CRITICALLY APPRAISED TOPIC

FOCUSED CLINICAL QUESTION

For a 31 year old military male suffering from more than one concussion in the past year, does progressive return-to-activity (PRA) dependent on symptoms or a graded progression independent of symptoms result in lower concussion-related disability ratings (physical, cognitive, psychological) in the long term (>10 years)?

AUTHOR

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CLINICAL SCENARIO

DM is a 31 year old military male, who has sustained two concussions within a six month period, which have went untreated for two years. His symptoms include headache, dizziness, and nausea with strenuous exertion between 7-10 on the Borg CR10 Rate of Perceived Exertion (RPE) scale. He has a history of additional concussions when he was 16 and 27 years old. Other pertinent medical history includes heavy caffeine use, alcohol abuse, and childhood sexual trauma. DM is otherwise healthy.

SUMMARY OF SEARCH

Eight studies were identified that met the inclusion/exclusion criteria, two of which were Level 1 randomised controlled trials and selected for review and analysis. Key findings from each study are as follows.

Mild to moderate aerobic exertion between 0-6 RPE on the Borg neither increases nor decreases recovery time, but it does decrease symptom intensity during the recovery period, compared to strenuous aerobic exertion between 7-10 RPE on the Borg which increases symptom intensity and increases recovery time.[1]

12 weeks of aerobic exertion at a heartrate (HR) just below an individual's symptomatic threshold HR significantly decreases post-concussion symptoms, significantly increases threshold HR to near age-predicted HR maximum (HR_{max}), and restores normal brain activity patterns during cognitive exertion.[2]

CLINICAL BOTTOM LINE

Current military-specific evidence suggests that progressive return-to-activity (PRA) is the optimal intervention for servicemembers who have had a previous concussion in the past 12 months and are experiencing symptoms exacerbation with exertion.[3,4] However, this military-specific evidence is predominantly Level 5, with expert opinions and conclusions based on sports concussion literature. Therefore, it is unclear if PRA is actually best practice for servicemembers, especially those who have suffered multiple concussions over many years before seeking treatment. Patients who have gone untreated may have avoided noxious stimuli during early recovery and become hypersensitive to motion and exertion, in which case a graded-approach independent of symptoms - similar to return-to-activity following chronic pain – may provide superior results in long term symptom remittance and recovery.

This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor

The above information should fit onto the first page of your CAT

SEARCH STRATEGY

<table>
<tr><th colspan="5">Terms used to guide the search strategy</th></tr>
<tr><td colspan="2"><u>P</u>atient/Client Group</td><td><u>I</u>ntervention (or Assessment)</td><td><u>C</u>omparison</td><td><u>O</u>utcome(s)</td></tr>
<tr><td rowspan="2">Military
Servicemember
Army / Soldier
Navy / Sailor
Air Force / Airmen
Marine Corps / Marine
Conventional
Unconventional
Special Operat*
Warfighter
Officer
Enlisted
Noncommissioned Officer
Veteran</td><td>Concussi*
Mild Traumatic Brain Injury (mTBI)
Chronic
Multiple</td><td rowspan="2">“Progress* Return to Activity”, PRA
Borg, “Borg Scale”
“Perceived Rate of Exertion”, PRE
Exert*
“Pain Scale”
“Modified Borg Rating Scale for Dizziness”, MBRSD
“Visual Vertigo Analog Scale”, VVAS
“Patient Health Questionnaire”, PHQ-2, PHQ-9
Asymptomatic</td><td rowspan="2">“Graded Approach”
“Graded Progress*”
“Symptom Independent”, “independent of symptoms”, “regardless of symptoms”
heartrate, “heartrate variability”
Treadmill, aerobic*, cardio*</td><td rowspan="2">“Long term”, 10 years
Disab*
“Veterans Administration” VA, “disability rating”, “disability benefits”
Compensat*
Function*
Impair*
Physical
Psychological
Cognitive
“Return to Activity”
“Return to Work”
“Return to Duty”
Asymptomatic</td></tr>
<tr><td>Post-Concussi* Syndrome
Symptom*
Headache, cervical, ocular
“Post-traumatic migraine”
Nause*
Vision, blurred
Dizz*
Vestibular, vertigo
Mood, change, disturbance
Depress*
Anxiety
Aggress*
Insomnia, difficulty sleeping</td></tr>
</table>

