Sport-Related Concussion

Randomized Controlled Trial Evaluating Aerobic Training and Common Sport-Related Concussion Outcomes in Healthy Participants

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Context: Aerobic exercise interventions are increasingly being prescribed for concussion rehabilitation, but whether aerobic training protocols influence clinical concussion diagnosis and management assessments is unknown.

Objective: To investigate the effects of a brief aerobic exercise intervention on clinical concussion outcomes in healthy, active participants.

Design: Randomized controlled clinical trial.

Setting: Laboratory.

Patients or Other Participants: Healthy (uninjured) participants (n = 40) who exercised ≥3 times/week.

Intervention(s): Participants were randomized into the acute concussion therapy intervention (ACTIVE) training or nontraining group. All participants completed symptom, cognitive, balance, and vision assessments during 2 test sessions approximately 14 days apart. Participants randomized to ACTIVE training completed six 30-minute exercise sessions that progressed from 60% to 80% of individualized maximal oxygen consumption (\(\dot{V}O_{2\text{max}}\)) across test sessions, while the nontraining group received no intervention.

Main Outcome Measure(s): The CNS Vital Signs standardized scores, Vestibular/Ocular Motor Screening near-point convergence distance (cm), and Graded Symptom Checklist, Balance Error Scoring System, and Standardized Assessment of Concussion total scores.

Results: An interaction effect was found for total symptom score (\(P = .01\)); the intervention group had improved symptom scores between sessions (session 1: 5.1 ± 5.8; session 2: 1.9 ± 3.6). Cognitive flexibility, executive functioning, reasoning, and total symptom score outcomes were better but composite memory, verbal memory, and near-point convergence distance scores were worse at the second session (all \(P\) values < .05). However, few changes exceeded the 80% reliable change indices calculated for this study, and effect sizes were generally small to negligible.

Conclusions: A brief aerobic training protocol had few meaningful effects on clinical concussion assessment in healthy participants, suggesting that current concussion-diagnostic and -assessment tools remain clinically stable in response to aerobic exercise training. This provides normative data for future researchers, who should further evaluate the effect of ACTIVE training on clinical outcomes among concussed populations.

Trial Registration Number: ClinicalTrials.gov: NCT02872480

Key Words: exercise, symptoms, balance, cognition, vision, mild traumatic brain injuries

Key Points

- Short-term aerobic training did not alter clinical concussion assessments in clinically significant ways among healthy participants.
- Clinical concussion assessments were susceptible to learning effects over a 2-week interval; computerized neuropsychological testing showed the largest effects.
- Clinicians can interpret scores from clinical concussion assessments as currently advised, regardless of whether a patient has undergone aerobic exercise therapy.

Sport-related concussions (SRCs) are among the most common form of traumatic brain injury\(^1\) and account for approximately 5% of all injuries reported in National Collegiate Athletic Association athletes.\(^2\) Current SRC diagnosis and management is centered on a clinical evaluation by an experienced medical provider, which includes symptom, balance, and cognitive testing.\(^3\) Best-practice guidelines\(^4\) have previously advocated for physical and cognitive rest until symptom resolution, with most concussion-related deficits resolving within 7 to 10 days. However, a small but significant minority of individuals fail to fully recover with rest alone and show persistent...
concussive deficits for weeks or months after injury. Experts' recommendations are shifting toward more active recovery strategies in hopes of improving outcomes and mitigating persistent concussive dysfunction.

Aerobic exercise is a novel SRC rehabilitation method. Previous authors have reported mixed results when evaluating symptom changes immediately after a single exercise bout in concussed cohorts, with some describing increased symptoms and others finding decreased emotional or cognitive symptoms postexercise. The literature is more conclusive for sustained aerobic exercise training, showing decreased symptom scores after exercise interventions compared with either rest or placebo (ie, stretching) protocols.

Previous SRC rehabilitation studies focused mainly on symptom outcomes, and little information exists regarding the effect of exercise interventions on other recovery domains after concussion. Some evidence supports the positive effects of aerobic training on balance, cognitive, and mood outcomes. Yet these studies were often limited by long time intervals between injury and exercise onset, and recent international guidelines supported earlier intervention after concussion.

