CARDIORESPIRATORY FITNESS IS ASSOCIATED WITH INDICES OF NEUROCOGNITIVE FUNCTION IN ADULTS

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ABSTRACT

Koehler RJ, Martens DM, Henderson JK. Cardiorespiratory Fitness is Associated With Indices of Neurocognitive Function in Adults. Journal of Undergraduate Kinesiology Research 2007;3(1):62-71. Purpose: Much is known of the relationship between physical fitness and health in aging adults. However, less is known about the relationship between cardiorespiratory fitness and cognitive functioning as the human body ages. The purpose of our study was to see how cardiorespiratory fitness correlates with cognitive functioning across a large age range. Methods: Our study consisted of 6 men and 7 women ranging from ages 20 to 60. Peak VO₂ levels were gathered using Viasys and MedGraphics equipment. Cognitive functioning was measured using ImPACT software. Statistical analysis was done using Statistical Package for the Social Sciences, Version 14.0 (SPSS, Inc, Chicago, IL) Pearson r was calculated to determine the correlation between cardiorespiratory fitness and composite neurocognitive scores (verbal memory, visual memory, visual motor speed, and reaction time) from the ImPACT testing software. Results: The correlation between cardiorespiratory fitness and composite neurocognitive scores were significant (p < 0.05) at 0.7039, 0.7954, 0.8276, and -0.9218 for verbal memory, visual memory, visual motor speed, and reaction time, respectively. However, a significant correlation was also observed between cardiorespiratory fitness and age (-0.9507). Conclusion: The results of this study demonstrate that neurocognitive function is associated with aerobic fitness. However, this association was shown to be age-dependent, suggesting age rather than cardiorespiratory fitness level as a predictor of neurocognitive ability.

Key Words: Memory, Symbol Match, Reaction Time, Processing, Psychology, Aging, Mental Health, Exercise, Maximal Oxygen Uptake
INTRODUCTION
As the human body ages, its functional capacity can become diminished from chronic neglect or abuse throughout a lifetime (1). The human brain structure begins to decline in the third decade of life (2-3). The frontal, parietal, and temporal lobes of the brain appear to be the most susceptible to this deterioration (3). These regions have been shown to be associated with working memory, task switching, and inhibition of irrelevant information (4,5). As more people continue to live longer, prevention and care for these conditions of “aging” should be of national interest (1).

Cognitive function can be assessed using Immediate Post-Concussion Assessment and Cognitive Testing software V.2005 (ImPACT Applications, Pittsburg, Pennsylvania). The software was designed after 10 years of University-based grant-supported research, and is currently the most widely utilized computerized concussion assessment software in the world (6). Computer-based tests of word discrimination, design matching, symbol matching, color matching, working memory, and visual processing speed provide an overview of cognitive function (6). These neurocognitive tests have been found to be both valid and accurate at measuring memory, processing speed, and reaction time in making return to play decisions in concussed athletes (6).

Physical inactivity has been linked to serious mental conditions such as schizophrenia, dementia, and Alzheimer’s disease (3). In a study of 10,308 middle-aged British civil servants, low levels of physical activity have been associated with poor performance on intelligence testing and poor cognitive functioning (3). In contrast, gray and white matter volume has been shown to increase in older adults exercising three days per week at moderate intensity for six months (4). In addition to physical activity, aerobic fitness alone has been correlated with cognitive preservation. In a cross sectional analysis of adults age 55-79, aerobic fitness levels were positively correlated to greater gray and white matter density maps using high-resolution Magnetic Resonance Images (MRI) (5). Moderate intensity aerobic exercise bouts of as little as 40 minutes have also been correlated to improved executive processing and short term memory immediately following exercise in young adults (7). These studies indicate that an inexpensive and effective treatment for many types of chronic mental disease may be a lifestyle intervention that includes an exercise prescription (1).