Final search strategy (history):

#1 (military or warfighter OR service member OR veteran)

#2 (concussi* OR traumatic brain injury OR mTBI OR (mild NEAR TBI))

#3 (progress* return to activity OR exert* OR symptom dependent)

#1 AND #2 AND #3

Databases and Sites Searched	Number of results	Limits applied, revised number of results (if applicable)
PubMed	44	Human, Publication date within 5 years
Cochrane	20	Not applicable
Embase	5	Not applicable

INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria
Studies investigating *military* or sport-related *mild* TBI Studies investigating *intervention* for symptom remission and return-to-duty/activity
Exclusion Criteria
Studies with subject populations *<17* years old Studies investigating *severe* TBI Studies investigating drug therapies

RESULTS OF SEARCH

Summary of articles retrieved that met inclusion and exclusion criteria

Author (Year)	Risk of bias (quality score)*	Level of Evidence**	Relevance	Study design
Maerlender 2015 [1]	D&B 17/27	1b	moderate	Randomised Controlled Trial
Leddy 2013 [2]	D&B 16/27	1b	moderate	Randomised Controlled Trial
Schneider 2017 [5]	AMSTAR 7/11	2a	moderate	Systematic Review of case studies and series (non-RCT)
Schneider 2013 [6]	AMSTAR 4/11	2a	moderate	Systematic Review of case studies and series (non-RCT)
McLeod 2017 [7]	AMSTAR 7/11	2a	moderate	Systematic Review of case studies and series (non-RCT)
Helmic 2014 [8]	Not Applicable	5	high	Narrative Review
McCulloch 2015 [9]	Not Applicable	5	high	Narrative Review
Conder 2014 [10]	Not Applicable	5	moderate	Narrative Review

*Indicate tool name and score

**Use Portney & Watkins Table 16.1 (2009); if downgraded, indicate reason why

BEST EVIDENCE

The following 2 studies were identified as the 'best' evidence and selected for critical appraisal. Rationale for selecting these studies were:

- Maerlender 2015
- Leddy 2013

Although these the subjects (adult athletes) in these studies are only moderately relevant to the patient (military servicemember), they inform the topic (return-to-activity) with Level 1 evidence, and, whereas only Level 5 evidence exists specific to the patient's population and questioned intervention, these level 1 studies provide higher quality conclusions that can be applied from one physically fit population to another.

SUMMARY OF BEST EVIDENCE

(1) Description and appraisal of Programmed Physical Exertion in Recovery from Sports-Related Concussion: a randomized pilot study by (Arthur Maerlender, Wanda Rieman, Jonathan Lichtenstein, C Condiracci, 2015[1]

Aim/Objective of the Study/Systematic Review:
The aim of this study was to determine the effect of moderate physical exertion on recovery from concussion.
Study Design
In this pilot randomised controlled trial, subjects were assigned to either the control or exertion group, without proof of true randomisation, allocation concealment, or blinding. However, the computer-based Immediate Post-concussion Assessment and Cognitive Test (ImPACT) was used to compare subjects' previous pre-concussion scores with post-concussion scores in verbal memory, visual memory, visual-motor speed, reaction time, and total symptoms, in order to distribute subjects with varying symptom severity amongst the two groups. All subjects met daily with a research-trained athletic trainer (ATC) to monitor activity and symptom status until recovery was achieved. The primary outcome measure was recovery, which was operationally defined as the point in time at which test scores, balance, and symptoms returned to baseline. This included being asymptomatic after exertion.
Setting
University of Nebraska at Lincoln athletic department
Participants
There were 28 subjects included in this RCT. They were purposively recruited among college athletes who were assessed by university ATCs as having recently sustained a sports related concussion but whose injuries did not prevent them from performing the exercise protocol. The control group contained 12 females and 3 males and the exertion group contained 8 females and 5 males, with no significant between group differences in gender, age, time since injury, symptom severity, and number of previous concussions at baseline. One subject was medically dropped due to poor recovery progress, but not due to increased symptoms with exertion. Three subjects taking >50 days to recover were deemed incompliant with the study's protocol and removed from analysis. One subject had missing actigraph data and was excluded from actigraph analysis.
Intervention Investigated
Control
The control group received standard concussion care through the college athletic department and were instructed not to exert themselves beyond normal activities such as walking to class and studying. Treatment was supervised by a research-trained ATC, who met daily with each subject to monitor progress.
Experimental
The exertion group received standard concussion care through the college athletic department and rode a Schwinn Airdyne stationary bicycle daily for 20 minutes at a Rate of Perceived Exertion (RPE) between 0 (mild) and 6 (moderate) on the Borg CR10 RPE Scale. Treatment was supervised by a research-trained ATC, who met daily with each subject to monitor progress. If any symptoms emerged, then exercise ceased for 24 hours before being reinstituted.
Outcome Measures
The Borg CR10 Rated Perceived Exertion (RPE) Scale is a 10-point visual analog scale with scores ranging from 0 for "no exertion" to 10 for "very, very hard exertion". The Borg CR10 RPE was administered by a research-trained ATC to guide exertion between 0 to 6 during cycling, and subjects rated their overall RPE immediately after each ride. The Post-Ride Symptom Change Rating is an experimental scale to rate a change in 14 symptoms that can be provoked by exertion. Each symptom is rated as either "same or better", "slightly worse", "moderately worse", or "significantly worse". Rated symptoms include headache, dizziness, fatigue, blurred vision, poor concentration, processing time, light sensitivity, nausea, double vision, noise sensitivity, restlessness,

