The Safety and Efficacy of Sub-Symptom Threshold Exercise as a Treatment for Post-Concussion Symptoms in Adolescents

Peter Kingsley

Evidence Based Medicine

Arcadia University

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Abstract

Introduction: Concussions are an unfortunately common injury sustained by many young athletes participating in a variety of sports throughout the country. Concussions are notoriously difficult to diagnose and may lead to serious, long-term difficulties if left untreated or treated incorrectly. Severe or repeated concussions can lead to many physical, psychological, neurological, and other symptoms that could potentially lead to death. Current concussion treatment is largely physical and cognitive rest. This research study aims to identify how limited exercise may decrease the duration of symptoms and make it safer for athletes to resume participation in their sport.

Methods: A literature search was performed and completed in November of 2019 using the PUBMED and EBSCO search databases. 11 articles were chosen based on inclusion/exclusion criteria as well as the date they were completed. These articles were then analyzed and their data were compared.

Results: The studies evaluated demonstrated benefits to the use of exercise in decreasing post concussive symptoms. Several studies also evaluated and demonstrated the safety and tolerability of exercise programs in adolescents with neurologic symptoms post tbi or concussion. These studies used a variety of metrics, evaluation tools, and statistical tests to demonstrate improvements. However, only a few studies were able to collect follow up data at various points post evaluation. Also, a few studies were not able to use an adequate control group to demonstrate the success of the treatment across different populations. Finally, almost all studies were done on too small of sample sizes to allow for broad extrapolation of data.

Discussion: The data collected from the studies were able to show strong data in support of sub-symptom threshold exercise as a better treatment option for adolescents with post-concussion symptoms than strict rest. Despite this, there are many factors that limit the generalizability of the data to state adequately that the exercise treatment is always both safer and more efficacious. More data must be collected through studies with larger sample sizes that extend over much longer periods of time to evaluate future health outcomes must be completed. One important finding of these data is that the findings were found to be safe, and negative findings were extremely minimal. Future, more robust studies should continue to employ and evaluate sub-symptom threshold exercise as a treatment plan for adolescents with post-concussion symptoms.

Conclusion: Concussions continue to be a very common issue in adolescent athletes, and a solution on how best to treat them continues to be a mystery. Previous treatment plans have stuck largely to a program of strict cognitive and physical rest until the symptoms improve. As demonstrated in the studies highlighted, properly implemented and monitored exercise has shown data indicating its efficacy as a superior treatment. However, further, more robust studies must be completed to show increased generalizability and long term success before these exercise treatments can be implemented as a mainstream treatment. The demonstrated safety of the exercise and positive findings shown make further research crucial and worthwhile to improve treatment for these millions of adolescent athletes.

Introduction

A concussion is defined as a complex pathophysiological process affecting the brain (McCrory et al., 2008). This type of brain change is caused by some type of trauma leading to a form of traumatic brain injury referred to as a concussion. At the 3rd international conference on concussion in sport (McCrory et al., 2008), the physicians identified concussion symptoms as "a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course; however, it is important to note that in a small percentage of cases, however, post concussive symptoms may be prolonged." This definition can then be broken down further to say that these symptoms include somatic symptoms such as a headache or emotional symptoms, physical signs including amnesia or loss of consciousness, behavioral changes such as irritability, cognitive impairment including slower reaction times, and/or sleep disturbances. A concussion may be suspected for diagnosis if one or more of those categories of symptoms are met by the patient. These concussions are certainly a problem for the individuals sustaining the blows and putting themselves at risk, but the burden of these concussions is also a public health problem. The societal impact of concussions can be felt when the epidemiology of these concussions is laid out. 38 million children participate in organized sports in the United States alone. These young athletes are then coupled with the additional 170 million adults that participate in physical activities including similar organized sports (Daneshvar et al., 2011). The number of traumatic brain injuries resulting in concussions and subsequent hospitalizations from sports and recreation activities has also been greatly increased. The CDC reported that from 2001 through 2009, the annual traumatic brain injury related visits to emergency rooms increase from 153,375 per year to 248,418 per year (Nonfatal Traumatic Brain Injuries Related to Sports and Recreation Activities Among Persons Aged ≤19 Years, n.d.). Also, it was reported that the highest rates of

hospitalizations came from males ranging in age from 10 to 19 years old. Many people around sports have heard of the short-term symptoms described above, including but certainly not limited to headache, neck pain, vision problems, sleep issues, cognitive deficits, and emotional changes (Junn, Bell, Shenouda, & Hoffman, 2015). These symptoms have been seen before in athletes in many forms with variations depending on both the athlete herself and the severity of the concussion from the blow to the head. However, it is often discounted that these symptoms are not always easily shaken and, unlike a bruise or cut, can be made significantly worse and leave permanent damage to the athlete beyond simply on the field abilities if left untreated. Concussions left untreated or unmanaged can cause not only the short-term symptoms mentioned, but long-term deficits can cause major issues for the athlete as well. The long-term symptoms include lingering short-term symptoms that make everyday life difficult, but also other neuropsychological outcomes due to alterations in brain physiology due to the injury/injuries sustained by the trauma. These potential outcomes include issues with executive function, attentional dysfunction, memory problems, slowed processing speeds, altered moods, and major depression symptoms (Carman et al., 2015). These lasting symptoms are also much more prevalent in those experiencing concussions than many individuals realize. A longitudinal study completed by Theadom et al. (2016) recruited adults over the age of 16 to completed assessments regarding their cognitive functioning, global functioning, post-concussion symptoms, mood, and quality of life a year after an injury resulting in a concussion. The results showed that after a full year, 47.9% of the participants reported still experiencing four or more of the post-concussion symptoms. Additionally, 10.9% of the participants reported very low cognitive functioning. Concussion treatments have been an area of some mystery as more and more information continues to surface about their outcomes. Previously, a very common

