

# Exercise as treatment for Concussion and Persisting Concussion Symptoms

8th Annual Concussion Research Symposium  
University Health Network (UHN)  
February 26, 2021

John Leddy, MD FACSM FACP FAMSSM

Professor of Clinical Orthopaedics and  
Rehabilitation Sciences

Director – University at Buffalo Concussion Management Clinic  
Team Physician- State University of New York at Buffalo

# **DISCLOSURES**

**John Leddy MD**

**Receives grant/research support from: NIH, DoD, AMSSM.**

**Is a member of the Scientific Advisory Board for: Neurologix,  
Highmark Innovations, and Stage 2 Contract Engineering.**

**Commercial Support was not received for this activity.**

## LEARNING OBJECTIVES

- The Learner will understand aspects of the Physiology of Concussion soon after injury with respect to The Autonomic Nervous System.
- The Learner will understand how to assess exercise tolerance systematically with the Buffalo Concussion Treadmill Test.
- The Learner will understand the role of individualized sub-threshold aerobic exercise for the treatment of acute sport-related concussion (SRC) and persistent post-concussive symptoms (PPCS).

# MD Concussion



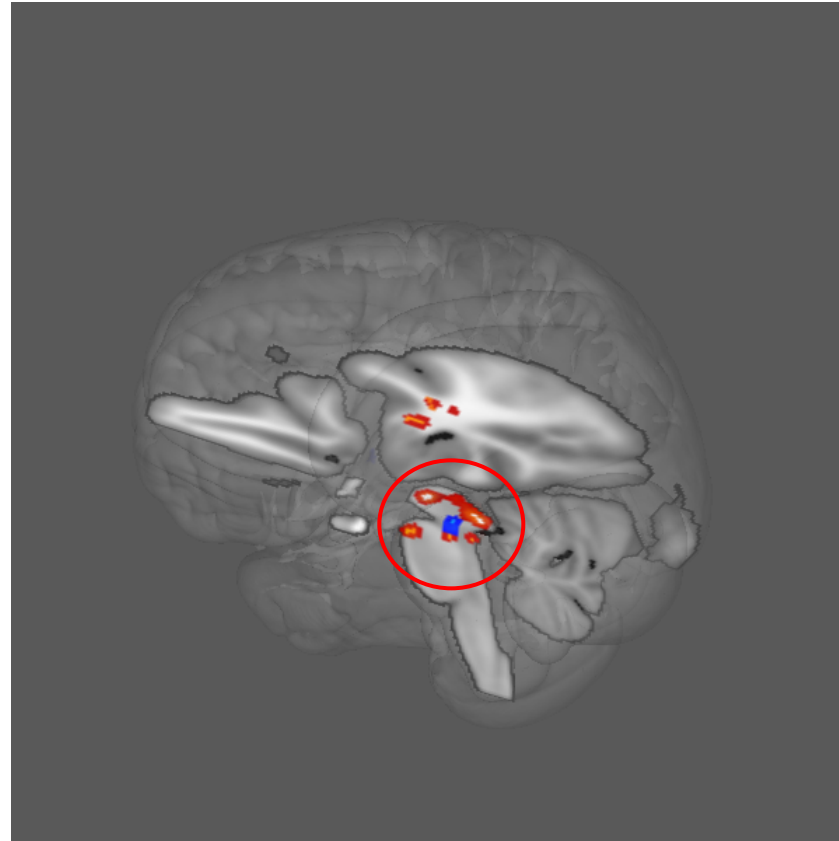
# The Physiology of Concussion soon after Injury

The Autonomic Nervous System  
and Acute SRC



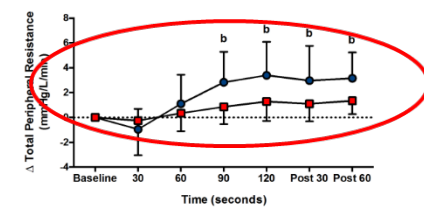
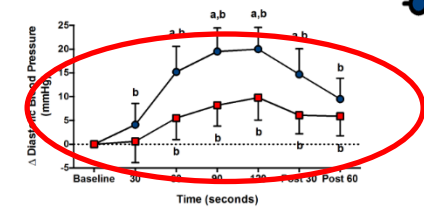
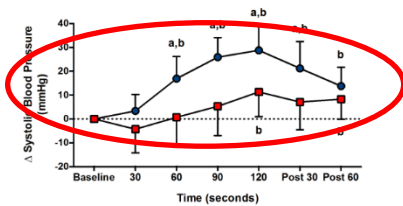
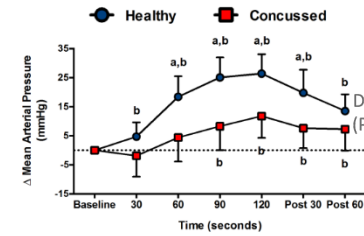
# DTI Brainstem injury in Concussion

Polak et al *J Head Trauma Rehabil* 2014

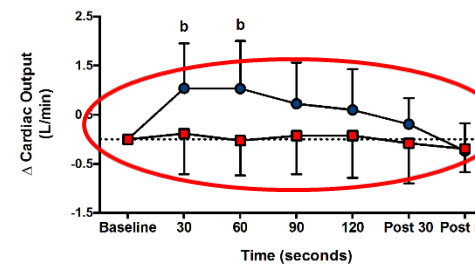
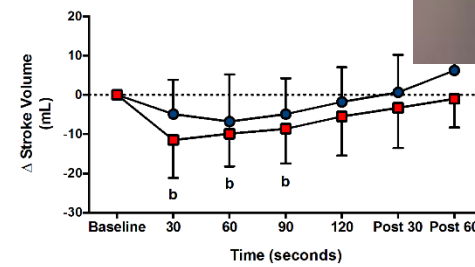
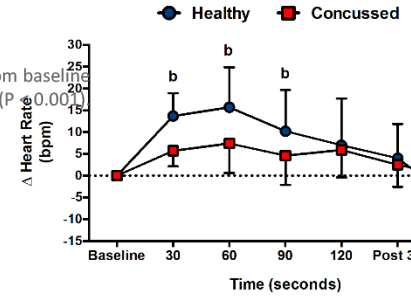