irritability, depression, and frustration. It was administered by a research-trained ATC immediately after each ride.

Actical Actigraph was used to continuously monitored subjects' ambient physical activity each 24 hour period, in order to compare normal activities levels between the groups. The actigraph device was outfitted by a research-trained ATC, and vigorous activity was measured in average minutes per day.

Main Findings

Measure	Mean	Range	Confidence Interval	P-Value
Days to Recovery with Exertion	15 days compared to 13 days in control group	Control 6-56 days Exertion 5-61 days	Not published	0.705

There was not a significant between-group difference in recovery time (p = 0.705). Although recovery for 53% of subjects in the exertion group exceeded two weeks, compared to 40% of subjects in the control group, this between-group difference was not statistically significant either (p = 0.464).

Based on Post-Ride Symptom Change Ratings, the most commonly provoked symptoms were headache, dizziness, and fatigue. Rides performed compliantly at mild exertion increased an average of 1.8 symptoms, rides performed compliantly at moderate exertion increased an average of 0.55 symptoms, and rides performed incompliantly at strenuous exertion increased an average of 7 symptoms (p-values not published). Notably, moderate exertion only provoked symptoms during initial rides and quickly dissipated over subsequent rides. Conversely, strenuous exertion prolonged symptom exacerbation and increased recovery time. Likewise, based on actigraph analysis, more vigorous physical daily activity increased recovery time by an average of 7 days +/-2 days (p = 0.039)

Original Authors' Conclusions

Mild to moderate physical exertion following a sports related concussion does not significantly impact recovery time. However, strenuous exertion exacerbates symptoms and have deleterious effects on recovery.

Critical Appraisal

Validity

Overall, this study's evidence is of fair quality.

Internal validity: Equal distribution of gender, age, time since injury, injury severity, and previous concussion between the control and experimental groups contributes to high internal validity. Likewise, the control group was appropriately used to inform the true treatment effect of exertion. However, though dropping a subject based on failure to recover may have been medically warranted for the subject's safety, excluding the subject's data from analysis indicates potential bias.

External validity: Results may be less applicable in the general population of individuals who are older, nonathletic, non-college educated, or male. Also, dropping three subjects for incompliance associated with delayed recovery detracts from external validity. If young, fit, athletically regimented individuals in a controlled university athletic department environment have difficulty complying, then the general population is likely to have difficulty complying as well. It is possible that parameters of the exercise protocol make it difficult to apply to and, thus, would contribute to the intervention's inefficacy in the general population.

Strengths: Although assignments were not random, they were controlled to equalize subject demographics between groups, which compensated for a small sample size. The exercise protocol was also well controlled, conducted in the university athletic department under the supervision of a research-trained ATC. Although there is no proof of ATC blinding, all measures were self-report or computer-generated, which at least somewhat mitigates evaluator bias, assuming ATCs did not influence subjects' self-reports. Although the control group may not have been exclusively designed as a placebo control, subjects may have felt that their instruction to limit exertion was in their best interest toward recovery, accounting for the placebo effect.