In animals, up regulation of neurotransmitters and neurotrophic factors release have been observed (8). In rats with abnormally low brain dopamine levels, exercise increased brain dopamine secretion through calcium/calmodulin-dependent synthesis (8). Exercise also increases circulating and brain levels of neurotrophic factor such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor (IGF-1) (8,9). IGF-1 appears to have a regulatory effect on BDNF, which has been shown to regulate dopaminergic and cholinergic neurotransmitters related to improved learning ability (4). In humans, initially high dopamine and BDNF levels have been associated with greater information retention and immediate learning success following intense exercise (9). While this evidence suggests a possible link between cognitive function and aerobic exercise, not all research has demonstrated a positive correlation.

A meta-analytic review found that aerobic fitness had a negative relationship to cognitive function when compared pre-post test (10). This study also determined that there is not a significant linear or curvilinear relationship between aerobic fitness and cognitive performance effect sizes in cross-sectional and posttest studies (10). In a study of recreational college athletes; verbal, delayed, and immediate recall memory were shown to be reduced by an average of 6-9 composite points immediately following the performance of a VO_{2max} test (11).

Evidence supports both a positive and negative correlation between aerobic fitness and cognitive function, with the majority suggesting a positive relationship (3-5,7-9). However, to the best of our
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knowledge, these previous studies have failed to test the relationship between maximal oxygen uptake and performance on a neurocognitive test battery. Therefore, the purpose of our study is to determine if there is an age-independent correlation between aerobic fitness measured by a VO$_2$peak test and cognitive function as assessed by ImPACT neurocognitive test battery. We hypothesize that improved neurocognitive function will be associated with higher levels of cardiorespiratory fitness independent of age.

METHODS

Subjects

Subjects consisted of 6 male and 7 female participants between 20 to 60 years of age. Subjects were recruited from an on-campus Community Fitness Program, upper division Kinesiology course, and word of mouth. Subjects were screened through the neurocognitive history questionnaire on the ImPACT software. Exclusion criterion included current or previous mental disorder, recent concussion, or an invalid test as defined by the ImPACT software (6). All subjects were required to sign a written informed consent form before participating in the study. The study was approved by the University Human Subjects Institutional Review Board.

Instrumentation

Aerobic fitness testing required a thermometer from Control Co. in Friendswood, TX (Serial No. 97218913) to calibrate temperature and a Swift Scientist Barometer was from Swift Instruments Incorporated in France to calibrate barometric pressure.

The Med Graphics Cardiopulmonary Diagnostic Systems Cart Cardio 2 (Model No. 790602-001R, Serial No. 140000033) and Gas Module (Model No. 762014-202R, Serial No. 132000098) from Medical Graphics Corporation in St. Paul, MN was used along with the Trackmaster treadmill by JAS (Model No. 215Ac, Serial No. 15777) made in Newton, KS to measure maximal oxygen uptake (VO$_2$peak) and ventilatory threshold. With the Med Graphics Cart we used the MedGraphics Cardiorespiratory Diagnostic System 3.0 liter Calibration System syringe (P/N 704001-003) to calibrate the Med Graphics Diagnostic Systems Cart Cardio 2.

We also use the Analyzer Assembly Vmax Encore 229C Metabolic Cart manufactured by Viasys Health Care Company in Palm Springs, California. The Woodway USA Treadmill (Model No. DESMO-S, Serial No. 8716105) from Waukesha, WI was also used to measure maximal oxygen uptake and ventilatory threshold. Also, the Swift Scientist Barometer was from Swift Instruments Incorporated in France COSMED Pulmonary Function Equipment 3-liter Calibration Syringe (Part n. C00600-01-11) from Rome, Italy was used to calibrate the Vmax Encore 229C Metabolic Cart manufactured by Viasys Health Care Company.

A Polar Heart Rate Monitor a1 from Polar Electro Incorporated in Woodbury, NY was used for accurately measuring heart rate during VO$_2$max testing. For the cognitive test the subjects will be using the Post-Concussion Assessment and Cognitive testing (ImPACT) V.2005 (ImPACT Applications, Pittsburg, Pennsylvania).

