Does Early Low-Intensity Aerobic Exercise Hasten Recovery in Adolescents With Sport-Related Concussion?

Ryan D. Henke, Savana M. Kettner, Stephanie M. Jensen, Augustus C.K. Greife, and Christopher J. Durall

Clinical Scenario: Low-intensity aerobic exercise (LIAEX) below the threshold of symptom exacerbation has been shown to be superior to rest for resolving prolonged (>4 wk) symptoms following sport-related concussion (SRC), but the effects of LIAEX earlier than 4 weeks after SRC need to be elucidated. **Focused Clinical Question:** Does LIAEX within the first 4 weeks following SRC hasten symptom resolution? **Summary of Key Findings:** Two randomized controlled trials (RCT) and 1 nonrandomized trial involving adolescent athletes (10–19 y) were included. One RCT reported faster recovery time with LIAEX versus placebo stretching. Likewise, recovery time was faster with LIAEX versus rest in the nonrandomized trial, but not in the underpowered RCT, although effect sizes were similar between these studies (0.5 and 0.4, respectively). All 3 studies reported a reduction in concussion symptom severity with LIAEX; however, the magnitude of symptom reduction across the recovery timeline was greater in the LIAEX group than the rest group in the nonrandomized trial, but not the 2 RCTs. Importantly, no adverse effects or incidence of delayed recovery from LIAEX were reported in any of the studies. **Clinical Bottom Line:** LIAEX initiated within 10 days after SRC may facilitate a faster recovery time versus placebo stretching or rest, although additional clinical trials are strongly advised to verify this. **Strength of Recommendation:** Level 1b and 2b evidence suggests subsymptom exacerbation LIAEX may decrease Postconcussion Symptom Scale scores and hasten symptom resolution in adolescent athletes following SRC.

Keywords: mild traumatic brain injury, active rehabilitation, return to sport, subsymptom exacerbation

Clinical Scenario

Historically, adolescent athletes with sport-related concussion (SRC) have been advised to abstain from physical activity until asymptomatic, at which point they may begin a graduated return to sport protocol.¹ Some researchers, however, have proposed that subsymptom exacerbation low-intensity aerobic exercise (LIAEX) may expedite concussion recovery via increased levels of brain-derived neurotrophic factor.^{2–5} Subsymptom exacerbation LIAEX, starting a minimum of 4 weeks after an SRC, has been reported to be more beneficial than rest,⁶ but the effects of LIAEX earlier than 4 weeks need to be elucidated. This review was conducted to determine if evidence supports initiating subsymptom exacerbation LIAEX within the first 4 weeks following SRC. The review was limited to adolescent athletes (aged 10–19 y), because, historically, this group experiences high rates of SRC and appears to be more vulnerable to prolonged recovery.^{1,7}

Focused Clinical Question

Does subsymptom exacerbation LIAEX within the first 4 weeks following SRC hasten symptom resolution in adolescent athletes?

Summary of Search, “Best Evidence” Appraised, and Key Findings

- The literature was searched for studies on the effects of early (within 4 wk) subsymptom exacerbation LIAEX after medically diagnosed SRC in adolescents.
- The search yielded 3 articles^{2,7,8} that fit inclusion/exclusion criteria. One level 1b randomized controlled trial (RCT),² and 1 level 2b nonrandomized trial (NRT)⁷ compared LIAEX initiated within 10 days after SRC with usual care (ie, rest). A second level 1b RCT⁸ compared LIAEX initiated within 10 days after SRC with placebo stretching.
- Recovery in the studies was defined as symptom resolution per the Postconcussion Symptom Scale (PCSS) and/or examination by a physician.
- One RCT⁸ found a significant difference in days to recovery favoring the LIAEX group compared with the stretching group. Likewise, the NRT by the same group of investigators showed faster recovery with LIAEX versus usual care (ie, rest). By contrast, the other RCT² did not find a significant between-group difference in days to recovery, although this study appears to have been underpowered.
- Notably, there were no reports of adverse effects with LIAEX in any of the reviewed studies.