Weaknesses: Sample size was small for the between group analysis, posing the potential for error and contributing to poor external validity. Not all demographic and baseline data was presented, limiting ability of readers to draw conclusions about the impact of variables such as number of previous concussions. The Post-Ride Symptom Change Rating did not differentiate between same and better in its symptom ratings, rendering it unable to capture the full potential benefit of mild to moderate exertion on post-concussion symptoms. After symptom remittance, it is unclear how control subjects were confirmed as recovered, as they should have underwent at least a 20 minute bike ride at mild-moderate exertion without symptoms in order to be compared to the experimental group. Lastly, the ImPACT could have been used again post-intervention to validate recovery, although results could have been skewed by learner effect.

Interpretation of Results
Mild to moderate exertion neither improved nor impaired recovery time, but it did improve symptoms during the recovery period, which may contribute to cognitive and psychosomatic aspects of recovery beyond those symptoms measured in this study. Furthermore, moderate exertion appears to be the most effective intensity for symptom remission. Conversely, strenuous exertion actually worsens recovery time, confirmed by actigraph data of vigorous activity associated with deleterious effects that prolong recovery time (p = 0.39). Although confidence intervals are necessary to confirm clinical significance, the difference in symptom exacerbation between moderate and strenuous exertion appears clinically significant, with moderate exertion exacerbating only an average of 0.55 of 14 symptoms compared to strenuous exertion exacerbating an average of 7 out of 14 symptoms. Additionally, the .55 symptoms exacerbated by moderate exertion quickly dissipate, while the 7 symptoms exacerbated by strenuous exertion prolonged symptoms and increased recovery time.
Applicability of Study Results
Similar to DM, subjects were physically fit and college educated, likely representing a near equal neurologic reserve post-concussion. However, the high proportion of females in the study may have masked gender differences applicable to DM, who is male. Likewise, the impact of exertion on subjects' acute injury (average of 2 days since injury) may be less applicable to the chronicity of DM's injury and symptoms. Military operational tempo decreases the feasibility of both military provider and patient being able to meet daily for 20 minutes of supervised exertion. Though the intervention could be modified so that servicemembers self-guide their own exercise, this would rely on servicemembers' adherence to stopping exercise for 24 hours after symptom presentation. Yet, this self-limiting behaviour is counter to the military mindset and warrior ethos of "never quit", indicating that this intervention may only be effective in the military population if supervised by a medical provider. Subjects' history of previous concussions suggests increased applicability to DM, who has suffered multiple concussions, though published data would be more informative.

(2) Description and appraisal of Exercise Treatment for Post-concussion Syndrome: A Pilot Study of Changes in Functional Magnetic Resonance Imaging Activation, Physiology, and Symptoms by John Leddy, Jennifer Cox, John Baker, David Wack, David Pendergast, Robert Zivadinov, Barry Willer, 2013[2]

Aim/Objective
The aim of this study was to compare neural activation patterns during a cognitive task amongst healthy controls, post-concussion syndrome (PCS) subjects receiving a placebo intervention, and PCS subjects receiving an exercise intervention.
Study Design
In this pilot randomised controlled trial (RCT), the first five subjects with PCS were assigned to the experimental exercise group and the next five subjects with PCS were assigned to the placebo stretching group. While this assignment indicates lack of true randomisation and allocation concealment, it was done in an effort to blind subjects and equalize placebo effects among the two PCS groups. Prior to intervention, PCS subjects reported baseline symptoms using the post-concussion scale under the following conditions: (1) at rest, (2) after cognitive exertion, and (3) during physical exertion. The cognitive condition utilized the Automated Neuropsychological Assessment Metrics (ANAM) Math Processing subtest. The physical condition utilized the Balke treadmill test was used to identify each subject's threshold HR at which symptoms were exacerbated. Symptoms under the same conditions were recorded again upon recovery or at 12 weeks after intervention, under the same rest, cognitive, and exercise parameters. In addition to symptoms, functional magnetic resonance imaging (fMRI) was administered during rest and during cognitive exertion at baseline and again upon recovery or at approximately 12 weeks after intervention. fMRI was analysed with Statistical Parametric Mapping 5 software, providing true evaluator blinding. Recovery was operationally defined as the point in time at which subjects were able to exercise at age-predicted HR maximums without symptom exacerbation.