Procedures

Testing was conducted on 2 non-consecutive days. The cognitive test was administered at least 3 days post VO$_2$peak testing as previous research indicated that maximal testing depressed cognitive ability for 3 days (11).

For cognitive testing, the subjects were instructed to come well rested with high intensity activity at least 3 days prior. During this meeting the subjects were given a cognitive assessment with the
ImPACT software. ImPACT Tests was computer administered, and took approximately 45 minutes to 1 hour to complete. The first section assessed the subject’s neurological background. The second section consisted of 8 neurocognitive tests. The software is set up to take a baseline test that is then used following a concussion to determine if cognitive function has returned to normal. For this study, only baseline testing was done to generate memory, processing speed, and reaction time data. For further information on this software or detailed description of each test, please visit http://www.impacttest.com.

For the VO\textsubscript{2}peak test the subjects were instructed to come to the Exercise Physiology Lab (UWEC) well rested, hydrated, wearing comfortable clothing (e.g. Shorts, t-shirt, comfortable running shoes), and having no strenuous activity in the previous 24 hours. First we started out by having the subjects put on a Polar Heart Rate Monitor which was lightly saturated with water to conduct the electrical impulses from the heart more efficiently. Prior to beginning the test the valves on both gas tanks were opened to start the calibration, and calibration included entering the correct room temperature (in Celsius), and room humidity (in grams of H\textsubscript{2}O per kilogram of air), and barometric pressure (kg/m\textsuperscript{3}). We turned on the vacuum pump, purged with the pneumotach with the 3-liter syringe, and then started the gas analyzers using known and consistent gas concentrations. The protocol we used in this study was individualized, but with standard increment changes, which were manually controlled by the researchers to maintain control of the study on the treadmill. Subjects first started out at a brisk walk of 3.0 miles per hour, increasing by .5 miles per hour every 10 seconds for the first minute while at a 0 degree grade. After the first minute only grade was increased (unless subject wanted speed increased) keeping speed constant at 6 miles per hour. Once the subjects reach their set speed we increased the grade by 1 degree every minute until they gave maximal effort. Achievement of VO\textsubscript{2} max was validated by meeting 2-3 of the following: RPE of 10 (scaled range 1-10), plateau in O\textsubscript{2}, volitional fatigue, RER above 1.15, or reaching 90% age predicted heart rate.

Statistical Analyses
All analyses were performed using Statistical Package for the Social Sciences, Version 14.0 (SPSS, Inc, Chicago, IL). Measures of centrality and spread are presented as mean ± SD. Pearson \( r \) was calculated to determine the correlation between cardiorespiratory fitness and composite neurocognitive scores (verbal memory, visual memory, visual motor speed, and reaction time) from the ImPACT testing software. The probability of making a Type I error was set at \( p \leq 0.05 \) for all statistical analyses. Graphical analysis was performed using GraphPad Prism, Version 5.00 for Windows (GraphPad Software, San Diego, CA).

RESULTS
Characteristics of the studied subjects are presented in Table 1. The reaction time composite score was shown to have the strongest correlation to cardiorespiratory fitness of all neurocognitive tests analyzed with a negative Pearson correlation of -0.9218 (Figure 1). This correlation was found to be significant \((p<0.001)\). The verbal memory composite score was shown to have the weakest correlation at a Pearson correlation of 0.7039 (Figure 2). This was still found to be a significant positive correlation \((p=0.007)\). A positive correlation was also demonstrated between visual memory composite scores and cardiorespiratory fitness, with a Pearson correlation of 0.7954 (Figure 3). This correlation was found to be significant \((p=0.001)\). Visual motor speed composite scores were found to have a positive correlation to cardiorespiratory fitness levels at a Pearson correlation of 0.8276 (Figure 4). This was also considered to be significant \((p<0.001)\).