recommendation to treat concussion symptoms was a period of strict rest. A study by Thomas et al. (2015) investigated the effectiveness of increasing a specifying that period of rest. In this study, patients randomly assigned to the control group rested one or two days before returning to school and returning to physical activity after the symptoms had resolved. If strict rest was beneficial, the researchers predicted more favorable outcomes with a longer, stricter rest regiment. The intervention group was told to maintain a strict rest period of five days. This included no school, work, or physical activity during those days. The results of this study, however, showed that this strict rest period added no benefit to the intervention group. There were no significant changes in the symptom scale reports (PCSS), the neurocognitive assessment, or the balance assessment (BEESS). In fact, patients in the intervention group experienced higher total symptoms over the course of the study ($P<0.03$). Many emerging treatments have become relevant recently creating more options for healthcare providers and patients to search for treatments that best suit their specific needs. One such treatment is an earlier use of sub-symptom threshold exercise as part of the recovery process. Data from this treatment approach continue to be positive and should be taken seriously as part of a patient's treatment plan. The goal of this study is to investigate: in adolescent athletes, ages 11-19, does a limited regiment of sub-symptom, aerobic exercise decrease the duration of symptoms (headache, concentration issues, irritability, sleep disturbances) as compared to strict rest?

Methods

A literature search was performed in November of 2019 in the PUBMED search database using the terms "aerobic exercise concussion treatment sports related adolescents." This search yielded 47 articles. This group was then narrowed down to articles written within the last 5 years leaving 38 articles. These remaining articles were then evaluated and excluded if they: 1. If they

contained a review or used secondary data, 2. If they did not contain a randomized trial, 3. Were using exercise as anything other than a treatment (I.e. prevention), 4. If they contained animals or anything other than human participants, and 5. If they did not contain the proper age group. This searched yielded 9 articles to be used.

Another, similar, literature search was completed using the EBSCO database. This search was conducted using keywords "aerobic exercise or aerobic training or physical activity or exercise or physical exercise AND concussion or mild traumatic brain injury or mild tbi or mtbi AND adolescents or teenagers or young adults." This search was also limited to articles written in 2014 or later. These criteria yielded 84 articles. These articles were then evaluated using the same exclusion criteria from above. Articles that were found in the PUBMED search were also excluded to prevent repeats. This search yielded 2 articles to be used

Results

Chrisman, Sara P. D., Kathryn B. Whitlock, Jason A. Mendoza, Monique S. Burton, Ellie Somers, Albert Hsu, Lauren Fay, Tonya M. Palermo, and Frederick P. Rivara. "Pilot Randomized Controlled Trial of an Exercise Program Requiring Minimal In-Person Visits for Youth With Persistent Sport-Related Concussion." *Frontiers in Neurology* 10 (2019). https://doi.org/10.3389/fneur.2019.00623.

The goals of this study were to conduct a 6-week, randomized control trial that assessed the feasibility and acceptability of the approach, collected pilot data on the effects of the STEP trajectory on concussive symptoms, and explored the impact of moderate vigorous physical activity. This study also introduced a component of minimal in-person visits. This research is very relevant as it further investigates the feasibility of programs that are easy and affordable to treat concussions using sub-symptom threshold, aerobic exercise. The research questions are very clear and are explicitly stated in the appropriate location. There are several research questions and identifying the main question is difficult. These research questions are descriptive

in their identification of the minimal visit aspect, and the STEP program. But they are casual in the one variable approach to see how the aerobic exercise impacts the sports related concussion recovery time in the adolescents.

This study used a randomized control trial for its study design. The study recruited participants from clinics at Seattle Children's Hospital as well as on-line. The participants were required to be between the ages of 12-18 and have been diagnosed with a sports related concussion by a clinician experienced with concussion management. Concussive symptoms (>/= 2) must also be present for inclusion. The study then randomized the participants in blocks of four. The groups were stratified by age and sex, however, allocation was weighted 2:1 toward the intervention group because the study wanted more data on feasibility and acceptability of the program. The participants then completed either the sub-threshold exercise program (STEP) or the control, stretching program.

One area of possible bias in the study was that the groups were blinded only to the randomization. It was obviously easy to tell which group was the exercise group and which was the stretching group.

The study consisted of 30 participants of which 17 were female and the average age was 15.5. 90% of the youth beginning the study completed it. Reasons were not given as to why these individuals did not complete the program.

Chi-square tests were used to assess overall demographics between the groups and interquartile ranges were used and compared to students t-tests. Acceptability and feasibility were measured using descriptive surveys. Finally, an exponential decay model was used to track recovery in both groups.

The data from this study support the conclusions that the sub-threshold exercise program (STEP) was both accepted, feasible, and effective. The intervention group showed significant decrease in recovery times when compared to the control, stretching group)

Limitations of this study include a small sample size (30) that do not allow the results to be extrapolated to larger groups of people due to the possibility of confounding variables.

These finding are important because they show not only that a program like STEP (sub-symptom threshold aerobic exercise) is beneficial in the treatment of sports related concussions, but that people as a whole are becoming accepting of these programs and a good treatment option for adolescents.

Cordingley, Dean, Richard Girardin, Karen Reimer, Lesley Ritchie, Jeff Leiter, Kelly Russell, and Michael J. Ellis. "Graded Aerobic Treadmill Testing in Pediatric Sports-Related Concussion: Safety, Clinical Use, and Patient Outcomes." ***Journal of Neurosurgery. Pediatrics*** **25, no. 6 (December 2016): 693–702. https://doi.org/10.3171/2016.5.PEDS16139.**

This study aimed to evaluate the safety, tolerability, and clinical use of graded aerobic treadmill exercise as both a tool for evaluation as well as treatment in pediatric patients who had recently received a sports related concussion. The study also aimed to discover if a submaximal aerobic exercise prescription had any effects on clinical outcomes in patients with post-concussion disorders. These questions were both very relevant after the background information was presented. Exercise has been researched as a new method of concussion treatment, however, few studies have been completed to evaluate the safety and efficacy with regards to pediatric patients. Many sports related concussions are suffered by young athletes and this research will be very important in treatment plans and assessments for their recovery. The research questions were very easily identified in the study and are located and presented appropriately. They are

explicitly stated as the last paragraph after the background and justification before going into the methods of the study.