Setting
State University of New York at Buffalo concussion clinic, gym, and subjects' homes
Participants
There were 15 subjects included in this RCT. The five healthy controls were purposively recruited among competitive and recreational athletes in the university community without a history of prior concussion. One was male and four were female, and their ages ranged from 18-29 years old. One healthy control was dropped due to a scheduling conflict. The 10 subjects with PCS were purposively recruited among competitive and recreational university athletes who had been experiencing post-concussive symptoms for at least six weeks but no more than 12 months, with a heart rate threshold for symptom exacerbation. PCS subjects in the placebo group consisted of 1 female and three males, aged 17-27. PCS subjects in the exercise group consisted of three females and one male, aged 18-33. Some PCS subjects had a history of prior concussions, but this data was not reported. One subject was dropped from the placebo group and one subject was dropped from the experimental group after initial fMRI revealed confounding posttraumatic stress disorder and suspected malingering, respectively. The average time since injury (symptom duration) was 171 days for PCS subjects assigned to the experimental exercise group and 65 days for PCS subjects assigned to the placebo stretching group. There were no significant differences in fMRI among PCS subjects at baseline.
Intervention Investigated
Healthy Control
Healthy controls did not receive an intervention and only received two fMRI scans separated by approximately the same 12 week interval as PCS groups.
Placebo Control
An investigator instructed the PCS placebo group to perform stretching and breathing exercises according to a published brochure for 20 minutes six days per week at home or in the gym, wearing a Polar HR monitor to maintain a HR below 40-50% of age predicted maximum. Stretching and breathing exercises included quadriceps stretch, hamstring stretch, and double and single knee to chest stretch, which were "progressed" according to the brochure while subjects continued maintaining the same target HR.
Experimental
An investigator instructed the PCS experimental group to perform aerobic exercise for 20 minutes six days per week at home or in the gym, wearing a Polar HR monitor to maintain a HR at 80% of their symptomatic threshold HR. Investigators progressed exercise intensity at higher HRs as subjects' symptomatic HR threshold increased.
Outcome Measures
Outcome measures were administered by investigators in the university concussion clinic. An fMRI measures brain activity through blood oxygenation level dependent (BOLD) imaging that represents local cerebral blood flow. Score ranges are not applicable; rather, peak voxels map the highest BOLD response in the brain in order to represent blood flow and activity relative to varying brain areas, task conditions, time points, or other individuals' fMRI images. The ANAM Math Processing subtest measures processing speed and working memory during 72 simple addition and subtraction tasks over the course of 5 minutes. Subjects left click the computer mouse if the equation equals <5 and right click the computer mouse if the equation equals >5. Possible scores include percent accuracy ranging from 0-100% and mean reaction time ranging from 0 seconds to 5 minutes. Age-predicted maximum HR (HR_{max} = 220 – age) was used to measure the threshold HR at which symptoms became exacerbated. Maximum possible threshold HR was 100% HR_{max}. Investigators outfitted subjects with Polar HR monitors to collect and analyse HR measurements from treadmill testing in the clinic and interventions at home or at the gym. The post-concussion scale measured the number of symptoms under each condition. Possible scores ranged from 0 to 22.

Main Findings

Measure	Mean Difference	Range	Confidence Interval	P-Value
Threshold HR for Symptom Exacerbation (% age predicted maximum)	HC not tested Pre to Post Stretch: -0.75% Pre to Post Exercise: +20.75%	HC not tested Pre to Post Stretch: -6 to +5% Pre to Post Exercise: +17 to +26%	No published	0.75 0.001
Post-concussion Scale (number of symptoms)	HC not tested Pre to Post Stretch: remission of 4 symptoms Pre to Post Exercise: remission of 15.5 symptom	HC not tested Pre to Post Stretch: remission of 0 to 10 symptoms Pre to Post Exercise: remission of 13 to 17 symptoms	Not published	0.16 0.004

At baseline, fMRI of healthy controls revealed significantly more peak voxels in the posterior cingulate gyrus, lingual gyrus, and cerebellum during cognitive exertion, compared to PCS subjects (p = 0.05). At 12 weeks post-intervention, there was no significant difference in fMRI results between healthy controls and the experimental exercise group, while the placebo stretching group demonstrated significantly fewer peak voxels in the anterior cingulate gyrus, thalamus, and cerebellum than healthy controls (p = 0.001).