# SNS function in College athletes within 1 week of SRC

10 concussed v. 10 HC after Cold Water Immersion. (20 y, 5 d from injury)- Johnson BD et al JAT 2020

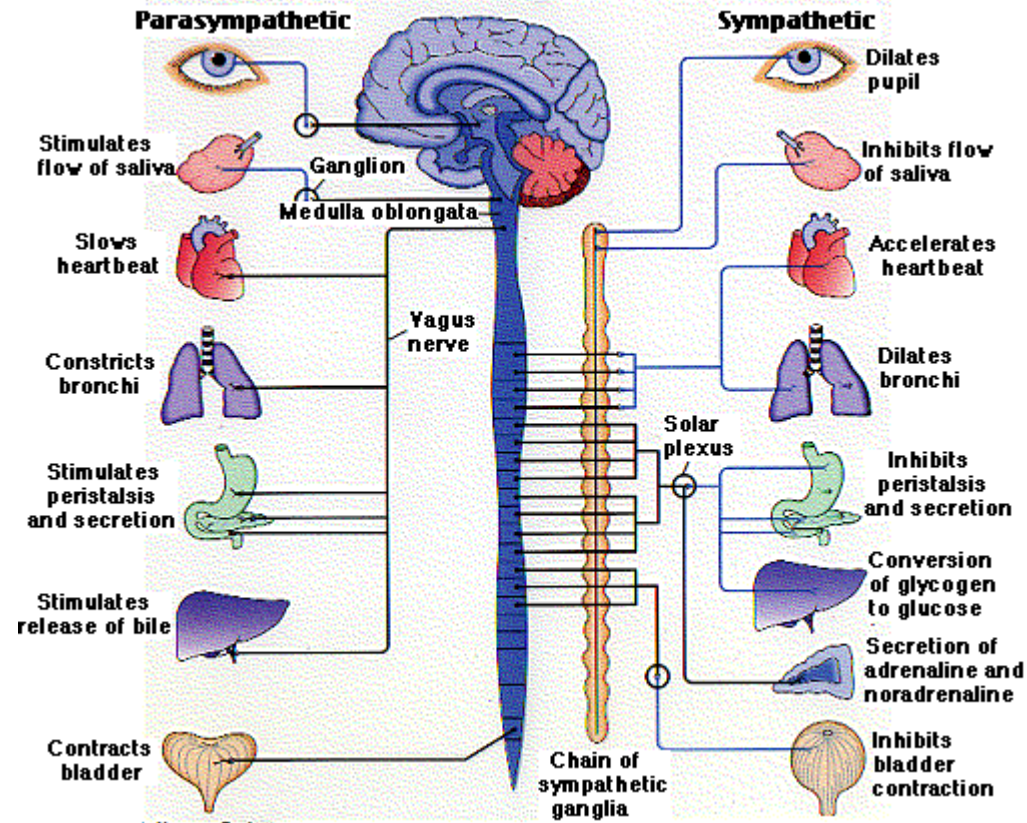


● Healthy ■ Concussed



# The Autonomic Nervous System

## A “switching problem” after mTBI





# Why consider Exercise to improve Concussion Physiology?

## Concussion and deconditioning adverse effects

- **Autonomic Nervous System**
- **Cerebral Blood Flow**
- Neuroplasticity
- Psychological
- Sleep



## Exercise beneficial effects

- Improves ANS balance and CO<sub>2</sub> sensitivity
- Improves CBF regulation
- Upregulates BDNF genes
- Improves Mood
- Improves sleep

# Evaluation of Exercise Tolerance after Concussion

## The Buffalo Concussion Treadmill Test



# The Buffalo Concussion Treadmill Test (BCTT)

- Modified Balke Protocol
  - Submaximal symptom-limited threshold = acutely concussed or not recovered.
    - Threshold is represented by the HR at symptom exacerbation.
    - HR used to prescribe sub-threshold exercise.
  - Maximum exertion without symptom limit = cardio- and cerebro-vascularly physiologically recovered.
  - And introducing the Buffalo Concussion Bike Test (BCBT) (Leddy et al CSMR 2018)



BCTT is safe and reliable in PPCS

(Leddy et al Clin J Sport Med 2010, 2011)