This research questions are causal questions that are asking about the effects of the aerobic exercise on the concussion symptoms. There is also a descriptive component to the primary research question because it asks if the aerobic exercise is well tolerated in the pediatric population being evaluated. However, overall the study is evaluating how one variable, the aerobic exercise treatment, affects the children with post-concussion syndrome or post-concussion disorder.

Participants for his study were gathered using data gathered over a two-year period between 2014 and 2016 in a retrospective chart review. The study used only data from patients under the age of 19 who underwent aerobic treadmill testing. All of the patients were required to have a diagnosis of acute sports related concussion or post-concussion syndrome secondary to a sports related concussion. After being identified, the patients would report for more data collection regarding past medical and concussion history as well as epidemiological data. The patients would then complete a post-concussion symptom scale as well as a full physical exam before beginning the graded exercise treadmill testing. These results were then reviewed, and the patients were separated into groups (physically recovered, physiological post-concussion disorder, vestibulo-ovular post-concussion disorder, and cervicogenic post-concussion disorder). Patients qualifying for post-concussion disorder were then given a tailored submaximal exercise program as a treatment. The patients and their progress were routinely monitored and evaluated by the neurosurgeon. These methods were appropriate for the study because they were continuously identifying new patients based on diagnoses concussion disorders. The study methods were safe for the patients. However, using these methods, the study could conclude only

that the treatment and aerobic evaluations were safe to use on the pediatric population. The lack of control group does not allow for the study to extrapolate any improvement over other treatments such as strict rest. Instead of random separation to control for demographic factors and other variable, the studied separated individuals by their performance on the graded treadmill exercise that lead to slightly different diagnoses. This then led to differences in the tailored submaximal aerobic exercise treatment plan. This certainly limited the scope of the study.

Potential bias present in the study could include the area in which the study took place (Canada) and possible differences in the current treatment of concussions or possibly how these injuries are viewed in the public and reported compared to the US. There are also likely differences in activities leading to the concussions.

In total, 106 patients with sports related concussions completed the aerobic graded treadmill test. The median age was 15.1 years and 43.4% of the patients were male. 8.5% of the patients were lost to follow up. The study was not uniform for all patients and some were either not able to return to sports due to continuing treatment (8.5%) or were classified as clinically not improved by the study (6.9%).

The conclusion of the study indicates that the graded treadmill exam was well tolerated by the patients and gave valuable information on the state of recovery for the patients. These concussions are supported by the data because there were 90.2% clinical recovery and return to play following the exercise. The study concluded that more research must be done to identify how necessary it would be for patients to use these tools given that they require access to specialized personnel and equipment.

Limitations for the study included that only patients who were in clinics and therefore likely had more severe injuries were included in the study. Another limitation was that the

sample size, while not meaninglessly small, was not large enough to extrapolate data to whole populations of people. Finally, as discussed earlier, the lack of control group significantly hindered the findings of the study and what can be taken from the results.

This study adds greatly to the knowledge of the field because it allows other researchers to use these data as justification for the safety of the protocols used. It will allow future researchers to build on these findings and perform more rigorous tests and studies with the knowledge that the testing is indeed safe for the population.

Grabowski P, Wilson J, Walker A, Enz D, Wang S. Multimodal impairment-based physical therapy for the treatment of patients with post-concussion syndrome: A retrospective analysis on safety and feasibility. *Physical Therapy in Sport.* 2017;23:22-30. doi:10.1016/j.ptsp.2016.06.001.

The purpose of this study was to assess how combining sub-symptom threshold exercise with comprehensive cervicovestibular physical therapy would affect the treatment of post-concussion symptoms. This research question is very important because it assesses how combining newer methods of concussion treatment will affect the recovery of the patient.

The study will be a retrospective study that will analyze the outcomes of 25 patients who were treated at the University of Wisconsin Hospitals and Clinics. Participant cases in this studied were required to be between the ages of 12 and 20 and be diagnosed with a sports related concussion based on World Health Organization criteria. These criteria included cognitive deficits in attention and/or memory. The symptoms had to be present for at least 3 weeks but no longer than 36 weeks and at least 2 PT visits were required. In addition to at least 3 weeks of symptoms, the case needed to include at least one other modifier: female, younger than 18, history of prior concussion, history of cognitive or affective disorder, dizziness, fogginess or

retrograde amnesia noted at time of injury, post-injury PCSS score of greater than 18, post-injury PCSS migraine score greater than 15. Any patient with symptoms lasting longer that 6 weeks were also admitted.

The cases had all been evaluated by physical therapists, and specific aerobic evaluation tests were used to classify symptoms. After this evaluation, the patients performed specific PT exercises based on the exam findings that consisted of 3 specific components; sub-symptom threshold cardiovascular exercise, vestibular/oculomotor therapeutic exercised, and cervicothoracic manual therapy and therapeutic exercise. The prescribed exercise was to be completed 5-6 days per week at an intensity of 80% of the symptom threshold heart rate identified during the initial testing. Walking, jogging, and stationary biking were acceptable forms of exercise. Home exercise programs were also prescribed as part of the physical therapy to work on the participants' balance, gaze, and convergence training.

Of the 33 initial cases, 8 were excluded leaving 25 for analysis. PCSS was used as a tool for evaluation as the study progressed. BESS and GXTs were also collected from the cases records. A mixed linear affects model was used to evaluate the change in outcomes based on age, gender, initial PCSS score, history of prior concussion, cognitive or affective disorder, and migraines or chronic tension headaches. PCS was evaluated after PT evaluations for physiologic, vestibular/oculomotor, and cervicogenic symptoms over a 3-month time span. Significant patient education was also given over this time period.