At 12 weeks post-intervention, there was a significant difference in threshold HR and number of symptoms between the experimental exercise and placebo stretching groups (p = 0.05). There were significant improvements in threshold HR and number of symptoms between pre- and post-intervention for the experimental exercise group (p = 0.001, p = 0.004). Conversely, mean threshold HR decreased between pre- and post-intervention for the placebo stretching group, but this worsening was statistically insignificant (p = 0.75). Neither was there a statistically significant difference in the number of symptoms between pre- and post-intervention for the placebo stretching group (p = 0.16). There were no significant differences between ANAM scores among the three groups before or after intervention.

Original Authors' Conclusions

In patients with PCS, controlled sub-symptomatic aerobic exercise may restore cerebral blood flow and, thus, normalize brain activation patterns, at least as represented by fMRI BOLD.

Critical Appraisal

Validity

Overall, this study's evidence is of fair quality.

Internal validity: This study is potentially confounded by participant demographics. Healthy controls were all female, compared to 25% female PCS placebo stretching subjects and 75% female PCS experimental exercise subjects. Thus, PCS experimental subjects' fMRI results may have been predisposed toward more similarities with the health controls.

External validity: Subjects were predominantly female, which may cause results to be less applicable to males in the general population. Due to athletic status in either competitive or recreational sports, subjects' fitness levels may have affected recovery, causing results to be less applicable to non-athletes in the general population. Likewise, results from the exercise protocol may not be applicable outside the clinic, home, or gym.

Strengths: Utilization of a healthy control provided for pre-injury comparisons and use of a placebo group accounted for the placebo effect. The placebo group also provided data demonstrating that too little exercise may impair recovery. Use of computer software in fMRI analysis eliminated evaluator bias through blinding.

Weakness: Lack of true randomization and allocation concealment suggests potential selection bias and led to aforementioned shortcomings in internal and external validity. Disparity between placebo and experimental group's time since injury (symptom duration) may have led to findings based more on group differences than treatment effect. It is possible that improvements in the experimental exercise group was influenced by natural recovery, since their average time since injury was 106 days longer than the placebo group. Likewise, subjects' exertion levels prior to intervention remain unknown but may greater aerobic fitness and symptomatic threshold HR may have impacted recovery, as suggested by the study's results.

Interpretation of Results

Although this study's sample size is small, it's effect size appears to be clinically significant, with sub-symptomatic aerobic exertion increasing average threshold HR by 20% of HR_{max}, decreasing an average of 15.5 out of 22 PCS exertional symptoms, and restoring normal brain activity patterns in 12 weeks. Conversely, lack of exertion through activities that are too far below threshold HRs may fail to habituate and rehabilitate brain and autonomic nervous system function, contributing to prolonged symptoms. It is possible that lack of exertional habituation could contribute to fear avoidance, which may psychosomatically exacerbate an increased number of symptoms at a lower HR.

In addition to affecting physical symptoms such as headache, dizziness, and nausea, fMRI results suggest that sub-symptomatic exertion may improve common cognitive symptoms, with increased activity in the posterior cingulate gyrus, lingual gyrus, and cerebellum representing improvements in memory, visual processing, and executive function, respectively. Likewise, lack of exertion may exacerbate cognitive symptoms, with decreased activity in the thalamus, anterior cingulate gyrus, and cerebellum representing deficits in visual attention, selection process, and execute function, respectively.

Applicability of Study Results

Although some subjects were as young as 17 years old, the study included other subjects closer to DM's age, which indicates applicability of results. However, the predominance of females in the study's health control and experimental groups may make results less applicable to DM, who is male. Likewise, the results of recreational athletes may not less applicable to DM's higher level of elite tactical athleticism.

The 12 week exercise intervention is very feasible, requiring only 20 minutes and a Polar HR monitor at home or at the gym. With the exception of fMRI – which is not available in the typical clinic – all other statistically significant outcomes are easily measured through HR_{max} and the post-concussion scale.

However, results of this exercise protocol may not be applicable outside the clinic, home, gym, or even athletic field. For instance, much military training takes place in dynamic environments, from dense woodland to complex urban terrain. Proprioceptive demands of trail running and obstacle navigating may challenges servicemembers' vestibular systems, and passing trees and room clearing tasks may further exacerbate vestibular post-concussion symptoms at lower HRs than identified in this protocol.