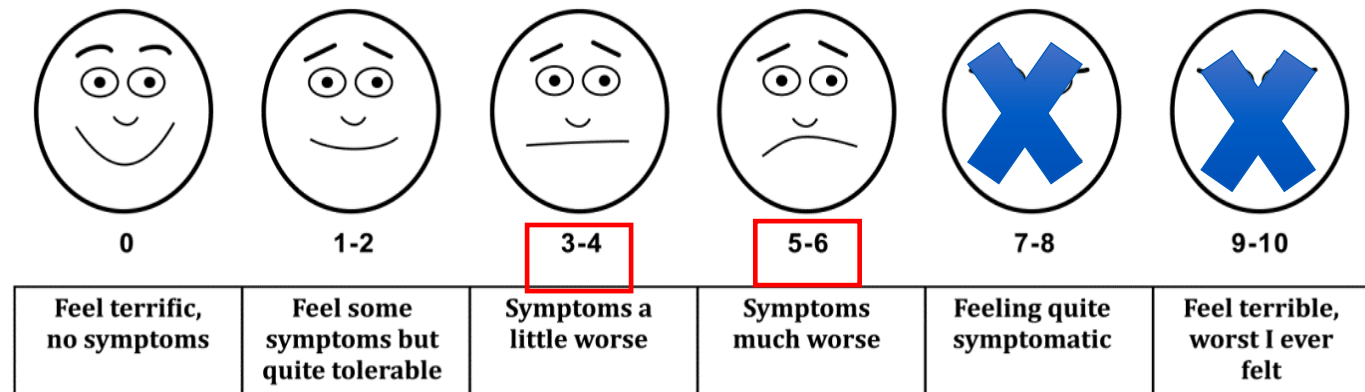
# Stopping Criteria during the BCTT

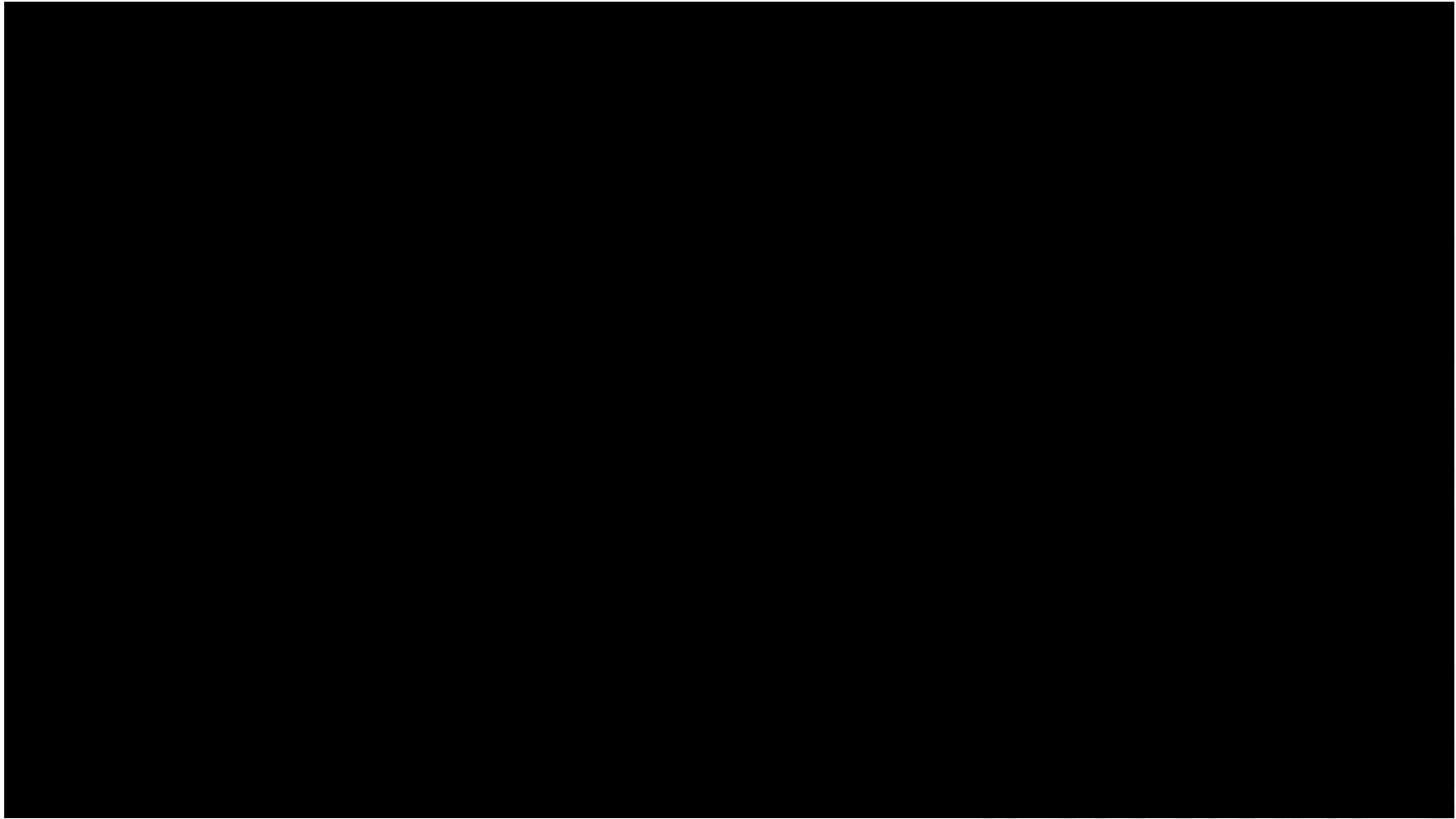
Defines the symptom-exacerbation threshold

Threshold =  $\Delta \geq 3$  points from baseline

Increase in headache or dizziness by 3 points or a new symptom appears (one point for each)