Clinical Bottom Line

Regarding the posed clinical question, evidence from 1 level 1b RCT⁸ and 1 level 2b NRT⁷ suggests subsymptom exacerbation LIAEX started within 10 days after SRC is associated with a faster

Henke, Kettner, Jensen, Greife, and Durall are with the Doctor of Physical Therapy Program, University of Wisconsin-La Crosse, La Crosse, WI. Durall is also with Physical Therapy Unit, Student Health Center, University of Wisconsin-La Crosse, La Crosse, WI. Henke (rdhenke12@gmail.com) is corresponding author.

overall recovery time when compared with rest or placebo stretching, although additional data are needed to substantiate this conclusion. Moderately strong (level 1 and 2) evidence from all 3 studies indicates that SRC symptom severity decreased across the study interval in response to LIAEX. In the reviewed studies, no adverse effects were reported when LIAEX was performed 5 to 7 days per week on a stationary bike or treadmill for 10 to 20 minutes at 50% to 70% of age-predicted maximal heart rate² or at 80% of symptom-threshold heart rate.^{7,8}

Strength of Recommendation

Level 1 evidence from 2 RCTs and level 2 evidence from 1 NRT support early (<10 d) subsymptom exacerbation LIAEX for adolescents with SRC. It is important to acknowledge that the RCT by Micay et al² in this review appears to have been underpowered with a total sample size of 15. This small sample may have prevented detection of between-group differences. The NRT by Leddy et al^{8,9} compared convenience sample data from 2 different published studies, and thus group assignment was not random. Finally, the RCT by Leddy et al⁸ did not have a true control group, rather, a placebo stretching group that was compared with the LIAEX group. Given the limited number of studies on this topic and the methodological shortcomings described earlier, additional data from studies with greater methodological quality and homogeneity are advised before widespread adoption should be advocated.

Search Strategy

Terms Used to Guide Search Strategy

- Patient/Client group: (adolescents OR athletes OR youth) AND (concussion OR traumatic brain injury OR mTBI)
- Intervention/Assessment: (symptom*OR sub-symptom*OR symptom threshold) AND (graded exercise program OR aerobic OR active rehab*)
- Comparison: rest OR no activity
- Outcomes: time OR duration OR symptom resolution OR symptom relief OR return to sport

Sources of Evidence Searched

- CINAHL Plus with Full Text
- Cochrane Central Register of Controlled Trials
- Cochrane Clinical Answers
- Cochrane Database of Systematic Reviews
- MEDLINE
- MEDLINE with Full Text
- SPORTDiscus with Full Text

Inclusion and Exclusion Criteria

Inclusion

- Limited to human subjects 10–19 years old
- Aerobic exercise initiated within 4 weeks after SRC diagnosis
- Published in English language

Exclusion

- Aerobic exercise initiated ≥ 4 weeks after SRC

Results of Search

The initial search in October 2018 yielded 24 studies that were reviewed for appropriateness based on inclusion and exclusion criteria. Of these, 2 articles^{2,7} were selected for critical appraisal. An additional article, published in February 2019, was identified on PubMed.⁸ A summary of the selected articles is provided in Tables 1 and 2.

Best Evidence

The studies in Tables 1 and 2 were identified as the best available evidence for this review. Two studies were level 1b evidence RCT and 1 study was a level 2b evidence NRT. Levels of evidence for this review were based on the Centre for Evidence-Based Medicine 2009 criteria.¹⁰

Implications for Practice, Education, and Future Research

Using LIAEX after SRC is a relatively recent practice, and, accordingly, the safety and efficacy of this approach need to be well established by high-quality research before widespread clinical adoption should be considered. The reviewed studies reported no adverse effects in symptomatic adolescents following subsymptom exacerbation LIAEX started within 10 days post-SRC. In the NRT, none of the 24 participants in the LIAEX group had delayed recovery, while 4 of the 30 (13%) rest group participants had delayed recovery.⁷ In addition, in the RCT by Leddy et al,⁸ 2 of the 52 (3.8%) participants with acute SRC in the LIAEX group had delayed recovery, while 7 of the 51 (13.7%) stretching group participants had delayed recovery. Therefore, a potentially important advantage of exercise-based treatment early in the SRC recovery process may be the reduced incidence of delayed recovery.