The study showed a statistically significant decreasing trend ($p<0.01$) for total PCSS scores as the study progressed. 2 patients reported mild symptom exacerbation while performing at home exercises that required alteration of the exercise prescription. These data demonstrated that this multimodal approach that included both individualized PT and sub-symptom threshold

aerobic exercise is feasible, safe, and viable as a treatment plan for individuals recovering from post concussive symptoms. This type of study shows that those suffering from sports related concussions can improve more quickly without suffering many negative effects of inactivity, however, they can remain safe from the major problems associated with early return to athletics.

Limitations in this study include a lack of a control group. This does not allow the results to be directly attributed to the treatment. The symptom decline could have been due to many other variables not accounted for by a control group. Also, many of the exercises were done at home, allowing for other, unaccounted for variable, to have made an impact on the recovery time of participants. There was also a wide variability in the timing, frequency, and number of physical therapy appointments within the case cohort. Finally, the sample size (25) was too small to extrapolate large scale population of individuals with concussion symptoms.

This research is very important as it provides further data on the importance of large-scale studies. The data are also important in showing how individualized, multimodal treatments are beneficial to patients recovering from concussions.

Gagnon I, Grilli L, Friedman D, Iverson GL. A pilot study of active rehabilitation for adolescents who are slow to recover from sport-related concussion. *Scandinavian Journal of Medicine & Science in Sports*. 2015;26(3):299-306. doi:10.1111/sms.12441.

This study aimed to examine the use of an active rehabilitation program to speed the recovery of children and adolescents who were slow to recover following a concussion. The study question is very relevant, and its efficacy was justified using in the background section by supplying past research highlighting the safety and positive results of the exercise regiments on concussion/post traumatic head injury rehabilitation. The research is further justified in the background by explaining how some children experience persistent concussion symptoms after

the expected recovery timeframe. A problem for clinicians is that, for a long time, rest was the treatment of choice for adolescent athletes and almost anyone suffering post-concussion symptoms. These protocols also did not have a specified time frame about how long the rest should be maintained. This research aims to show that rest is not the only treatment and that other, better treatments can be used to actively rehabilitate concussions to prevent further damage of young athletes.

The studied used 10 adolescents between the ages of 14 and 18 who were referred consecutively to the Concussion Clinic of the Montreal Children's Hospital Trauma Center. These adolescents were included in the study due to their slow recovery from a sports related concussion. The criteria for the slow recovery was concussion symptoms lasting more than one-month post injury. Before beginning the program, the participants were screened for coexisting cervical, oculomotor, and/or vestibular impairments. Finally, before beginning the program, information was collected on the participant's pre-injury characteristics, trauma history (including previous concussions), mechanism of injury, and recovery to date.

The participants were then started on the aerobic exercise regimen where they were asked to choose between walking/jogging on the treadmill or using a stationary bicycle. There activities were also combined with an interactive gaming system (Nintendo wii) to distract the participants and make the activities more enjoyable. Heart rate and heart rate variability were measured throughout the exercises using portable heart rate monitors that were provided to the participants. The goal of the exercise was for the participants to exercise at 60% of their maximum heart rate capacity for a maximum of 15 minutes. Their heart rate maximum was predicted using the 220 - age formula. There were also coordination exercises that were chosen by the participant based on a sport of choice. Participants were instructed to complete these exercises, which included

sliding on a board as if ice skating, soccer ball drills, hockey stick handling, and more, for a maximum of 10 minutes. Heart rate was also measured here. Finally, visualization and imagery techniques were used along with workouts, where the participant was instructed to choose a motor component of a sport and practices positive visualization under the instruction of the physical therapist. The program lasted for 6 weeks at which time the participants were re-evaluated.

The participants in this study were evaluated by an external evaluator. The primary method of evaluation was the use of the post-concussion scale. Other evaluation methods included mood, energy level, balance, coordination, and anxiety. Paired sample t-tests were used to assess outcomes.

The study was able to show positive results and decreased in symptoms in the participants after the 6-week examination. The data from this study showed that all participants showed symptom improvement and were able to return to full activity participation following their sports related concussion. The study was also able to show that the program was safe and feasible for the participants to complete.

Problems with this study stem from its lack of both a control group and randomization. These missing aspects of the study do not allow for the positive results to be attributed only to the program. Also, if the program was solely responsible for the symptom improvement, there is no way to know which parts were beneficial and which parts were not. The sample size of this experiment was also very small.

This research is important as it gives justification to complete a more robust, randomized control trial to fully examine how efficacious the aerobic exercise is on concussion rehabilitation.

Leddy JJ, Haider MN, Hinds AL, Darling S, Willer BS. A Preliminary Study of the Effect of Early Aerobic Exercise Treatment for Sport-Related Concussion in Males. *Clinical Journal of Sport Medicine*. 2019;29(5):353-360. doi:10.1097/jsm.0000000000000663.

The purpose of this study was to compare the affects sub-symptom aerobic exercise has on specific symptoms compared to a strict rest treatment. Because current recommendations for concussion rehabilitation are no longer strict rest, a historic cohort was used as a control group. The researchers were hypothesizing that the aerobic treatment would lead to shorter recovery times. The study also planned to examine daily symptom scores to examine differences in physical, cognitive, sleep, and affective symptoms between the cohorts. This research is important in assessing how specific symptoms are affected in a specific population by the sub-symptom threshold exercise.

Despite the groups not being randomly distributed, both were similar in age, sex, and athletic background. Both groups included adolescent males between the ages of 13 and 18 that presented to the University Concussion Management Clinics less than 10 days post concussive injury. All participants were diagnosed with a concussion by an experienced sports medicine clinician. Participants were to be excluded from the study if they showed; evidence of focal neurological deficit, an inability to exercise, increased cardiac risk, current diagnosis of ADHD, learning disorder, depression, or anxiety, history of moderate to severe traumatic brain injury, the inability to understand English, recovery in 2 days or less from initial visit, sustaining another head injury before recovery, having an initial PCSS score of 5 or less, not completing at least 75% of daily reports. In the exercise group, the Buffalo Concussion Treadmill Test was performed to get a baseline and calculate exercise prescription. The rest group was instructed to strictly rest according to previous treatment guidelines, while the exercise group was instructed

to complete their individualized sub-symptom threshold exercise regimen that included a heart rate goal of 80% of symptom exacerbation heart rate based on initial treadmill test. Both groups reported symptoms on an online data form every night for 2 weeks.