As exercise training interventions evolve and shift toward more acute implementation after concussion, a critical first step is to understand how these interventions may affect clinical assessments of healthy participants. In uninjured cohorts, somatic and fatigue-related symptoms increased postexercise, while cognitive and emotional symptoms decreased, particularly in female participants. Exercise intensity seemed to further complicate the relationship between concussion-like symptoms and physical activity in healthy participants, with more intense exercise resulting in an increased symptom burden. Acute exercise bouts negatively affected clinical balance outcomes, with Balance Error Scoring System (BESS) scores not returning to baseline until after at least 13 minutes of rest. Cognition appeared to be less influenced by acute exercise, with most cognitive domains showing no change after activity.

The effect of exercise on clinical visual assessments is unknown. To the best of our knowledge, no authors have evaluated how an aerobic training protocol designed to assess the effect of acute concussion therapy intervention (ACTIVE) training on clinical outcomes. Recreationally active participants were randomized into ACTIVE training (intervention) or nontraining (no-intervention) groups on study enrollment using a computer-generated randomization sequence with block sizes of 4.

All participants completed clinical concussion metrics and a maximal exercise-cycling protocol (Lode, Groningen, The Netherlands) at 2 test sessions approximately 14 days apart in a controlled laboratory setting. An orientation session was provided to familiarize participants with the cycling protocol and equipment. After a brief warm-up, the maximal exercise test began at 50 W; intensity was increased by 50 W for the first 2 stages and by 30 W every stage thereafter. Each stage lasted for 2 minutes for the first 10 minutes, followed by 1-minute stages until volitional exhaustion.

The ACTIVE training participants completed six 30-minute training bouts between test sessions, with a warm-up and cool-down (3 minutes each) provided. Training intensity was progressive, with the first session starting at 60% of maximal oxygen consumption (V\textsubscript{O\text{\textsubscript{2max}}}) achieved during the first maximal exercise test and increasing until the final session, conducted at 80% of V\textsubscript{O\text{\textsubscript{2max}}}. Oxygen consumption levels were checked periodically (5-, 15-, and 25-minute marks) during training.

METHODS

Participants

A convenience sample of university students and staff between the ages of 18 and 30 years who participated in at least 30 minutes of physical activity, 3 or more days per week, was recruited for this study. Volunteers were excluded if they self-reported a diagnosed head injury within the past year, had any lower extremity injury that would prevent them from stationary cycling or balancing on 1 leg, or used recreational drugs. They were also excluded if they had any cardiovascular abnormalities incompatible with maximal exercise testing, which were evaluated using an electrocardiogram, the Physical Activity Readiness Questionnaire, and a health history questionnaire. A study physician reviewed all medical documents and provided medical clearance for all participants enrolled in the study. Informed consent was provided, and the study was approved by the institutional review board at the university (No. 15-2387).

Intervention

A parallel-groups, unblinded randomized controlled trial was designed to assess the effect of aerobic exercise training on clinical outcomes. Recreationally active participants were randomized into ACTIVE training (intervention) or nontraining (no-intervention) groups on study enrollment using a computer-generated randomization sequence with block sizes of 4.
ensure that the target exercise intensity was achieved. The maximal exercise and training protocols used in this study both aligned with the exercise prescription guidelines set forth by the American College of Sports Medicine. Nontraining group participants received no intervention between test sessions.

The lead author (E.F.T.), with more than 7 years of experience using the clinical concussion metrics in this study, supervised all sessions for all participants. The lead author was also responsible for generating the random allocation sequence, enrolling participants, and assigning participants to randomization arms. An experienced exercise physiologist (C.L.B., with more than 20 years of experience in exercise prescriptions in clinical populations) supervised the maximal exercise testing. The maximal exercise test and ACTIVE training protocols were developed by the lead author and the exercise physiologist. A progressive baseline assessment, exercise, training at 80% of the baseline assessment maximal, and 30-minute training sessions were all conducted in accordance with the current literature regarding exercise rehabilitation among SRC populations.