Regarding the efficacy of subsymptom exacerbation LIAEX for concussed adolescents, all 3 studies reported a reduction in SRC symptom severity across their study intervals. The magnitude of symptom reduction across the recovery timeline was greater in the LIAEX group than the rest group in the NRT,⁷ but not the 2 RCTs.^{2,8} Reviewers calculated effect sizes for between-group symptom severity reduction (via PCSS scores) from the data provided in the Micay et al² RCT; effect sizes were considered clinically significant (2.8 between weeks 1 and 3; 1.6 between

Table 1 Summary of Study Designs of Retrieved Articles

Level of evidence	Study design/methodology	Number located	Study
1b	RCT	2	Micay et al ² Leddy et al ⁸
2b	Quasi-experimental NRT	1	Leddy et al ⁷

Abbreviations: NRT, nonrandomized trial; RCT, randomized controlled trial.

Table 2 Summary of Best Evidence

	Micay et al ²	Leddy et al ⁷	Leddy et al ⁸
Study design	Randomized controlled trial	Nonrandomized trial	Randomized controlled trial
Participants	15 male athletes diagnosed with SRC and symptomatic at day 5 postinjury were randomized into EXG or UCG.	54 male athletes diagnosed with SRC 1–9 d prior to study enrollment. Data for EXG were extracted from another randomized controlled trial on subthreshold aerobic exercise prescription. ⁸	103 athletes (F=48, M=55) diagnosed with SRC 1–9 d prior to study enrollment were randomized into EXG or placebo stretching group. No interventions were started earlier than 48 h postinjury.
Intervention investigated	Age = 14–18 y, mean age = 15 y Demographic variables did not differ between groups at the start of the study. EXG (n = 8) participated in 8 sessions of supervised aerobic exercise on a stationary cycle ergometer wearing an HR monitor. Sessions started on day 6 postinjury. Each session included a 5-min warm-up and 5-min cooldown. Session 1 was 10 min in duration at 50% of age-predicted HR _{max} . Session 2 was 20 min at 50% HR _{max} . Subsequent sessions were 20 min in duration, but intensity was increased by 5% of HR _{max} until 70% HR _{max} was achieved. Participants exercised at this intensity during all subsequent sessions. Exercise sessions occurred on 2 consecutive days followed by a rest day. PCSS scores were obtained before, during, and after each exercise session.	Age = 13–18 y, mean age = 15 y Demographic variables did not differ between groups at the start of the study. EXG (n = 24) participated in daily supervised 20-min aerobic exercise sessions on a treadmill or stationary bike at 80% subthreshold HR wearing an HR monitor. Sessions started within 9 d postinjury. Each session included a 5-min warm-up and 5- to 10-min cooldown. Prior to first exercise session, the BCTT was used to determine HR at symptom exacerbation (≥3-point increase on VAS) or voluntary fatigue (≥ 17 RPE). Participants were instructed to stop exercising if symptom exacerbation occurred during daily exercise sessions.	Age = 13–18 y, mean age = 15 y Demographic variables did not differ between groups at the start of the study. EXG (n = 52) participated in 20-min daily aerobic exercise on a treadmill or stationary bike at 80% subthreshold HR wearing an HR monitor. Supervised LIAEX was performed at home or in a gym. Sessions started within 9 d postinjury. Prior to first exercise session, the BCTT was used to determine HR at symptom exacerbation. Participants were instructed to stop exercising if symptom exacerbation occurred during exercise sessions at home (≥2-point increase on VAS). Participants completed a weekly BCTT to calculate a new target HR.
Control	The UCG (n = 7) were progressed through a 6-stage progression of activity protocol (per Berlin 2016 Guidelines), under the direction of their sports medicine physician.	The UCG (n = 30) was a subset from a previously published study. ⁹ Participants were instructed to follow standard care model for return to sport/school. Activity levels were not strictly monitored.	The stretching group (n = 51) was instructed to follow a gentle, whole-body stretching program that was not intended to noticeably raise HR. Stretching was progressed each week. Participants completed a weekly BCTT during clinic visits.
Outcome measure(s)	Symptom severity and exacerbation per PCSS. Time (in days) to medical clearance.	Time (in days) to recovery from initial visit. Return to baseline symptoms per PCSS.	Time (in days) to recovery since date of injury. Return to baseline symptoms per PCSS.
Primary findings	No significant difference between groups in average time to medical clearance ($P = .87$; Cohen $d = 0.4$). PCSS scores significantly decreased in both groups, although differences between groups were not significant. Large between-groups effect sizes favored EXG for reducing PCSS scores (effect sizes were calculated, not reported): (1) Weeks 1–3 (Cohen $d = 2.8$) (2) Weeks 1–4 (Cohen $d = 1.6$)	Recovery time from initial visit was significantly faster for EXG than UCG ($P = .048$) with a moderate effect size (calculated Cohen $d = 0.5$) favoring EXG. Percentage of participants not recovered (total, physical, cognitive, and sleep symptoms) by day 14 was significantly different between groups favoring EXG.	EXG recovered significantly faster than stretching group ($z = 2.82$, $P = .01$). EXG recovered in a median of 13 vs 17 d in stretching group ($P = .01$). Total self-reported symptom scores appeared to decrease more rapidly in the EXG. Decreases in symptom scores for the EXG achieved significance on days 5, 12, and 18, but not for the other 18 d of the study.
Secondary findings	No participants experienced symptom exacerbation during intervention; participants completed all intervention sessions.	No EXG participants experienced prolonged recovery (>30 d) vs 4/30 (13%) in the EXG had prolonged recovery.	Seven participants in the stretching group experienced delayed recovery since injury (>30 d) compared with 2 participants in the EXG; this was not found to be significant ($P = .08$)
Level of evidence	1b	2b	1b
Validity score	PEDro score: 6/10	PEDro score: 4/10	PEDro score: 5/10