2 sample t tests with unequal variances were used to assess recovery times between the groups based on age, previous concussions, days from injury to initial visit, and symptoms at first visit. There were 67 participants used in the study with 2 withdraws from the exercise group and 3 from the rest group. due to non-compliance with the exercises. The data were able to show that recovery time was significantly faster in the exercise group compared to the rest group. This was true in all symptom categories examined.

These results are very important because they were able to safely show the efficacy of the exercise on concussion symptom recovery as well as its statistical superiority over strict rest. These data are important to further show the safety of this type of exercise following a concussive injury.

Issues with this study include that it was not fully randomized, so the results cannot be completely externally extrapolated to larger groups. The sample size of this experiment was also rather small. Finally, this study only used males of a small age group.

This research is very important to call for larger studies on the wide efficacy of this type of treatment for concussive symptoms.

Leddy, John J., Mohammad N. Haider, Michael J. Ellis, Rebekah Mannix, Scott R. Darling, Michael S. Freitas, Heidi N. Suffoletto, Jeff Leiter, Dean M. Cordingley, and Barry Willer. "Early Subthreshold Aerobic Exercise for Sport-Related Concussion: A Randomized Clinical Trial." *JAMA Pediatrics* 173, no. 4 (April 1, 2019): 319–25. https://doi.org/10.1001/jamapediatrics.2018.4397.

The goal of this study was to evaluate the use of individualized, sub-symptom threshold aerobic exercise and its effectiveness in speeding the recovery in adolescents with sports related

concussions vs a placebo group. The research question is very relevant because it fills a very critical role in the literature where it will begin testing, with a control, the effectiveness of the sub-symptom threshold exercise on sports related concussion recovery. The current protocol for concussion recovery, as discussed by the article in its introduction, is “rest is best.” This protocol comes from studies done on animals and has since been challenged by data about exercise as a better treatment alternative. Previous studies have evaluated the safety of the exercise post sports related concussion, but this study aimed to evaluate its efficacy. The research question in the study is easily identified in the last paragraph of the background where it is explicitly stated. The research questions is causal and will evaluate one variable, sub-symptom threshold exercise, and its effects on sports related concussion recovery.

The design for this study was a parallel randomized control trial. The two groups for the trail were the exercise group and the placebo stretching group. The study lasted 30 days after which those still requiring treatment were provided interdisciplinary care. The study located participants by using 3 outpatient concussion management clinics. The participants were required to be between the ages of 13 and 18 and needed to present with a sports related concussion in the last 10 days. The concussion required diagnosis from a sports medicine physician. The patients then all underwent a baseline assessment that included a symptom questionnaire, a physical exam, a cognitive exam, and an exercise tolerance treadmill test. The participants were then randomly sorted participants into either the aerobic exercise or the stretching group. The groups were stratified by sex as well as location to ensure the groups were as similar from a demographic perspective as possible. The groups then completed their program which was either 1) using aerobic exercise to achieve 80% of symptom threshold heart rate or 2) a prescribed stretching program. This study design was appropriate because it allowed researchers a means to

compare the aerobic exercise to a more common (resting) protocol, while still allowing for control of the placebo effect because participants in the stretching group did not know that they were the control. The randomized control trial is the gold standard for this kind of research, making this a strong study design for this research question.

One area for potential bias is that the researchers were able to see clearly which group was which, allowing for potential bias when evaluating results. Another potential, yet unlikely, area for bias is that the participants could tell which group they were in. This bias was accounted for in that the participants did not know which group was the control. However, it is possible that they had a predilection for one intervention, it could introduce bias.

The sample size of the study began with 165 participants but was narrowed down to 113 participants randomized into the groups due to inclusion/exclusion criteria. There were no differences in age, sex, or other demographic variable between the groups. The groups were not different in previous concussions, time since injury, or initial symptom score. 10 participants did not complete the study due to loss to follow up (7) or were forced to discontinue due to illness or another reason (unspecified).

The study evaluated recovery time and daily symptom reporting to analyze the effectiveness of the intervention. The recovery time was evaluated using a logistic parametric survival model. The results showed that the aerobic exercise group recovered from the concussions significantly faster than the stretching group. The incidence of delayed recovery was also higher in the stretching group than the aerobic exercise group. The conclusions of this study are supported by the data, which show shorter recovery times in the aerobic exercise group, after controlling for age, sex, concussion history, and other variables taken into account which all affect recovery times.

Limitations for this study include that the participants were not constantly monitored. This leaves the question of "how much did they stick to the treatment" up to individual reporting. Also, other potential variable in the participant's lives could potentially account for some changes, as the patients were not constantly monitored.

These results contribute greatly to knowledge in this field. They give great data about how "rest is best" may not be the best treatment for adolescent recovery from sports related concussions. More, larger scale studies must be done to expand on these results, as well as evaluate a "dose" or exercise that is best for individual patients.

Willer BS, Haider MN, Bezherano I, et al. Comparison of Rest to Aerobic Exercise and Placebo-like Treatment of Acute Sport-Related Concussion in Male and Female Adolescents. ***Archives of Physical Medicine and Rehabilitation*****. 2019;100(12):2267-2275. doi:10.1016/j.apmr.2019.07.003.**

This study used a comparison of cohorts to compare 3 different treatments of concussion rehabilitation. The study intended to differentiate between a prescribed rest group, a placebo group, and an exercise group. This study also wanted to differentiate recovery between the genders within the groups. This research is very relevant as concussions and rehabilitation from them continues to rise in importance in the world of sports and athletics. As more data continues to surface on the consequences of untreated concussions, more research must be done on how effectively and analytically to rehabilitate athletes with concussions. This study is important because it more directly compares the placebo effect of exercise with actual sub-symptom threshold exercise as well as a group that is placed on strict rest.