SYNTHESIS AND CLINICAL IMPLICATIONS

Evidence Synthesis

Overall, the quality and validity of these studies is fair. Although Maerlender et al defined recovery behaviourally as asymptomatic exertion and Leddy et al defined recovery physiologically as normal fMRI brain activity, analysis suggests that 20 minutes of aerobic exercise 6-7 days per week at moderate intensity on the Rate of Perceived Exertion (RPE) scale or just below symptomatic threshold HR significantly decreases post-concussive symptoms, restores cerebral blood flow, normalized brain activation patterns during cognitive tasks, and increases threshold HR near age-predicted HR maximum (HR_{max}) in approximately 6-12 weeks. Conversely, too little exertion below 40-50% HR_{max} or too much exertion between 7-10 RPE worsens symptoms and delays recovery. However, neither Maerlender et al or Leddy et al investigated the impact of such aerobic exercise on long term recovery or disability outcomes.

These studies are generally applicable to DM as they include near aged, college educated, physically fit subjects. However, subjects were predominantly female and varied in athletic elitism, which may cause results to be less applicable to DM as a male servicemember.

Implications for Clinical Practice

Evidence suggests that 20 minutes of aerobic exercise at moderate intensity or just below symptomatic threshold HR may be used to effectively treat and improve symptoms of both physical and cognitive exertion post-concussion. In addition to maintaining aerobic exercise at moderate intensity or just below symptomatic threshold HR, another important parameter for this protocol is that exercise must be non-contact in order to avoid the compounding effects of a subsequent concussion prior to recovery.

Also, mechanism of exercise (i.e. bicycle, treadmill, trail running, plyometrics) may be clinically prescribed based on individual patients' balance impairment and associated falls risk, which are common post-concussion. Patients with severe balance impairment may benefit from performing aerobic exercise on a stationary bike in a quiet room, at least initially. As symptoms such as vestibular dizziness contributing to balance impairment begin to decrease, then patients may benefit from progression to more dynamic aerobic exercise such as on a treadmill or in a crowded gym, while continue to exert at the same PRE and HR_{max} parameters. Progression toward 100% HR_{max} without symptom exacerbation in a dynamic environment may especially help servicemembers ensure a successful return-to-duty in complex and demanding training and operational environments.

Tools to guide this progression feasibly include the post-concussion scale, RPE, and symptomatic threshold HR. Servicemember who are unable to afford a Polar HR monitor may use a less expensive FitBit, use the HR sensor built into gym equipment (i.e. bike, treadmill, elliptical), or use the RPE in lieu of threshold HR.

Overall, these aerobic exercise protocols are reflective of the military's progressive return-to-activity (PRA) clinical practice guidelines, especially the condition of stopping exercise for 24 hours if any new symptoms are provoked by exertion. This suggests that PRA is indeed best practice for rehabilitation of concussions within both acute and subacute (at least up to 75 days[2]) periods. Based on this evidence, it is likely that the efficacy of PRA extends to rehabilitation of DM's chronic concussions as well, compared to a graded-approach which would be more representative of exertion that was ether too mild below 40-50% HR_{max} or too strenuous between 7-10 RPE, which would increase symptoms and further delay recovery.

Implications for Future Research

Future studies are needed to compare the efficacy of progressing exertion based on RPE versus symptomatic threshold HR, and would benefit from true randomised with a much larger sample size to promote heterogeneity among groups, as well as multiple physical (post-concussion scale), cognitive (ImPACT, ANAM, fMRI), and psychosomatic outcome measures both pre- and post-intervention. For instance, studies that utilize the Fear Avoidance Belief questionnaire would enlighten the influence of mild intensity and low HR_{max} versus fear of symptom exacerbation on exertional symptoms and habituation. As for fMRI, it is possible that the cerebral blood flow deficits associated with symptom exacerbation during physical exertion are also responsible for symptom exacerbation during cognitive exertion, and research investigating this hypothesis could inform the role of physical exertion – which improves cerebral blood flow – in treating cognitive symptoms of concussion.[2] Additionally, comparison of fMRI during cognitive exertion, physical exertion, and a combined cognitive and physical dual task could enlighten the impacts of each intervention on the complex real-world return-to-duty standards that servicemembers must be able to meet.

Additionally, the effects of less than or greater than 20 minutes of aerobic exercise under these RPE and HR_{max} parameters could better inform exercise prescription and identify interventions. Finally, follow up at least six months or even up to 10 years after return to activity is needed to reveal which interventions provide the most sustainable improvements.

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