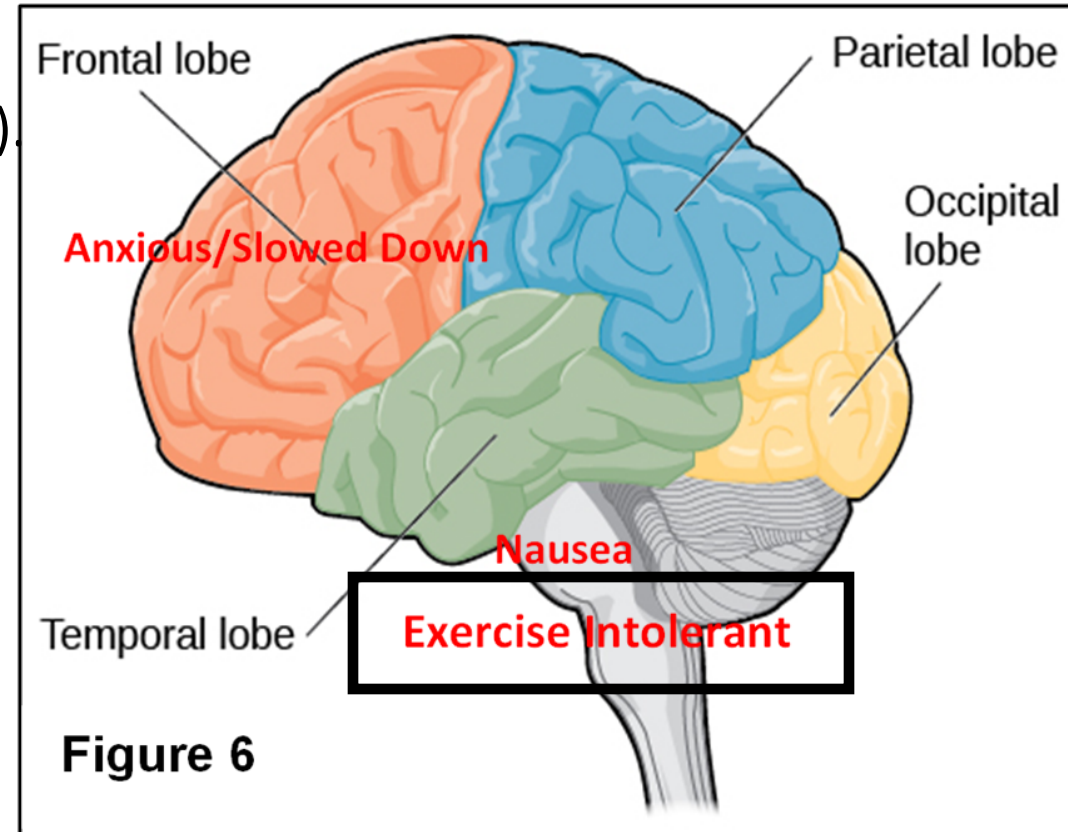
## Rate Your Overall Condition





# New Data: DTI, exercise intolerance and symptoms after concussion

- CA (n=32, 15.3 y, 56% male) 7 days since injury.
  - HC = age and sex-matched adolescents with no concussion in the past year (n=25, 15.7 y, 56% male).
- Pearson correlations analyzed symptoms and regional weighted mean DTI values.
- Exercise intolerance on BCTT was significantly associated, after Bonferroni correction, with brainstem FA ( $p=.01$ ) and with temporal lobe MD ( $p=.03$ ).
- Exercise intolerance is linked to brainstem DTI changes, where central autonomic control resides.



# WE CAN TREAT ACUTE CONCUSSION AND PPCS

The Best Way To Improve Control of  
ANS: **Aerobic Exercise training**

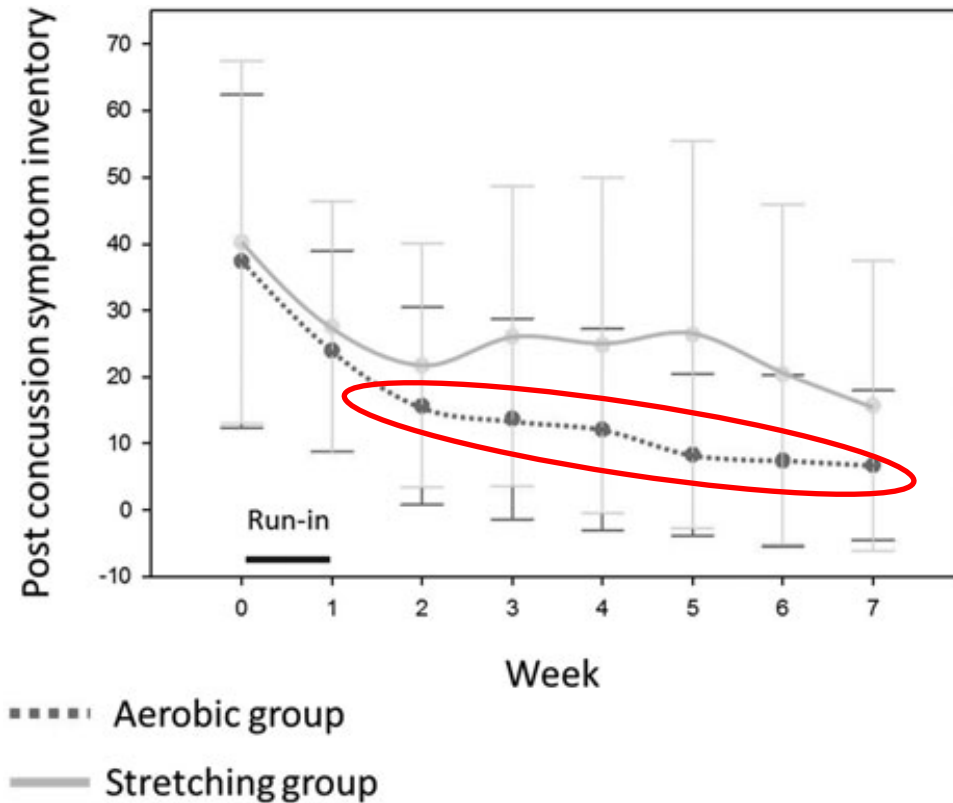
# Exercise is Medicine to treat Sport-related Concussion

- Establish the diagnosis by systematic evaluation of exercise tolerance
  - Symptom-limited threshold on the treadmill or the bike.
- Sub-threshold exercise prescription (“Exercise is Medicine”)
  - 90% of achieved HR on BCTT = target HR.
    - HR monitor is KEY to prevent athlete from over-exertion.
  - 20 min/day minimum at target HR with 5 min warmup and longer cool down.
    - Stop at symptom exacerbation. (2 point increase)
  - Bike first, then running. 6-7 d/wk.
  - Increase target HR 5-10 bpm q1-2 weeks (or re-test).
  - $\geq 80\%$  age-predicted max HR x 20 min without symptoms-  
“Cardiovascular and Cerebrovascular Physiological Recovery”