Each group in the study was made of both male and female adolescents between the ages of 13 and 18 presenting to a University of Buffalo concussion management clinic within 10 days

of sustaining a sports related concussion. The participants were then evaluated by sports medicine physicians where they were diagnosed based on international guidelines, questioned about concussion history, given a thorough cognitive evaluation, given a symptom questionnaire, and a specific physical examination. The participants were excluded from the study if they: showed evidence of focal neurologic deficit, had a history of moderate or severe traumatic brain injury, had a current diagnosis of attention deficit hyperactivity disorder, a learning disorder, depression, anxiety, or history of greater than 3 concussions, could not understand English, or had a symptom severity score of less than 5 on initial visit. The participants were then prescribed their treatment and followed up with the physician weekly for the first 4 weeks unless recovery came before then. The groups reported symptoms daily online at night.

The exercise group was prescribed sub-symptom threshold exercise at 80% of symptom heart rate that was identified at the initial evaluation. The participants were given heart rate monitors and instructed to walk, jog, or bike at home or in a gym for 20 minutes a day with a 5-minute warm up and 5-minute cool down. They were also instructed to stop exercising if they began to experience symptoms. The placebo group was prescribed a stretching and breathing exercise that was meant not to elevate the heart rate. They were provided a booklet from which to follow that detailed the exercises to be performed. They were to perform the exercises for 20 minutes a day. The rest group were told that they should rest to allow their brains to heal and limit any activities that could raise their heart rate. They were also told to avoid television, their phones, and social interactions as much as possible.

The primary outcome studied was the days to recovery from date of injury. And analyses were conducted to assess differences between the 3 groups. To do this, ANOVA and Chi-square tests were completed to compare the differences between the groups related to sex, prior

concussions, number of physical exam signs, and incidence of delayed recovery. Chi-square tests were again used to compare male and female participants in each group for all of the above differences as well as days to recovery.

There were a total of 169 participants in the study. Of those, 1 was lost from the exercise group, 1 from the placebo group, and 5 from the rest group. 3 participants from the exercise group, 4 from the placebo group, and 5 from the rest group were removed because they did not report their daily symptoms. The data were able to show that those in the exercise group had significantly shorter times to recovery compared to the placebo and the strict rest group. The strict rest and placebo groups did not differ significantly from each other in their times to recovery. Also, no significant difference was found in recovery times between males and females. This was true in all treatment groups.

Limitations in this studied included that the groups were not randomized and were in fact recruited a different times. The rest group also had a significantly smaller number of female students compared to the other 2 groups. Also, the study relied heavily on compliance and self-reporting of the participants. This lack of total control over the study could lead to other variables being introduced.

These data are very important because they allow for a further push for bigger and more robust studies to expand on these findings. These data show that older treatment protocols are worse for both genders compared to the exercise and more research must be done to see more differences between genders as well as between different levels of exercise.

Discussion

This search revealed several studies that fit the criteria for inclusion. The studies were able to shed light on many factors surrounding the research question. As shown on appendix 3, 6 of the studies were able to demonstrate positive results about the efficacy of sub-symptom threshold exercise as a treatment for concussions in adolescent athletes. Over 50% of the cases were randomized control trials that showed significant ($P<.05$) data supporting the hypothesis. Because of the age group specification, case reviews and retrospective cohorts were other easily obtained data to study that also demonstrated both the safety and efficacy of the treatment.

The strength of the data collected is that the data demonstrated overwhelmingly positive support for the treatment. All of the data collected showed support for the treatment and showed in that negative effects of the programs or treatments were rare outliers. Along with safety and efficacy, several studies also demonstrated that these programs were easily accomplished by the participants, meaning they were more likely to stick to and complete the treatment regimen. This is crucial in the treatment of concussions because most is done at home without the supervision of a clinician. Easy to do exercises that patients are likely to see to their completion is vital to the success of the treatment.

One issue with the data collected was the lack of long term follow up data on these patients. Appendix 1 demonstrates the lack of this aspect of clinical trials in the studies evaluated. Before these treatments become mainstream, it will be essential for both patients, their parents, and clinicians to know what long term health outcomes and risks can be attributed to these treatment programs. As discussed, concussions at a young age, such as the population in these studies, come with several long-term health risks. It will be important to have concrete,

generalizable data to show how this treatment program mitigates those risks or at least does not increase their likely hood or severity.

Another issue with these data is the lack of generalizability in the studies. As shown on appendix 2, several of the studies have small sample sizes. These will need to be increased vastly in order to produce data that is generalizable to the larger population of adolescent athletes from various backgrounds and medical histories. Accompanying this on appendix 2, much of the data were found to have bias attributed to the trial, therefore also making large-scale generalizability difficult.

While these data were able to demonstrate safety, efficacy, and sustainability of sub-symptom threshold exercise as a treatment for concussions in adolescent athletes, more data must be gathered to show long term success and generalizability of the success.

Conclusion

Concussions are a hugely prevalent issue in adolescent athletes that can lead to neurological deficits in both the short and long term in managed incorrectly. For decades, the symptoms of concussions have been managed exclusively through strict mental and physical rest. These data evaluated demonstrate that sub-symptom threshold exercise may be a more efficacious treatment that leads to shorter recovery times and fewer lasting symptoms than the strict rest treatment.

While these data are very promising, more studies that include larger sample sizes with less bias must be completed. In order for this treatment to become mainstay, it must be proven to work in large populations with various backgrounds, health histories, mechanisms of injury, and other confounding variables. These robust studies can rely on the studies evaluated here to demonstrate the safety of the programs as negative effects were very rare.

Another crucial aspect of future data must be studies that evaluate long-term health outcomes of adolescent athletes treated with strict rest and the exercise programs. The long-term health of these adolescent athletes is the main concern for clinicians when presented with these cases. Therefore, concrete data must be collected to ensure that all risk of long-term damage is mitigated and not worsened through the exercise treatment program.