No changes to methods or participant recruitment were made throughout the trial. As we focused on healthy, recreationally active participants, no guidelines for prematurely stopping a trial were implemented.

Main Outcome Measures

The primary outcome measures for this study were changes in clinical concussion metrics. Because individuals with SRCs are known to display deficits in symptoms, cognition, balance, and vision, we chose widely used clinical metrics to evaluate these domains. All primary outcome measures were assessed at both time points and counterbalanced across sessions. Clinical outcomes were always assessed before the maximal exercise test to eliminate any potential for physical fatigue to confound the results.

The CNS Vital Signs. The CNS Vital Signs (CNS) is a 30-minute computerized neuropsychological assessment that evaluates attention span, working memory, response variability, problem solving, and reaction time. This assessment uses stimulus randomization when possible to reduce practice effects; on-screen instructions and short practice tests are provided. The CNS assessment produces standardized scores that scale outcomes into categories (very low, low, average, above average) based on an age-matched normative data set ranging from ages 8 to 90 years. Standardized scores for neurocognitive index, composite memory, verbal memory, visual memory, psychomotor speed, reaction time, complex attention, cognitive flexibility, processing speed, executive function, reasoning, simple attention, and motor speed were used in this study. The CNS assessment has previously been shown to be a valid neuropsychological evaluation and reliable over time.

Standardized Assessment of Concussion. The Standardized Assessment of Concussion (SAC) is a 5-minute sideline evaluation that tests orientation, immediate and delayed memory, and concentration. Orientation is evaluated by asking the participant the month, date, day of the week, year, and time. Immediate memory requires the participant to repeat a list of 5 words that has been read out loud 3 times. Concentration is tested first by repeating a number string, followed by stating the months of the year, both in reverse order. Delayed memory asks participants to recall as many of the 5 words from the immediate memory word list as possible. Total SAC score (out of 30) is the primary outcome of interest from this assessment. The SAC has been studied extensively in both healthy and concussed populations and is a reliable and sensitive tool.

Balance Error Scoring System. The BESS uses double-legged, nondominant single-legged, and tandem stances (nondominant leg in back) on 2 support conditions (firm and foam) to assess static balance. Each 20-second trial is performed with the eyes closed and hands on the hips. Participants are scored on errors committed during each trial (maximum errors per trial = 10), including removing hands from hips, opening eyes, stepping or falling, hip abduction or flexion >30°, lifting the forehead or heel off the testing surface, and remaining out of the test position for more than 5 seconds. Total BESS score (out of 60) over all 6 conditions was used in this study, with lower scores representing better balance. The BESS has high intrater reliability (intraclass correlation coefficient = 0.87–0.98) and is used extensively among collegiate populations.

Graded Symptom Checklist. The Graded Symptom Checklist (GSC) is a list of 27 common symptoms that may be experienced after an SRC. Participants are asked to rank each symptom on a Likert scale from 0 (symptom not present) to 6 (severe symptom presence) based on how they feel at the time of the assessment. Answers to the GSC are summed to create a total symptom score ranging from 0 to 162, with higher scores indicating cumulatively greater symptom severity. The GSC is similar to the symptom checklist used in the Sport Concussion Assessment Tool, but we included it in this study to evaluate additional signs and symptoms (loss of consciousness, personality changes, ringing in ears, seeing stars, and vacant stare). The GSC has previously been found to be a sensitive, valid, and reliable assessment tool.

Vestibular/Ocular Motor Screening. The Vestibular/Ocular Motor Screening (VOMS) is a 5-minute visual assessment that can be completed on the sideline or in clinical settings. The VOMS evaluates saccade, pursuit, convergence, vestibular-ocular reflex, and visual motion sensitivity domains. Participants are asked to self-report 4 symptoms (headache, nausea, dizziness, and fogginess) before and immediately after assessment of each visual domain. Near-point convergence distance (in centimeters) was the outcome of interest in this study. The VOMS is sensitive to SRC.