Analysis of neurocognitive testing as associated to age produced contrasting results to cardiorespiratory fitness. Comparing cardiorespiratory fitness to age resulted in a very significant negative Pearson correlation of -0.9507 \((p<0.0001)\) (Figure 5). Verbal memory, visual memory, and
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visual motor speed showed similar significant negative Pearson correlations of 0.7739, 0.8403, and 0.7747, respectively (p = 0.0019, 0.0003, 0.0019, respectively) (Figures 6-8). Reaction time showed a significant positive association with age, with a Pearson correlation of 0.9108 (p<0.0001) (Figure 9).

Table 1. Subject Characteristics

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight</th>
<th>VO₂peak</th>
<th>Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>31.23±14.12 years</td>
<td>78.04±18.65 kg</td>
<td>49.70±11.90 ml/kg/min</td>
<td>15±1.87 years</td>
</tr>
</tbody>
</table>

Figure 1. The correlation between aerobic fitness level and reaction time composite score.

Figure 2. The correlation between aerobic fitness level and verbal memory composite score.

Figure 3. The correlation between aerobic fitness level and visual memory composite score.

Figure 4. The correlation between aerobic fitness level and verbal memory composite score.
Figure 5. The correlation between aerobic fitness level and age.

$R^2 = 0.9039$

Figure 6. The correlation between verbal memory composite score and age.

$R^2 = 0.5989$

Figure 7. The correlation between visual memory composite score and age.

$R^2 = 0.7062$

Figure 8. The correlation between visual motor speed composition score to age.

$R^2 = 0.6002$

Figure 9. The correlation between reaction time composite score and age.

$R^2 = 0.8295$
DISCUSSION
Results from the current study demonstrated that neurocognitive performance was significantly associated with aerobic fitness levels. However, this correlation appeared to be primarily due to the age-related decline of the human body. When older subjects were removed from analysis of data, no significant associations were observed between cognitive function testing and cardiorespiratory fitness, data not presented. Our results support previous research that has identified decreases in cardiovascular and mental function related to age, but failed to support our hypothesis that improved neurocognitive function would be associated with cardiovascular fitness, independent of age (3-5,7-10,12-15). Our results also demonstrated visual motor speed and reaction time showed a stronger relationship to cardiorespiratory fitness rather than age. This association marginally supports research suggesting that aerobic training has a neuroprotective effect on the brain (3-5,12).

The physiological effects of aerobic training are well understood in most systems of the body. However, the mechanisms of how brain function is moderated by aerobic fitness remain to be fully understood. Recent human clinical trials have produced some interesting findings. In a meta-analytical review, aerobic fitness training influenced a variety of cognitive functions, most profoundly the executive control processes (12). The executive control processes include things such as planning, scheduling, working memory, inhibitory processes, and multitasking (12). These processes tend to show the greatest age-related declines in older adults (12).

In the present study, we demonstrated that improved executive control processes such as visual motor speed and reaction time were correlated to higher cardiorespiratory fitness levels (Figure 1,3). Reaction time was shown to have a negative correlation to cardiorespiratory fitness because lower scores on reaction time functions indicate improved levels of brain function. Reaction time is important for activities of daily living such as driving and preventing falls, and improved or maintained function is important for overall quality of life.

It has also been demonstrated that individuals who continue to work or exercise between the 62-70 years of age have improved cerebral blood flow and do better on cognitive testing than sedentary retirees of the same age (3). This increased blood flow has been suggested as a potential mechanism for increased neuron proliferation, increased dendrite production, as well as a growth in brain capillary beds in subjects participating in aerobic training (3,5). These subjects were also shown to increase both gray and white matter in the prefrontal and temporal cortices, which have been reported to show most substantial age-related deterioration (5). The pre-frontal cortex is often associated with short term or working memory, while the temporal cortex is recognized as an important area for long term memory as is evidenced by atrophy in this region associated with Alzheimer’s disease.