This study demonstrates a positive step towards the 1st line use of these exercise treatment programs. The data show that they are safe, efficacious, and that patients reliably complete them. More data must be collected to ensure their full success, but these data can be used as a foundation on which to justify the completion of those large-scale studies. This treatment, or ones like it, could help lessen the burden of the negative health impacts of concussions on young athletes in communities across the country and the world, and the pursuit of these data must remain paramount to the research community.

References

Carman, Aaron J., Rennie Ferguson, Robert Cantu, R. Dawn Comstock, Penny A. Dacks, Steven T. DeKosky, Sam Gandy, et al. "Expert Consensus Document: Mind the Gaps—Advancing Research into Short-Term and Long-Term Neuropsychological Outcomes of Youth Sports-Related Concussions." *Nature Reviews Neurology* 11, no. 4 (April 2015): 230–44. https://doi.org/10.1038/nrneurol.2015.30.

Chrisman, Sara P. D., Kathryn B. Whitlock, Jason A. Mendoza, Monique S. Burton, Ellie Somers, Albert Hsu, Lauren Fay, Tonya M. Palermo, and Frederick P. Rivara. "Pilot Randomized Controlled Trial of an Exercise Program Requiring Minimal In-Person Visits for Youth With Persistent Sport-Related Concussion." *Frontiers in Neurology* 10 (2019). https://doi.org/10.3389/fneur.2019.00623.

Cordingley, Dean, Richard Girardin, Karen Reimer, Lesley Ritchie, Jeff Leiter, Kelly Russell, and Michael J. Ellis. "Graded Aerobic Treadmill Testing in Pediatric Sports-Related Concussion: Safety, Clinical Use, and Patient Outcomes." *Journal of Neurosurgery. Pediatrics* 25, no. 6 (December 2016): 693–702. https://doi.org/10.3171/2016.5.PEDS16139.

Daneshvar, Daniel H., Christopher J. Nowinski, Ann McKee, and Robert C. Cantu. "The Epidemiology of Sport-Related Concussion." *Clinics in Sports Medicine* 30, no. 1 (January 2011): 1–17. https://doi.org/10.1016/j.csm.2010.08.006.

Gagnon I, Grilli L, Friedman D, Iverson GL. A pilot study of active rehabilitation for adolescents who are slow to recover from sport-related concussion. *Scandinavian Journal of Medicine & Science in Sports*. 2015;26(3):299-306. doi:10.1111/sms.12441.

Grabowski P, Wilson J, Walker A, Enz D, Wang S. Multimodal impairment-based physical therapy for the treatment of patients with post-concussion syndrome: A retrospective analysis on safety and feasibility. *Physical Therapy in Sport*. 2017;23:22-30. doi:10.1016/j.ptsp.2016.06.001.

Junn, Cherry, Kathleen R. Bell, Christian Shenouda, and Jeanne M. Hoffman. "Symptoms of Concussion and Comorbid Disorders." *Current Pain and Headache Reports* 19, no. 9 (September 2015): 46. https://doi.org/10.1007/s11916-015-0519-7.

Leddy JJ, Haider MN, Hinds AL, Darling S, Willer BS. A Preliminary Study of the Effect of Early Aerobic Exercise Treatment for Sport-Related Concussion in Males. *Clinical Journal of Sport Medicine*. 2019;29(5):353-360. doi:10.1097/jsm.0000000000000663.

Leddy, John J., Mohammad N. Haider, Michael J. Ellis, Rebekah Mannix, Scott R. Darling, Michael S. Freitas, Heidi N. Suffoletto, Jeff Leiter, Dean M. Cordingley, and Barry Willer. "Early Subthreshold Aerobic Exercise for Sport-Related Concussion: A Randomized Clinical Trial." *JAMA Pediatrics* 173, no. 4 (April 1, 2019): 319–25. https://doi.org/10.1001/jamapediatrics.2018.4397.

McCrory, P., W. Meeuwisse, K. Johnston, J. Dvorak, M. Aubry, M. Molloy, and R. Cantu. "Consensus Statement on Concussion in Sport: The 3rd International Conference on Concussion in Sport Held in Zurich, November 2008." *British Journal of Sports Medicine* 43, no. Suppl 1 (May 1, 2009): i76–84. https://doi.org/10.1136/bjsm.2009.058248.

Nonfatal Traumatic Brain Injuries Related to Sports and Recreation Activities Among Persons Aged ≤19 Years --- United States, 2001--2009." Accessed October 5, 2018. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6039a1.htm.

Theadom, Alice, Varsha Parag, Tony Dowell, Kathryn McPherson, Nicola Starkey, Suzanne Barker-Collo, Kelly Jones, Shanthi Ameratunga, Valery L. Feigin, and BIONIC Research Group. "Persistent Problems 1 Year after Mild Traumatic Brain Injury: A Longitudinal Population Study in New Zealand." *The British Journal of General Practice: The Journal of the Royal College of General Practitioners* 66, no. 642 (January 2016): e16-23. https://doi.org/10.3399/bjgp16X683161.

Thomas, Danny George, Jennifer N. Apps, Raymond G. Hoffmann, Michael McCrea, and Thomas Hammeke. "Benefits of Strict Rest after Acute Concussion: A Randomized Controlled Trial." *Pediatrics* 135, no. 2 (February 2015): 213–23. https://doi.org/10.1542/peds.2014-0966.

Willer BS, Haider MN, Bezherano I, et al. Comparison of Rest to Aerobic Exercise and Placebo-like Treatment of Acute Sport-Related Concussion in Male and Female Adolescents. *Archives of Physical Medicine and Rehabilitation*. 2019;100(12):2267-2275. doi:10.1016/j.apmr.2019.07.003.