Statistical Analysis

All statistical analyses were completed in SAS (version 9.4; SAS Institute Inc, Cary, NC). Descriptive analyses were completed for demographic and primary outcomes. Intention-to-treat analyses were performed, meaning that we analyzed groups based on the randomization assigned on enrollment, regardless of adherence. Separate 2 (group) x 2 (session) analyses of variance were completed for all primary outcomes. Demographics and primary outcomes did not differ between groups at the first test session; therefore, no covariates were added to any statistical model.
We calculated means using a 10% Winsorized method to control for potential outliers without reducing the sample size. Tukey post hoc analyses were performed for all significant interactions, and adjusted P values are reported throughout to account for multiple comparisons. To assess if any changes had clinical relevance, we also calculated the 80% reliable change index (RCI) and effect sizes (Cohen d) for all outcomes. The RCIs were calculated using the methods of Moritz et al., which account for any practice or learning effects that may be present between sessions, and individual change scores were applied to the calculated RCIs. Because the majority of cells had fewer than 5 observations, Fisher exact tests were performed to determine if the proportion of individuals exceeding the reliable change was different between groups. The a priori α for all analyses was set to .05. Assuming a medium effect size, α = .05, power = 0.80, number of groups and time points = 2 each, and correlation among repeated measures = 0.49, the number of participants needed to adequately power all primary outcomes of interest was 36 (18 per group). Forty participants were recruited to account for potential attrition or missing data.

RESULTS

Participants were recruited from August 2016 to February 2017. Forty-five individuals were screened; 4 did not receive medical clearance from the study physician. One recruit who met the inclusion criteria declined participation. The remaining 40 participants were enrolled in the study, with no participants lost to follow-up (Figure). Participants were evenly randomized to the training and nontraining groups; no differences in baseline characteristics between groups were noted (Table 1). Eight intervention participants missed a total of 10 out of 120 scheduled training sessions (8.3%) because of inclement weather (n = 3), illness (n = 4), or forgetting about the scheduled session (n = 3). No unintended harms occurred throughout the study.

Primary outcomes by group and session are shown in Tables 2 and 3. A significant interaction effect was found for total symptom score (F136 = 4.41, P = .042), with the intervention group improving between test sessions. Main effects of session were present for composite memory (t37 = 2.34, P = .025), verbal memory (t37 = 2.09, P = .044), cognitive flexibility (t37 = 2.92, P = .006), executive function (t37 = 2.82, P = .008), reasoning (t34 = 2.42, P = .021), total symptom score (t36 = 2.36, P = .024), and near-point convergence (t36 = 2.05, P = .047). Both composite and verbal memory worsened at the second test session, while all other domains improved between sessions. The intervention group performed better on the complex-attention (t38 = 2.13, P = .040) and simple-attention (t38 = 2.07, P = .045) domains than the nontraining group; these group differences were not present at baseline. No significant main or interaction effects were found for the SAC (P > .28) or BESS (P > .48).

The proportion of participants with changes outside of the calculated 80% RCI was significant by group only for the simple-attention cognitive domain (P = .035), with a higher number of participants in the nontraining group (n = 5) having negative changes outside the 80% RCI (ie, worse performance) compared with the ACTIVE training participants (n = 0). For all other clinical outcomes, the proportion of individuals with changes exceeding the 80% RCI, either positively or negatively, did not differ by group. Effect sizes were also determined to provide further information on the clinical significance of any changes observed throughout the study. Overall effect sizes were small to negligible (Cohen d < 0.50) for both groups, with ACTIVE training displaying a medium-sized effect (Cohen d = 0.55) only on symptom scores (Table 4).

DISCUSSION

The ACTIVE training protocol produced few statistically significant changes in clinical concussion outcomes among a healthy population. Additionally, a significant portion of ACTIVE training individuals failed to improve beyond the 80% reliable change indices and effect sizes were small, indicating that the assessments used in this study were clinically stable (ie, no clinically meaningful changes were observed) in response to the ACTIVE training protocol. Exercise after SRC has been shown to improve clinical outcomes during the chronic recovery stages, and clinicians are beginning to evaluate its effectiveness more acutely. Few data exist to suggest if and how brief aerobic exercise training protocols, including those that mimic SRC rehabilitation paradigms, can influence clinical diagnostic and management tools, which can have profound effects on return-to-play and athlete safety outcomes. The ACTIVE
training was evaluated in healthy, recreationally active young adults to establish the expected exercise-response changes in common clinical metrics and help build the foundation for future research on athletes with SRC.