# Aerobic Exercise for Adolescents With Prolonged Symptoms After Mild Traumatic Brain Injury: An Exploratory RCT

Kurowski et al J Head Trauma Rehabil 2016

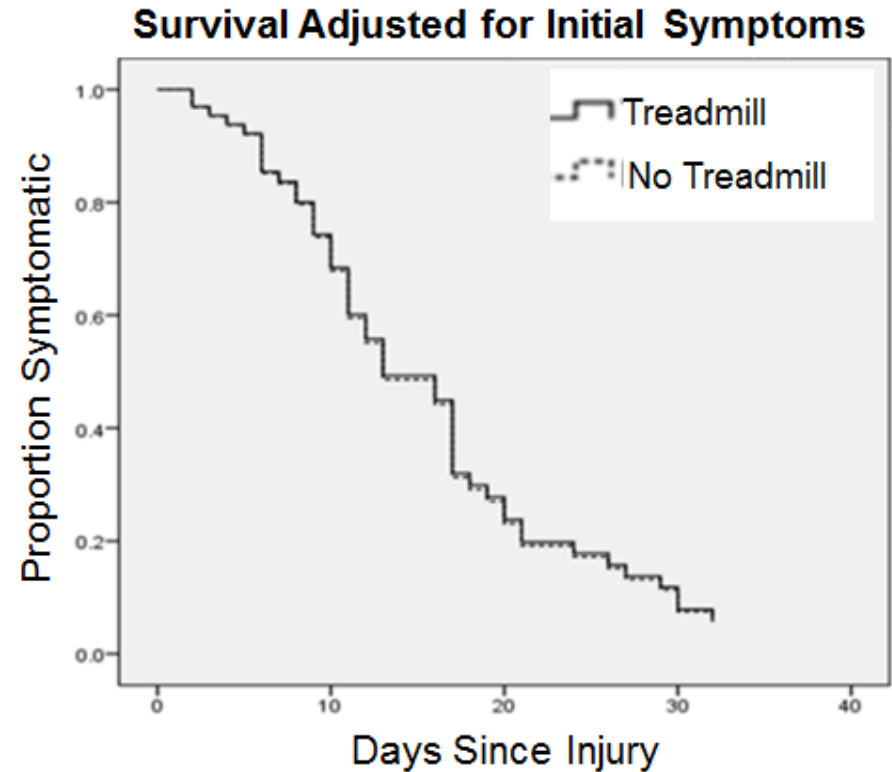


Greater rate of improvement in the sub-symptom threshold aerobic training group than in stretching group ( $P = .044$ ).

“Potential benefit of active rehabilitation programs for adolescents with persistent symptoms after mTBI”...

# Assessment of Exercise Tolerance within First Week of SRC is safe

(Leddy et al. CJSM 2018)



JAMA Pediatrics | [Original Investigation](#)

# Early Subthreshold Aerobic Exercise for Sport-Related Concussion A Randomized Clinical Trial

John J. Leddy, MD; Mohammad N. Haider, MD; Michael J. Ellis, MD; Rebekah Mannix, MD; Scott R. Darling, MD;  
Michael S. Freitas, MD; Heidi N. Suffoletto, MD; Jeff Leiter, PhD; Dean M. Cordingley, MSc; Barry Willer, PhD

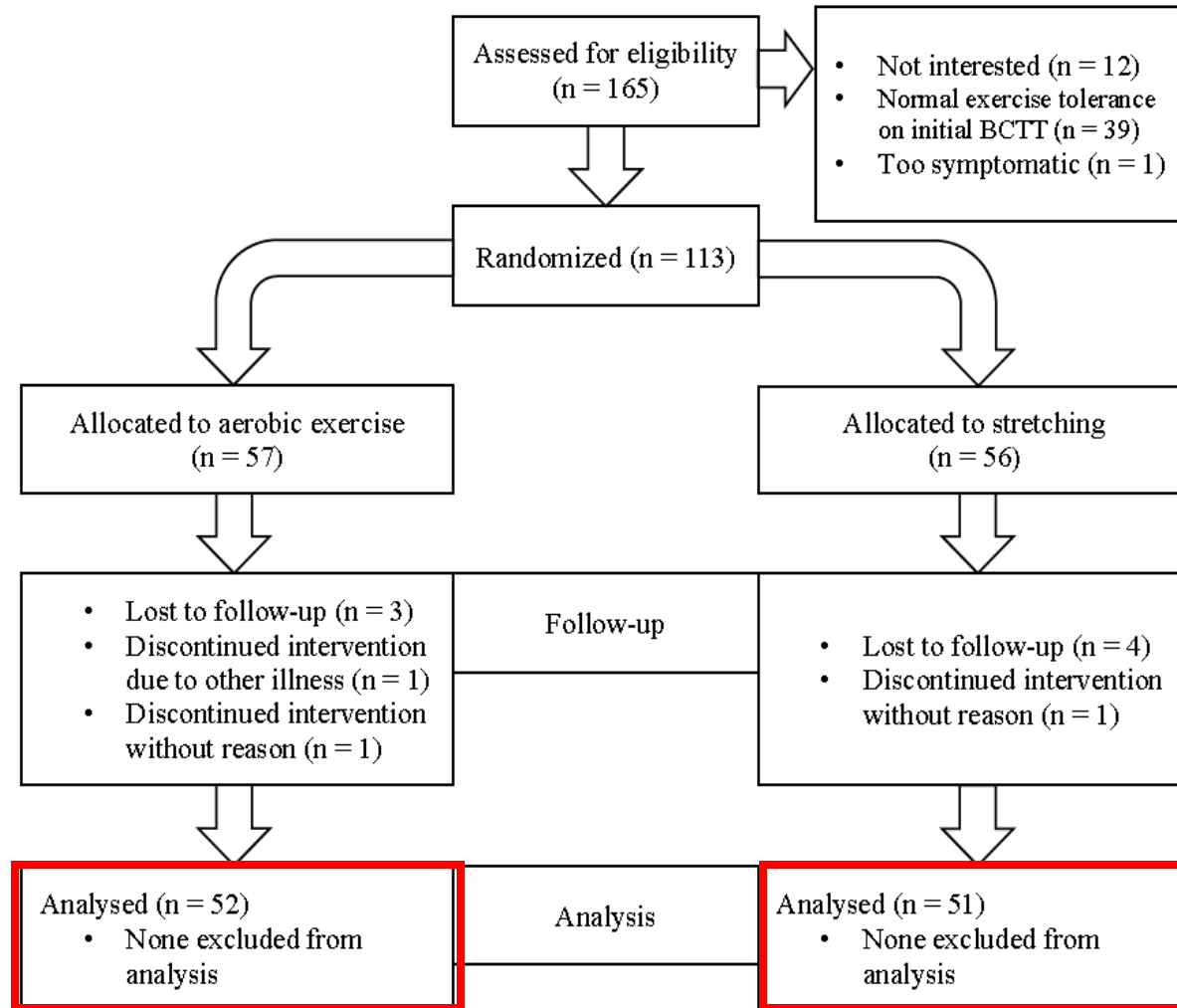
*JAMA Pediatr.* doi:10.1001/jamapediatrics.2018.4397  
Published online February 4, 2019.