(continued)

Table 2 (continued)

	Micay et al ²	Leddy et al ⁷	Leddy et al ⁸
Conclusion	In male adolescents diagnosed with SRC and symptomatic after 5 d, both LIAEX and rest were beneficial in decreasing symptom severity. LIAEX was not associated with a faster recovery time than rest, although the small sample may have hindered detection of between-group differences. Aerobic exercise did not cause symptom exacerbation and thus appears to be safe and feasible in potentially aiding symptom resolution.	Following SRC, an early individualized subthreshold LIAEX intervention may safely hasten symptom resolution in adolescent males. Accordingly, subthreshold LIAEX within 10 d following injury may reduce the number of patients who experience prolonged recovery.	Use of individualized subsymptom threshold aerobic exercise within the first week following SRC may safely speed recovery in male and female adolescents. Reduced incidence of delayed recovery appears to be the primary benefit of early subthreshold exercise treatment.

Abbreviations: BCTT, Buffalo Concussion Treadmill Test; EXG, exercise group; F, females; HR, heart rate; HR_{max}, maximal heart rate; LIAEX, low-intensity aerobic exercise; M, males; PCSS, Postconcussion Symptom Scale; RPE, rating of perceived exertion; SRC, sport-related concussion; UCG, usual care group; VAS, visual analog scale.

weeks 1 and 4), favoring the LIAEX group. In the NRT, adolescents who started LIAEX within 9 days of SRC had greater symptom reduction across the study period than the usual care (ie, rest) group. They also reported the LIAEX group had a significantly shorter recovery time than the usual care group, although their control data set was imported from another study, and group assignment was not randomized.⁷ By contrast, the RCT by Micay et al did not detect between-group differences in recovery time, although their small sample size (N = 15) may have lacked the statistical power to detect differences. According to Micay et al,² a calculated sample size of 30 would be needed to detect between-group differences with an effect size of 0.8. Calculated effect sizes for reduction in time to medical clearance were moderate in both the Micay et al² and Leddy et al⁷ studies (0.4 and 0.5, respectively). In the RCT by Leddy et al,⁸ both groups reported decreases in PCSS scores through the 21 days of the study; however, when compared with the stretching group, the LIAEX group reported significant PCSS score decreases on days 5, 12, and 18. Additional RCTs are needed to definitively answer the clinical question regarding the impact of subsymptom exacerbation LIAEX on overall SRC recovery time in this population, although the initial data are encouraging.