**Effect of Exercise on Clinical Concussion Assessment in Healthy Participants**

A significant overall interaction effect was found for symptom outcomes, driven by improvements in the intervention group. The intervention group had a mean symptom score of 5.10 at the first test session. Previous researchers showed that mean total symptom scores for healthy (uninjured) persons fluctuated by 1 to 3 points, suggesting that the intervention group, for unknown reasons, had high symptom scores at the first test session. Therefore, the improvement in symptom scores for the intervention group may represent a benefit due to exercise or a regression to the mean at the second test session. These results support the large variability of symptom reporting in response to exercise noted previously in both concussed and healthy samples. Similar to previous studies, cognitive-related and sleep-related symptoms improved after the exercise intervention. However, in contrast to the previous literature, sex differences in symptoms and improvements in emotion-related symptoms were not established in this study.

Significant main effects of group and time were observed for the computerized cognitive assessments. Composite and verbal memory scores declined for both groups at the second test session. Although these findings align with those of a previous study indicating decreased verbal memory scores measured via computerized neurocognitive evaluations acutely after a maximal exercise test, it is critical to note that all of the changes we saw were present in both groups in a rested state and were not specific to the intervention, with only 1 participant (1/20, 5%) endorsing more symptoms at the second session. Among the non-training group, 45% of participants (9/20) displayed an improvement in symptoms, while 25% (5/20) had worse symptoms at the second test session. These results support the large variability of symptom reporting in response to exercise noted previously in both concussed and healthy samples. Similar to previous studies, cognitive-related and sleep-related symptoms improved after the exercise intervention. However, in contrast to the previous literature, sex differences in symptoms and improvements in emotion-related symptoms were not established in this study.

**Table 2. All CNS Vital Signs Outcomes at Each Session for the ACTIVE Training and Nontraining Groups Extended on Next Page**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Nontraining (n = 20), Session</th>
<th>ACTIVE Training (n = 20), Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurocognitive index</td>
<td>97.60 ± 9.49 (93.16, 102.43)</td>
<td>98.55 ± 9.75 (93.99, 103.11)</td>
</tr>
<tr>
<td>Composite memory</td>
<td>105.45 ± 15.21 (98.34, 112.57)</td>
<td>98.15 ± 16.19 (90.57, 105.73)</td>
</tr>
<tr>
<td>Verbal memory</td>
<td>102.60 ± 15.26 (95.46, 109.74)</td>
<td>97.90 ± 16.17 (90.33, 105.47)</td>
</tr>
<tr>
<td>Visual memory</td>
<td>106.20 ± 13.24 (100.00, 112.40)</td>
<td>98.50 ± 16.43 (90.81, 106.19)</td>
</tr>
<tr>
<td>Psychomotor speed</td>
<td>105.15 ± 12.66 (99.23, 111.07)</td>
<td>105.55 ± 14.62 (98.71, 112.39)</td>
</tr>
<tr>
<td>Reaction time</td>
<td>88.00 ± 16.34 (80.35, 95.65)</td>
<td>90.60 ± 14.72 (83.71, 97.49)</td>
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<tr>
<td>Complex attention</td>
<td>95.10 ± 13.84 (88.62, 101.58)</td>
<td>95.70 ± 17.24 (87.63, 103.77)</td>
</tr>
<tr>
<td>Cognitive flexibility</td>
<td>94.35 ± 12.82 (88.35, 100.35)</td>
<td>100.45 ± 15.03 (93.42, 107.48)</td>
</tr>
<tr>
<td>Processing speed</td>
<td>105.20 ± 15.74 (97.83, 112.57)</td>
<td>107.70 ± 17.94 (99.30, 116.10)</td>
</tr>
<tr>
<td>Executive functioning</td>
<td>95.80 ± 12.40 (90.00, 101.60)</td>
<td>102.00 ± 14.23 (95.34, 108.66)</td>
</tr>
<tr>
<td>Reasoning</td>
<td>102.37 ± 13.28 (95.97, 108.29)</td>
<td>109.55 ± 13.53 (103.23, 115.88)</td>
</tr>
<tr>
<td>Simple attention</td>
<td>95.30 ± 18.62 (86.59, 104.01)</td>
<td>88.70 ± 24.03 (25.71, 114.57)</td>
</tr>
<tr>
<td>Motor speed</td>
<td>103.05 ± 11.21 (97.80, 108.29)</td>
<td>100.86 ± 12.68 (77.45, 99.95)</td>
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</tbody>
</table>