Sub-threshold exercise for the Rx of Acute Sport-related ConcussionLeddy et al. *JAMA Pediatrics* 2019

	Aerobic Exercise (n = 52)	Stretching (n = 51)	p- value
Age (years)	15.3 ± 1.6	15.4 ± 1.7	0.753
Sex	46% female	47% female	0.927
Previous concussions	0.71 ± 0.8	0.67 ± 0.9	0.773
Time since injury (days)	4.9 ± 2.2	4.8 ± 2.4	0.893
Initial Visit symptom score on PCSS	30.8 ± 16.5	33.3 ± 19.7	0.479
Initial Visit resting HR	74.5 ± 12.7	75.2 ± 12.3	0.796
Initial Visit HR at symptom exacerbation	136.9 ± 26	136.6 ± 21	0.952
Duration of Initial Visit BCTT (minutes)	8.65 ± 4.88	8.64 ± 4.32	0.717

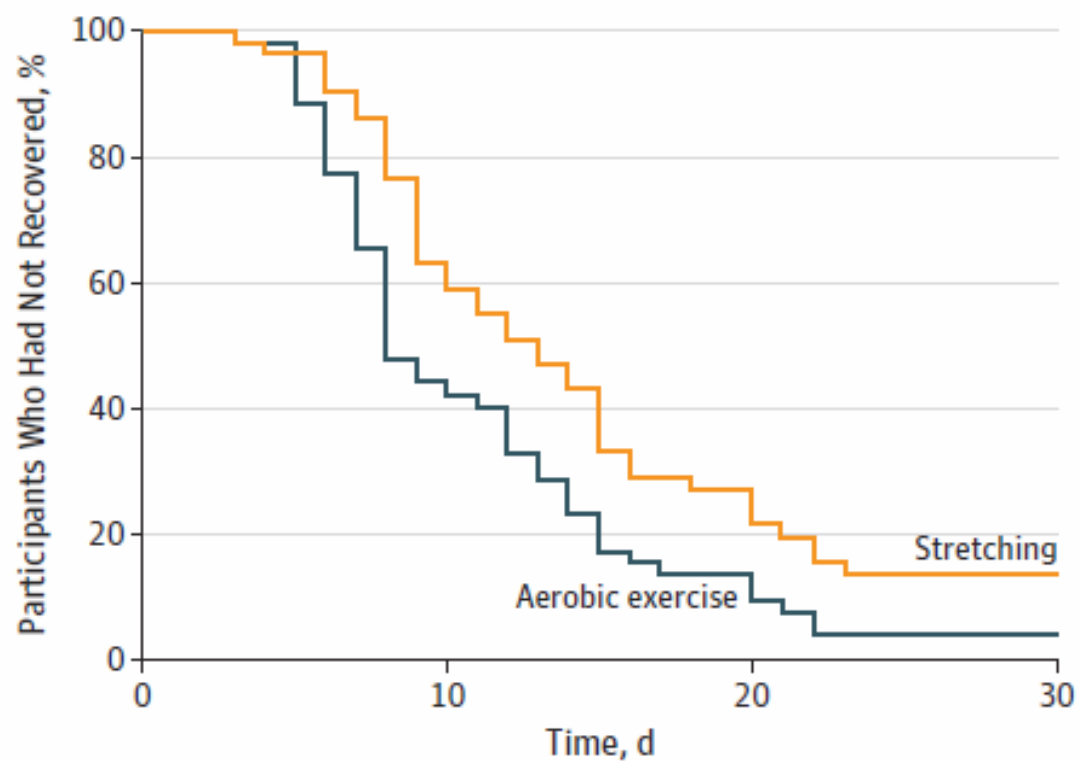
1 Figure 1. CONSORT Flow Diagram

2  
3  
4



Leddy et al *JAMA Pediatrics* 2019

Figure 2. Kaplan-Meier Estimates of Time to Recovery



No. at risk					
Aerobic exercise	52	23	7	2	
Stretching	51	32	14	7	

Survival analysis comparing groups; the aerobic exercise group recovered significantly faster than the stretching group after adjusting for age, sex, time from injury to first clinical visit, and concussion history ( $z = 2.82$ ;  $P = .005$ ).

# Aerobic v. Stretching RCT

Leddy et al. *JAMA Pediatrics* 2019

- Recovery was longer for stretching group (17 days [IQR 13, 23]) v. aerobic exercise group (13 days [IQR] 10, 18.5],  $p = .009$ ).
- There was a non-statistically significant lower incidence of delayed recovery in the aerobic exercise group (2 aerobic vs. 7 placebo participants,  $p = 0.076$ ).
- \*Females responded as well as males.