Clinicians should educate patients that aerobic exercise is beneficial for the human brain and that subsymptom exacerbation LIAEX does not appear to delay recovery, but it may speed recovery in adolescents with acute postconcussive symptoms. This seems concordant with a recent international consensus statement that recommends a more active approach to SRC treatment.¹ There is evidence that aerobic exercise can promote neuron growth and repair after concussions through increased levels of brain-derived neurotrophic factor.⁵ Levels of brain-derived neurotrophic factor have been shown to increase in healthy athletes immediately after cycle ergometry to exhaustion¹¹ and in rodents that initiated exercise within 1 to 3 days after concussion.¹² In the later study, concussed rodents that were exercised also had significant improvements in motor and cognitive functioning. Current evidence points to inferior neurocognitive performance of athletes engaging in high levels of activity following SRC when compared with athletes engaging in moderate levels of activity.¹³ Given this, clinicians should emphasize to their patients that any exercise or activity should be below the threshold of symptom exacerbation.

Future research on this topic would be strengthened by: (1) using mixed-gender participant groups, (2) including a control group and random group assignment for interventional comparisons, (3) determining optimal sample sizes a priori via a power

analysis, (4) employing a standardized LIAEX protocol, (5) using standardized outcomes measures to determine readiness to return to sport/activity (ie, medical clearance), and (6) reporting effect sizes so the clinical significance can be appreciated. The RCT by Micay et al² and the NRT by Leddy et al⁷ included male subjects only for convenience. Females, however, may be more likely to have a delayed recovery after SRC.¹⁴ As with the reviewed RCT by Leddy et al,⁸ inclusion of both males and females in future studies will improve generalizability. The consistent utilization of randomly assigned control or comparator groups will aid in estimating the influence of aerobic exercise post-SRC. In addition, sample size calculations should be performed to ensure studies on this topic are adequately powered.

There is a need to determine optimal exercise protocols that could be adopted by future researchers. Two of the studies in this review utilized daily subthreshold aerobic exercise lasting 20 to 30 minutes,^{7,8} while the third study used a prescribed progressive aerobic exercise program, based on age-predicted maximal heart rate, beginning at 10 minutes and increasing over time to 20 minutes.² In both articles by Leddy et al,^{7,8} the heart rate at symptom exacerbation was used to determine a target subsymptom threshold heart rate for aerobic exercise. Determination of optimal LIAEX dosage is needed, as 2 studies implemented daily exercise^{7,8} and the other prescribed exercise 5 days per week.² Ongoing research to develop a standardized aerobic exercise protocol for concussed patients is being conducted.¹⁵ Future researchers should aim to standardize outcome measures; all 3 of the reviewed studies included the PCSS as an outcome measure, although this is a highly subjective, symptom-based test. Furthermore, in the studies by Leddy et al,^{7,8} symptom recovery was defined as a PCSS score of <7 for 3 consecutive days, while Micay et al² relied solely on physician examination to determine recovery.² Thus, there is a need for more standardization in determining recovery and readiness for return to sport after SRC. As with many health care issues, greater methodological consistency in future studies should improve confidence in the validity of results and enhance clinical decision making.

The results of this review suggest subsymptom exacerbation LIAEX administered within 10 days following SRC in adolescents does not appear to delay recovery and may result in greater symptom reduction and faster medical clearance than rest. Clinicians who consider applying the LIAEX protocols, as described in the clinical bottom line, should emphasize to their patients that any exercise or activity should be below the threshold of symptom exacerbation. Information in this critically appraised topic should

be reviewed in 3 years or after the publication of high-quality RCTs on this topic to determine if the recommendations suggested earlier should be modified.

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