**Table 3. The SAC, BESS, GSC, and VOMS Outcomes at Each Session for the ACTIVE Training and Nontraining Groups Extended on Next Page**

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Outcome</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAC</td>
<td>Total score</td>
<td>28.80 ± 1.28 (28.20, 29.40)</td>
<td>28.30 ± 1.17 (27.75, 28.85)</td>
</tr>
<tr>
<td>BESS</td>
<td>Total score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15.35 ± 6.29 (12.41, 18.21)</td>
<td>16.20 ± 9.38 (11.81, 20.59)</td>
</tr>
<tr>
<td>GSC</td>
<td>Total symptom score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.50 ± 3.03 (1.08, 3.29)</td>
<td>2.30 ± 4.84 (0.04, 4.56)</td>
</tr>
<tr>
<td>VOMS</td>
<td>NPC distance&lt;sup&gt;b&lt;/sup&gt;, cm</td>
<td>4.58 ± 4.67 (2.40, 6.77)</td>
<td>4.66 ± 4.82 (2.34, 6.98)</td>
</tr>
</tbody>
</table>

Abbreviations: ACTIVE, acute concussion therapy intervention; BESS, Balance Error Scoring System; GSC, Graded Symptom Checklist; NPC, near-point convergence; SAC, Standardized Assessment of Concussion; VOMS, Vestibular/Ocular Motor Screening.

<sup>a</sup> P values were adjusted to account for multiple comparisons.

<sup>b</sup> Lower scores indicate better performance.
exercise intervention. Cognitive flexibility, executive functioning, and reasoning also improved at the second test session. Therefore, these changes were likely due to learning effects or inherent variability among the participants themselves. In addition, the large variability of these results, as evidenced by the relatively large standard deviations and 80% RCIs, may speak to the suboptimal test-retest reliability of computerized neuropsychological assessments, which has been noted in the literature.22,32

A main effect of session was evident in near-point convergence distance, with both groups having increased (worse) near-point convergence distance at the second test session, but group means for all sessions were within previously established normative values (<5 cm).33

No significant main or interaction effects were present for the SAC or BESS scores, indicating that the brief aerobic training protocol had no influence on sideline balance and mental status examinations. Our findings for the SAC agree with the literature in that sideline cognitive assessments were unaffected by exercise,16 although previous authors used a single bout of acute exercise as opposed to the 2-week training protocol we used. Most studies have shown that BESS scores worsened after acute physical activity and took up to 20 minutes to recover,14,34 whereas 1 study demonstrated improved BESS outcomes after acute exercise.35 Our results suggest that aerobic training had no effect on balance, which may be due to the rested state in which participants were evaluated or our use of stationary cycling as the exercise mode.

The RCIs were calculated for all clinical outcomes, with 80% intervals chosen to represent more clinically conservative values. Except for the simple-attention cognitive domain, no other clinical outcomes showed a group difference in the proportion of individuals exceeding the 80% RCI. The lack of positive improvements exceeding the RCI, along with the generally small effect sizes, indicate that a brief aerobic training intervention had little clinically meaningful effect on concussion diagnostic and management tools in healthy participants. However, several of the assessments are known to have ceiling (SAC) or floor (GSC and VOMS) effects, and clinically meaningful change would be impossible to observe if a participant was already at the floor or ceiling. We found no differences in the number of participants at the floor or ceiling level between sessions, but these effects remain a limitation.