JAMA Pediatrics | Original Investigation

# Early Subthreshold Aerobic Exercise for Sport-Related Concussion A Randomized Clinical Trial

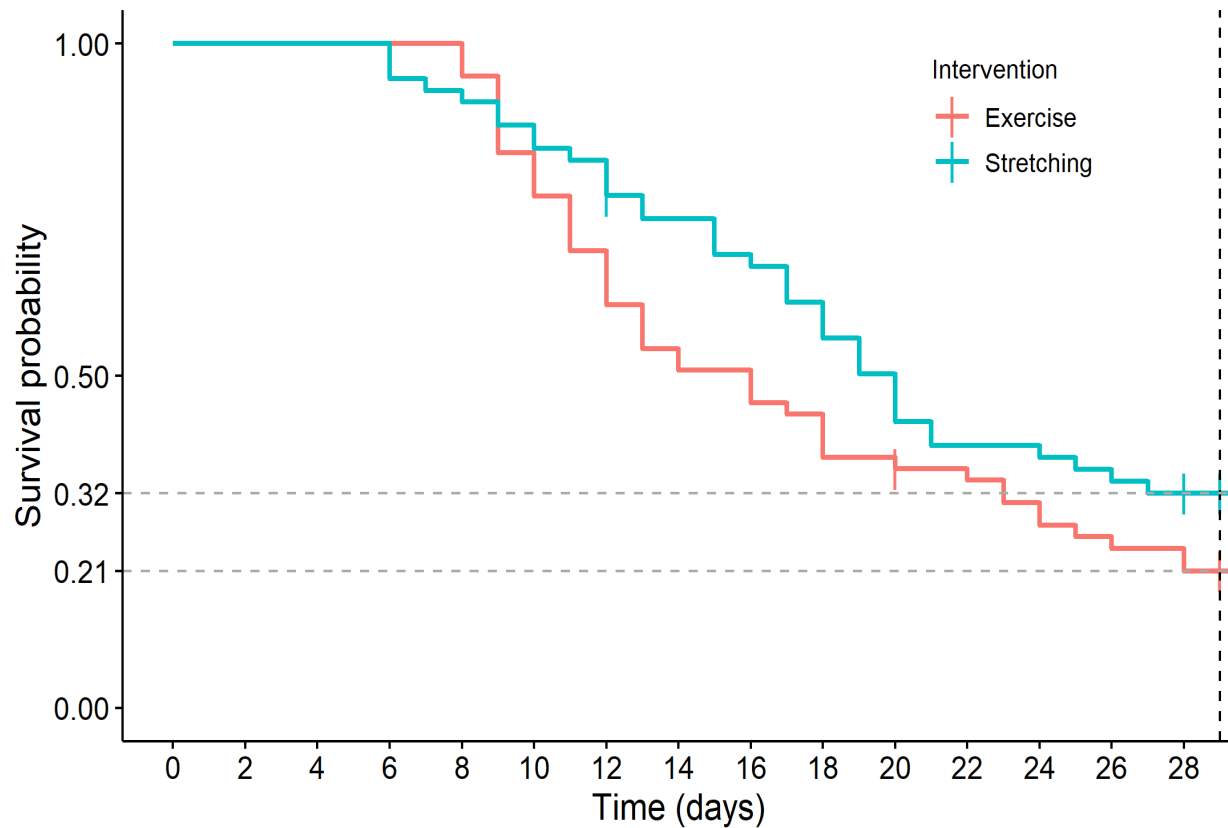
John J. Leddy, MD; Mohammad N. Haider, MD; Michael J. Ellis, MD; Rebekah Mannix, MD; Scott R. Darling, MD;  
Michael S. Freitas, MD; Heidi N. Suffoletto, MD; Jeff Leiter, PhD; Dean M. Cordingley, MSc; Barry Willer, PhD

*JAMA Pediatr.* doi:10.1001/jamapediatrics.2018.4397  
Published online February 4, 2019.

Rest after concussion in adolescents (Grool et al 2016): ~35% PPCS at one month  
Placebo Stretching Group: 15% PPCS  
Aerobic Exercise Group: 5% PPCS  
But... not statistically significant.



# New Multicenter RCT of Early Sub-threshold Aerobic Exercise and PPCS in Adolescent SRC (AMSSM CRN Grant)



- 21% of aerobic exercise (n=61, 1/3F) and 32% of stretching (n=57, 1/3F) participants did not recover by Day 29.
- On survival analysis, aerobic exercise participants had a significantly reduced incidence of PPCS ( $p = 0.042$ ) when controlling for sex ( $p = 0.915$ ) and site ( $p < 0.001$ ).
- Hazard ratio for PPCS in the aerobic exercise arm was 0.638 (0.415, 0.982), corresponding to a 36% reduction in PPCS versus stretching exercise.

# Practical Management: Prescribing Subsymptom Threshold Aerobic Exercise for Sport-Related Concussion in the Outpatient Setting

Itai Bezherano, BS,\* Mohammad N. Haider, MD,\*† Barry S. Willer, PhD,‡ and John J. Leddy, MD\*

Clin J Sports Med 2020;00:1-4

Age	Predicted HR <sub>max</sub> *	Stage 1 50%	Stage 2 55%	Stage 3 60%	Stage 4 65%	Stage 5 70%	Stage 6 75%	Stage 7 80%

\*maximal heart rate predicted by conventional Karvonen method (220 – age)

Day	Attempted stage	Target Heart rate	How were your symptoms (1-10) before exercise?	How were your symptoms (1-10) during exercise?	What stage will you be attempting tomorrow?*
1	1 (50%)				
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					

\*The following days' stage is dictated by the difference between symptom scores (see below) before and during exercise. This decision should be made according to the following:

**Method 1: Exercise Prescription With Exertion Testing and Heart Rate Monitor**

**Method 2: Exercise Prescription With Exertion Testing but Without a Heart Rate Monitor**

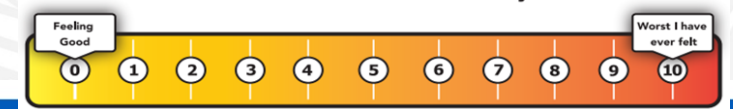
**Method 3: Exercise Prescription Without Exertion Testing**

Daily outcomes based on symptom score increase during exercise

- 0 Continue to next stage
- 1 Continue to next stage
- 2 Remain at same stage until 2 continuous days without symptom increase
- 3+ Attempt previous stage

**Rate Your Overall Condition**

Choose a number from 0 to 10 and describe your condition.