The ImPACT testing software incorporates both immediate and delayed memory recall into the composite scores for verbal and visual memory (6). In our study, we were able to demonstrate that higher levels of cardiorespiratory fitness were positively correlated to improved verbal and visual memory function (Figures 2,4), as well as a decrease in reaction time (Figure 1). However, these results were also shown to be strongly correlated to age. These results, along with previous researcher, suggest that much is still unknown about how exercise promotes the cellular and molecular processes within the brain.

For ethical reasons, limited in vivo research has been conducted on human subjects with regard to the cellular and molecular effects of exercise on memory in the brain; however, extensive research has been carried out in animals (3,13-15). Many studies have focused on hippocampus, which is a structure located within the medial temporal lobe of the cerebral cortex (3). As previously stated, this
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region shows a significant decrease in cell size and number in patients suffering from Alzheimer’s disease, and has been associated with amnesia (3). In mice, exercise has been reported to induce neuron proliferation in both young and aged subjects (13). In exercising rats, levels of brain-derived neurotrophic factor (BDNF) were elevated in the hippocampus of running animals, and these elevated levels may have led to increased learning and neuron generation in exercising animals (14). BDNF appears to have an effect on long-term potentiation, a cellular model of memory, and exercise increases levels in both young and aged brains (14). It also appears that exercise-induced release of BDNF has a regulatory effect on brain neurotransmitters dopamine, serotonin, and acetylcholine that enhances cognition (3). Insulin-like growth factor I (IGF-I) has been reported to regulate BDNF expression and acts to mediate BDNF improvements in neuron proliferation and enhanced cognition (15). The results of these studies provide useful information that would not be possible to obtain in human subjects and suggest some possible mechanisms for how the age-related decline in mental ability observed in the current study could be improved with exercise.

LIMITATIONS
The sample size used in the current study was our biggest limitation. With only 13 subjects, establishment of significant correlations are marginal at best. Also our population was heavily weighted with college students, due to ease of testing (9 of 13 subjects between 20-24 years of age).

Using the ImPACT testing software might not have been the most accurate way to assess cognitive ability in all subjects. Research done on the validity and accuracy of the software has focused on athletes from elementary to college age. While normative data was available for college-age students, no such data was available for older adults in the study. The test is computer based and older subjects seemed to have found it more challenging, as they were not as familiar with computers as the current college students. ImPACT software accessibility was also limited to a general access lab that could not be optimally controlled (temperature, humidity, and ambient noise), so testing was conducted in a non-ideal environment.

We also experienced some difficulties in collecting aerobic fitness measurements. Due to equipment failure, we were forced to do testing on two different metabolic carts during this study. Also due to time constraints imposed by the equipment failure we used data collected from protocols that varied from the one described in the methods. While criterion for a valid test was still met, this may have affected the accuracy and reliability of our results.

CONCLUSIONS
The results of this study and other studies indicate that declines in cardiorespiratory fitness and cognitive ability are significantly associated with aging. The present study failed to demonstrate an association between aerobic fitness and cognitive ability independent of age. Reaction time and visual motor speed demonstrated a greater relationship to cardiorespiratory fitness rather than age. These results are encouraging, because they suggest another way that exercise may help maintain or improve cognitive function as the body ages. While this study failed support previous research on exercise and improved cognitive function, it is our recommendation that future research look at this correlation through a longitudinal study rather than in a cross sectional design. The small sample size used in the present study could also be expanded to include more subjects. Since physical activity alone has been shown to improve cognitive function, we also suggest future research examines the effects of resistance training and flexibility on cognitive function. Overall, cardiorespiratory fitness is essential for longevity and prevention of chronic disease. Improvements in cardiorespiratory fitness are beneficial to people of all ages, but can be especially beneficial as we age, as it tends to diminish some of the negative aspects of aging.
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