Previous authors have exclusively evaluated clinical outcomes immediately (within 30 minutes) after exercise,

Table 3. Extended From Previous Page

<table>
<thead>
<tr>
<th>Group, Mean ± SD (95% Confidence Interval)</th>
<th>Adjusted P Valuea</th>
<th>80% Reliable Change Index</th>
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<tr>
<td>ACTIVE Training (n = 20), Session</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
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<tr>
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<td>28.35 ± 1.76 (27.53, 29.17)</td>
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<td>16.85 ± 6.46 (13.83, 19.87)</td>
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<tr>
<td>5.10 ± 5.75 (2.41, 7.79)</td>
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<tr>
<td>3.29 ± 1.74 (2.47, 4.10)</td>
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</table>
and, to the best of our knowledge, none have investigated how a longer period of aerobic exercise training affects clinical concussion outcomes in healthy populations. The general lack of significant interaction effects, absence of group differences exceeding 80% RCIs, and negligible effect sizes suggests that short-duration, aerobic exercise programs designed to mimic concussion rehabilitation interventions do not change common concussion outcomes in clinically meaningful ways among healthy participants. However, healthy participants who complete SRC assessments with optimal effort and motivation are likely to be performing at their maximum capacity and, therefore, have little to no room for improvement on subsequent assessments. It is important to note that concussed athletes will likely display suboptimal performance on acute SRC assessments due to injury-related deficits. Thus, patients with concussions have more room for improvement in SRC assessments after aerobic exercise interventions and, as aerobic exercise can target concussion-induced physiological dysfunction, they may have different and more clinically meaningful responses to aerobic exercise interventions.

**Translation of ACTIVE Training to Concussed Populations**

Controlled and progressive aerobic exercise is becoming a popular SRC treatment option as research suggested that

<table>
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<tbody>
<tr>
<td>CNS Vital Signs</td>
<td>Neurocognitive index</td>
<td>0.10</td>
<td>0.29</td>
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<tr>
<td></td>
<td>Composite memory</td>
<td>–0.48</td>
<td>–0.19</td>
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<td></td>
<td>Verbal memory</td>
<td>–0.31</td>
<td>–0.42</td>
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<td></td>
<td>Visual memory</td>
<td>–0.58</td>
<td>0.09</td>
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<tr>
<td></td>
<td>Psychomotor speed</td>
<td>0.03</td>
<td>0.21</td>
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<td>0.16</td>
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<td></td>
<td>Processing speed</td>
<td>0.15</td>
<td>0.17</td>
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<tr>
<td></td>
<td>Executive functioning</td>
<td>0.50</td>
<td>0.41</td>
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<td></td>
<td>Reasoning</td>
<td>0.54</td>
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<td></td>
<td>Simple attention</td>
<td>–0.35</td>
<td>0.49</td>
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<tr>
<td></td>
<td>Motor speed</td>
<td>–0.23</td>
<td>0.10</td>
</tr>
<tr>
<td>SAC</td>
<td>Total score</td>
<td>–0.39</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Total score</td>
<td>–0.13</td>
<td>0.16</td>
</tr>
<tr>
<td>GSC</td>
<td>Total symptom score</td>
<td>0.06</td>
<td>0.55</td>
</tr>
<tr>
<td>VOMS</td>
<td>NPC distance, cm</td>
<td>–0.02</td>
<td>–0.48</td>
</tr>
</tbody>
</table>

Abbreviations: ACTIVE, acute concussion therapy intervention; BESS, Balance Error Scoring System; GSC, Graded Symptom Checklist; NPC, near-point convergence; SAC, Standardized Assessment of Concussion; VOMS, Vestibular/Ocular Motor Screening.