# Benefit or No Harm of Moderate Physical Activity or Controlled Exercise for Acute Concussion and PPCS

- Moderate Physical Activity

- Majerske et al. (2008)- Retrospective
- Brown et al. (2014)- Retrospective.
- Thomas et al. (2015)- RCT
- Buckley et al. (2015)-Prospective cohort
- Silverberg et al. (2016)- Secondary analysis RCT
- Grool et al. (2016)-Prospective multicenter cohort
- Howell et al. (2016)-Prospective cohort
- Taubman et al. (2016)-Prospective cohort
- Sufrinko et al. (2017)- Secondary analysis RCT
- Lawrence et al. (2018)- Retrospective

- Prescribed Aerobic Exercise

- Gagnon et al. (2009)-Prospective case series
- Leddy et al. (2010)-Prospective case series
- Baker et al. (2012)- Retrospective
- Leddy et al. (2013)-Quasi experimental
- Clausen et al (2015)-Prospective cohort
- Dematteo et al. (2015)-Prospective X-sectional
- Maerlender et al. (2015)- RCT in acute SRC
- Cordingley et al. (2016)-Retrospective
- Gagnon et al. (2016)-Prospective case series
- Chrisman et al. (2017)-Retrospective in PPCS
- Kurowski et al. (2017)- RCT in PPCS.
- Leddy et al (2017)- RCT in acute SRC.
- Popovich et al. (2018)- Retrospective- subacute
- McGeown et al. (2018)- Prospective in PPCS
- Chan et al (2018)- RCT in PPCS.
- Leddy et al (2018)- Prospective cohort in acute SRC.
- Micay et al (2018)- RCT in acute SRC
- Rytter et al. (2019)- RCT in PPCS
- Leddy et al (2019) )- RCT in acute SRC
- Willer et al (2019)- quasi-experimental in acute SRC

# Activity After Concussion

Old view



Rest until symptoms resolve



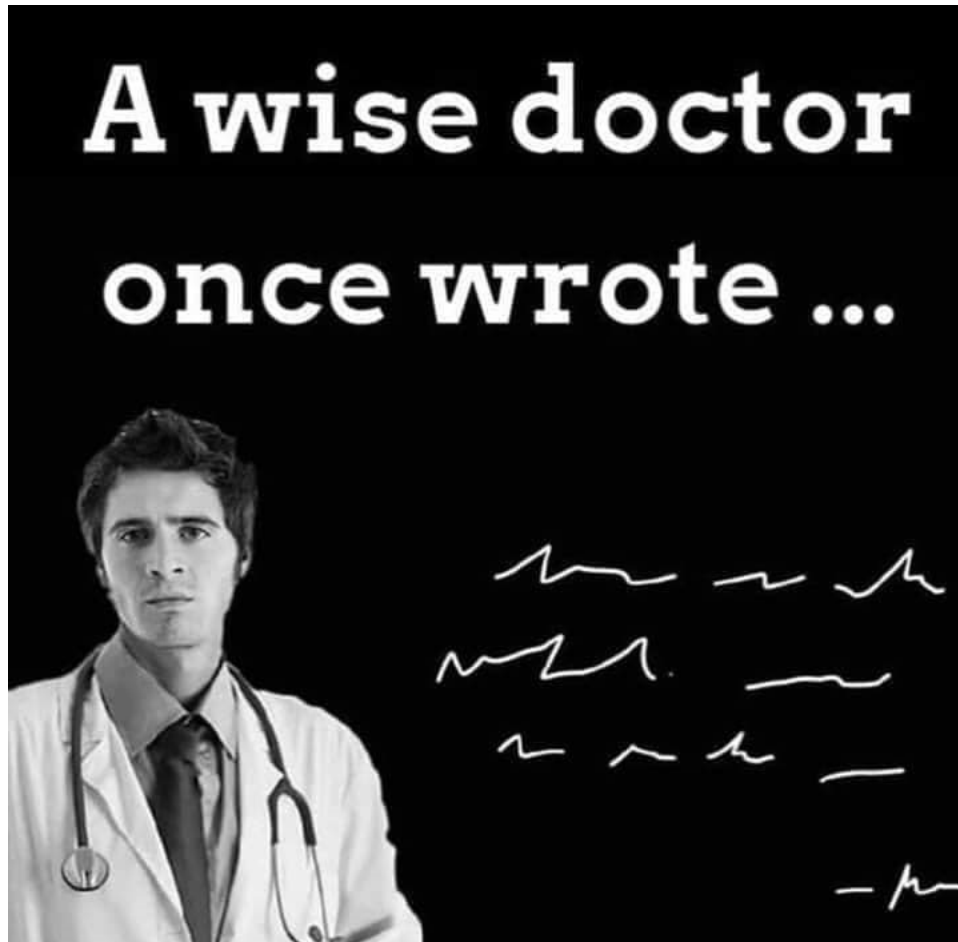
# Activity After Concussion - New view

Berlin CISG 2016 (BJSM 2017)

- “Relative Rest” for a couple of days.
  - May need to be “Radical Rest” for kids in school
- Once symptoms stabilize, get back into activity gradually staying below cognitive and physical symptom **thresholds**.
- There are active treatments for the physiological disturbances seen in SRC and PPCS:
  - **ANS (with sub-threshold aerobic exercise).**
  - **Oculomotor, vestibular, cervical, psychological, and cognitive/behavioral therapies.**



Please remember this important take home message that I wrote down just for you...



**Translation:** Don't "Cocoon" because sub-threshold aerobic exercise training is an evidence-based treatment aimed at the physiology of concussion that speeds recovery from SRC and can prevent PPCS.



“Some cause happiness  
wherever they go; others  
whenever they go”

*Oscar Wilde*

*and I'm gone....*

QUESTIONS?

[Concussion.ubmd.com](http://Concussion.ubmd.com)

[ledy@buffalo.edu](mailto:ledy@buffalo.edu)

716-829-5499

716-204-3200