Appendices

Appendix 1. Comparison of study designs investigating the use of exercise s/p sports related concussion

Study	Basic design	Population recruitment	Type of treatment	Duration of study	Follow up time
Chrisman et al. 2019	Randomized controlled trial	12-18 y/o from Seattle concussion clinic over 9-month period	Subthreshold exercise 10 minutes per/day increased by 10 minutes per week (60 minutes by end). Goal 80% symptom heart rate	6 weeks	3 and 6 month surveys
Cordingle et al. 2016	Retrospective chart review	<20 y/o patients with sports related concussions who underwent graded aerobic treadmill testing between 10/2014 and 2/2016 in Canada	Repeated treadmill testing	Na	Na
Gagnon et al. 2015	Case series	Montreal children's hospital concussion clinic	Gradual, light aerobic exercise, coordination exercise, mental imagery, reassurance, stress reduction strategies. 15 minutes at 60% max HR (220-age)	Symptom resolution	Na
Grabowski et al. 2017	Retrospective cohort	12-25 year old patients at university hospital sports medicine facility	Combining physical therapy, vestibular/oculomotor and cervical rehab, and sub-symptom threshold exercise	Na	Na
Leddy et al. 2019	Quasi-experimental	University sports medicine centers	Exercising 20 minutes daily at sub-symptom threshold levels	14 days	30 days
Leddy et al. 2019	Randomized clinical trial	13-18 y/o at university concussion senters	Treadmill exercise for 20 minutes per day	Symptom resolution	Na

Appendix 2. Comparison of evaluation methods of studies investigating the use of exercise s/p sports related concussion investigating the use of exercise s/p sports related concussion

Study	Sample size	Blinding	Lost to follow up	Statistical technique used	Bias	Generalizability
Chrisman et al. 2019	30	Adequate	2 – reasons unknown	Regression models of symptoms Qualitative interviews	Adequate	moderate/ inadequate
Cordingle et al. 2016	106	Na	Na	Dichotomous characteristics were proportioned or summarized by median and interquartile range	Moderate	Moderate
Gagnon et al. 2015	10	Na	Na	Paired sample t-tests	Inadequate	Poor
Grabowski et al. 2017	25	Na	Na	Paired t tests	Inadequate	poor
Leddy et al. 2019	54	Adequate	None	Mixed linear models	adequate	Moderate
Leddy et al. 2019	103	Adequate		Paired t test, models, ranges	Adequate	Adequate

Appendix 3. Comparison of study results of studies investigating the use of exercise s/p sports related concussion

Study	Research question	Outcomes measured	Results	Did results answer research question	Were results significant
Chrisman et al. 2019	Does minimal visit, subthreshold exercise decrease post-concussion symptoms compared to control group Does minimal visit STEP decrease fear/avoidance of exercise post TBI	Accelerometer measurements at baseline and at 6 weeks Weekly symptom assessments Fear surveys	Significant rate of decline of symptoms Improvement in reported quality of life "kinesiophobia" Significantly declined in parents Not in children	yes	P=.02 P=.0045 P= .0096 P=.13
Cordingle et al. 2016	Evaluate safety, tolerability, and clinical outcomes of submaximal aerobic exercise in patients with post concussion disorder	Post concussion scale surveys Graded treadmill testing	Recovery demonstrated in 96.9% of tested patients	yes	No, no control
Gagnon et al. 2015	Determine effectiveness of active rehabilitation on adolescents slow to recover from concussion	Heart rate during exercise	Decreased symptoms were shown in post concussion scale, increases in mood, energy level, balance and coordination were recorded with decreases in anxiety	Yes but without real comparison	No, no control
Grabowski et al. 2017	Is combining safe/feasible PT along with vestibular/ oculomotor therapy and sub symptom threshold exercise a safe and beneficial treatment for patients with post concussive symptoms	Post concussion symptom scale, maximum symptom free heart rate, gxt duration, balance error scoring, and adverse effect number	Significant decrease in post concussion symptom scale score 23% increase in gxt Bess errors decreased 52%	Yes	P<0.01 but no control group
Leddy et al. 2019	What effect does prescribed aerobic exercise have on acute, sport-concussion recovery compared to rest	Days to recovery, exercise tolerance	Recovery time was significantly shortened All symptoms decreased with time with no correlation to treatment Delayed recovery was 0% in exercise group but 13% in rest group	yes	P=0.048
Leddy et al. 2019	What is the effectiveness of sub-symptom threshold aerobic exercise vs placebo-like stretching	Time to recovery from symptoms	Recovery time was less in the exercise group than the placebo (Stretching) group	Yes	P=.009

Study	Research question	Outcomes measured		Did results answer research question	Were results significant
Chrisman et al. 2019	Does minimal visit, subthreshold exercise decrease post-concussion symptoms compared to control group Does minimal visit STEP decrease fear/avoidance of exercise post TBI	Accelerometer measurements at baseline and at 6 weeks Weekly symptom assessments Fear surveys		yes	P=.02 P=.0045 P=.0096 P=.13
Cordingle et al. 2016	Evaluate safety, tolerability, and clinical outcomes of submaximal aerobic exercise in patients with post concussion disorder	Post concussion scale surveys Graded treadmill testing		yes	No, no control
Gagnon et al. 2015	Determine effectiveness of active rehabilitation on adolescents slow to recover from concussion	Heart rate during exercise		Yes but without real comparison	No, no control
Grabowski et al. 2017	Is combining safe/feasible PT along with vestibular/ oculomotor therapy and sub symptom threshold exercise a safe and beneficial treatment for patients with post concussive symptoms	Post concussion symptom scale, maximum symptom free heart rate, gxt duration, balance error scoring, and adverse effect number		Yes	P<0.01 but no control group
Leddy et al. 2019	What effect does prescribed aerobic exercise have on acute, sport-concussion recovery compared to rest	Days to recovery, exercise tolerance		yes	P=0.048
Leddy et al. 2019	What is the effectiveness of sub-symptom threshold aerobic exercise vs placebo-like stretching	Time to recovery from symptoms		Yes	P=.009

Table 3. Comparison of study results of studies investigating the use of exer

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