrials.gov website (Clinical Trial Registration No.: NCT01294332).

## Participants

The inclusion/exclusion criteria for subject enrollment have been reported previously.[24] Briefly, subjects had a nonpenetrating head injury of $\geq$6 months, were ambulatory, and had no present contraindications to exercise. Subjects were also sedentary prior to enrollment and had not participated in regular moderate to vigorous exercise. A physician specializing in TBI performed the history and physical examination to determine subject eligibility and classification of TBI severity using Department of Veterans Affairs/Department of Defense guidelines.[25]

## Study design

Subjects completed neuropsychological assessments and self-report questionnaires prior to performing a treadmill cardiopulmonary exercise test (CPET) to volitional exhaustion. The CPET was performed on a treadmill as described previously.[24] After baseline assessments, subjects participated in a supervised aerobic exercise training program for 12 weeks.[24] Sessions were conducted on a treadmill 3 times a week, with subjects exercising at their target training heart rate range (70%−80% heart rate reserve) for 30 minutes. All baseline assessments were repeated after completion of the training program.

Measures of cardiorespiratory fitness, such as peak oxygen consumption per unit time ($\dot{V}O_2$), peak work rate (WR), and $\dot{V}O_2$ at the anaerobic threshold (AT), were collected during the CPET as described elsewhere.[24] The neuropsychological assessments performed included the Trail Making Test[26] and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).[27] The Trail Making Test Part A (TMT-A) measures speed of information processing, and the Trail Making Test Part B (TMT-B) measures select aspects of executive functioning.[28] Demographically corrected T scores were obtained and adjusted based on age, sex, and education level.[29] The RBANS is a brief screening test that evaluates abilities across 5 specific cognitive domains. A total scale index score is derived from the domain-specific index scores, and higher scores are indicative of better performance. The Pittsburgh Sleep Quality Index[30] was used to measure sleep quality, and a score >5 was used as a cutoff to indicate significant sleep disturbance.[30] The Beck Depression Inventory, version 2[31] was used to measure the severity of symptoms related to depression. The presence of depression was indicated by cutoff scores of 19 for those with mild TBI and 35 for moderate to severe TBI.[32]

## Statistical analysis

Data were analyzed using SPSS version 21.[a] The neuropsychological assessments, cardiorespiratory fitness measures, and questionnaires were compared using a paired-sample *t* test. A Pearson correlation was also performed between the main outcomes of the CPET and neuropsychological assessments. Significance was set at $P<.05$. Data are presented as mean ± 1 SD.

# Results

Nine subjects enrolled in the study and performed baseline neuropsychological testing prior to beginning the exercise program. As previously reported,[24] 2 of the subjects were administratively withdrawn from the study because of pregnancy (n=1) and for noncompliance (n=1). Complete data were available and analyzed for the 7 remaining subjects.

Characteristics of the subjects that completed participation are shown in table 1. Subjects demonstrated high adherence to the 12-week training program (93%±5% attendance) and were able to average between 74% and 80% of their target training heart rate (78%±3%). Exercise was performed at or above their target heart rate range for 99%±2% of the aerobic exercise time. Because of personal schedules and highly flexible session availabilities, subjects rarely exercised together with other subjects in this study. The supervised nature of the program resulted in significant interaction with research personnel. There were no serious adverse events reported during this study; however, minor lower-limb musculoskeletal injuries were observed, which was expected in sedentary individuals participating in an exercise program.[33] Cardiorespiratory fitness was improved after the aerobic exercise training program, indicated by greater peak $\dot{V}O_2$ (2.2±2.3mL/min/kg; $P=.044$), peak WR (72±47W; $P=.007$), and $\dot{V}O_2$ at the AT (2.8±1.8mL/min/kg; $P=.006$).

Table 2 displays results of the neuropsychological assessments and self-report questionnaires, with correlations for changes in cognitive outcomes and indices of cardiorespiratory fitness shown in figure 1. The standardized T scores for the Trail Making Test were significantly higher after exercise training, with improvements of 25%±18% ($P=.007$) and 26%±24% ($P=.001$)

***List of abbreviations:***

| | |
|---|---|
| **AT** | **anaerobic threshold** |
| **CPET** | **cardiopulmonary exercise test** |
| **RBANS** | **Repeatable Battery for the Assessment of Neuropsychological Status** |
| **TBI** | **traumatic brain injury** |
| **TMT-A** | **Trail Making Test Part A** |
| **TMT-B** | **Trail Making Test Part B** |
| **$\dot{V}O_2$** | **oxygen consumption per unit time** |
| **WR** | **work rate** |