*Negative signs indicate worse performance at the second test session.*
exercise positively influenced symptom, balance, and cognitive domains in populations experiencing prolonged recovery. Our results indicate that aerobic exercise training alone did not meaningfully influence balance, cognitive, or visual outcomes in healthy participants, although a potential for improving symptom outcomes may be present. Return-to-play decisions are often based, in part, on the return of clinical concussion assessments to preinjury values. Understanding how concussion rehabilitation interventions influence diagnostic and management assessments is critical for clinicians to make appropriate return-to-play decisions. As rehabilitation paradigms are initiated during more acute-recovery phases, when the risk of subsequent re-injury is at its peak, ensuring that athletes are not prematurely returned to play is paramount. Our study of healthy participants showed that ACTIVE training alone did not result in clinically meaningful improvements on any assessment. This is a critical finding, allowing clinicians prescribing exercise therapy to interpret outcomes as currently advised and eliminating the need for adjusted scores when patients with concussions receive exercise-related therapy. However, the serial management of concussions may require multiple administrations of these assessments as opposed to the 2 time points we tested. This possibility further highlights the need for future authors to conduct similar assessments in cohorts with acute concussions.

Limitations

Although assessing outcomes in healthy populations is considered the first phase of clinical trials, results in healthy individuals may not directly translate to participants with concussions, who may have a different response to exercise training. Physical activity will likely be restricted during their recovery. In many cases, supervised aerobic exercise interventions would be the only physical activity patients with concussions are permitted throughout recovery. We studied a convenience sample of healthy, physically active college students. As such, we were unable to prevent participants from completing additional forms of exercise outside of the ACTIVE training protocol during the 2-week period. How this may affect the translation of ACTIVE training to populations with concussions remains unknown. A subset of participants (n = 23; 11 nontraining, 12 ACTIVE training) wore Charge HR (Fitbit, Inc, Boston, MA) activity monitors throughout the study. The ACTIVE training participants completed approximately 30 more minutes of physical activity than nontraining participants, suggesting that ACTIVE training was completed in addition to any current physical activity and that the dose of ACTIVE training was appropriately administered. In addition, the majority of physical activity recorded for both groups was low intensity in nature, which could represent activity that participants with concussion would be permitted to complete (such as walking). As both concussion and aerobic exercise can affect psychological outcomes, future investigators should evaluate the influence of SRC rehabilitation on mental health outcomes, such as anxiety and depression. We tried to design the study and analysis to make the results as generalizable as possible, but future authors should evaluate the effects of aerobic training in other populations, including youth and elite-level athletes, as the findings may not directly transfer.

Conclusions

Aerobic exercise is a relatively safe, inexpensive, and easy form of rehabilitation for college-aged participants that has well-established cardiovascular and mental health benefits. Aerobic exercise may hold additional benefits for individuals with concussion as it can target the underlying physiological deficits after injury and expedite recovery; however, individuals with visual, vestibular, or cervicogenic dysfunction may continue to benefit from therapies supplementing exercise training. We conducted a phase I randomized controlled trial to assess the effect of an aerobic exercise program on clinical concussion outcomes in healthy participants. A significant interaction effect was found for total symptom score (P = .01), with the intervention group showing improved symptom scores between sessions. However, the intervention group did not show a higher proportion of participants with improvement exceeding the calculated 80% RCIs, and effect sizes were generally small, suggesting that the ACTIVE training had little clinical significance for outcomes in healthy participants. Because participants with concussion exhibit suboptimal performance on acute concussion assessments due to injury-related deficits, and the serial management of concussion differs from the pre-post design used in this study, they may have different results from those shown in healthy cohorts, and this should be examined in future studies.

Clinical Perspective

The management of SRC is continually evolving, and recent guidelines recommended earlier implementation of rehabilitation. Acrob exercise training is a novel rehabilitation protocol that has successfully mitigated persistent symptoms post-concussion. However, no information previously existed as to whether aerobic exercise training alone influences clinical concussion outcomes, which can have profound effects on return-to-play decisions and athletes’ safety. The results of our study in a healthy sample suggested that clinical concussion assessments remained stable in response to aerobic exercise training, and no clinically meaningful changes were observed. Thus, clinicians prescribing exercise therapy can interpret changes in their patient’s concussion assessments as currently advised, with no need to adjust scores. Also, improvements in clinical concussion outcomes in concussed patients undergoing exercise therapy may not be a by-product of increased physical activity alone and must be due to other factors, which should be further explored in future studies.

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