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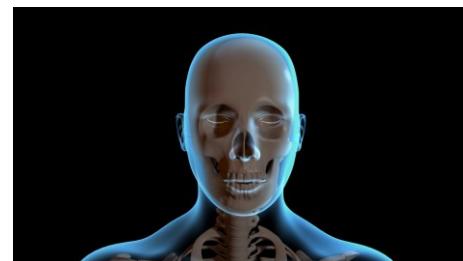
## Objectives

Upon completion, the participant will be able to describe the:

1. Autonomic nervous system physiology of concussion and its relation to post-concussion exercise intolerance.
2. Efficacy, safety, and the effect of adherence, of sub-symptom threshold aerobic exercise early after injury to speed recovery and to prevent delayed recovery in adolescents after sport-related concussion.
3. Role of aerobic exercise treatment in the Amsterdam return to sport/play strategy.

3

Concussion = Commotio Cerebri or "Shaken Brain"



4

## Signs and symptoms of Concussion/MTBI

\*Must appear within 72 hours of injury

Domains	Symptoms	Signs
Cognitive	Confusion Feeling "in a fog" or "Zoned Out" Inability to focus	Anterograde amnesia Retrograde amnesia Loss of Consciousness Drowsiness Delayed verbal and motor responses Vacant stare Slurred/Incoherent speech
Somatic	Headache Dizziness Nausea/vomiting Visual disturbances Photophobia, blurry/double vision Pain/pressure	Balance disruption Abnormal eye tracking Abnormal Vestibulo-ocular reflexes (VOR) Abnormal near point convergence
Affective	Emotional lability Irritability Fatigue Anxiety Sadness	Acts irritable Flat affect
Sleep Disturbances	Trouble falling asleep Sleeping more than usual Sleeping less than usual	Excessive drowsiness

5

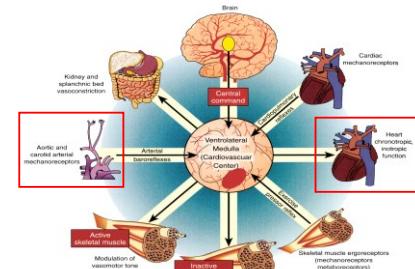
## Physiological Symptoms/Signs of Concussion

- **Orthostatic intolerance:** lightheadedness or dizziness upon standing suggests autonomic nervous system baroreflex impairment and/or vestibular impairment.
- **Abnormal vestibular** (e.g., tandem stance/gait) and **oculomotor** (e.g., repetitive saccades) exam findings.
- **Exercise intolerance:** inability to exercise to the maximum level expected for the patient due to exacerbation of concussion symptoms.

6

# The Physiology of Concussion soon after Injury

## The Autonomic Nervous System and Acute SRC



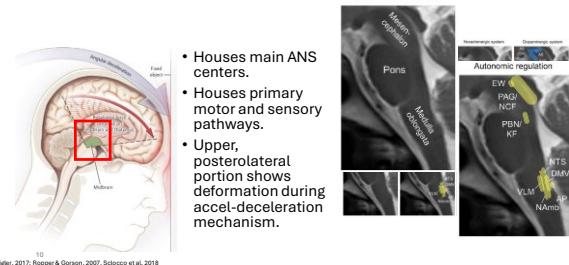
## Injury to the ANS

### Structure

### Autonomic Function

### Cerebral Blood Flow Regulation

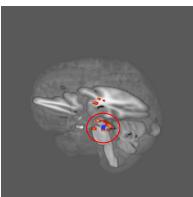
## Brainstem in SRC



## STRUCTURE

### DTI Brainstem injury in Concussion

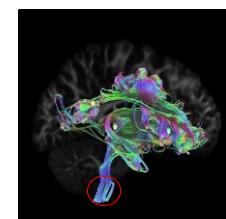
Polak et al. J Head Trauma Rehabil 2014



## Connectivity in the Central Autonomic Network (CAN)

### CAN

- Midbrain
- Hypothalamus
- Amygdala
- Cingulate gyrus
- Insula

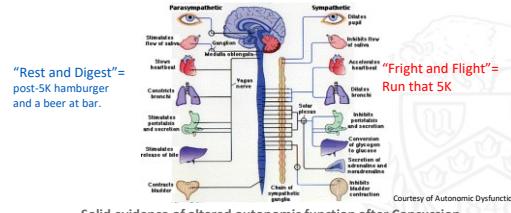


Tractogram reconstruction of key fiber pathways interconnecting regions of the CAN from diffusion MRI.

# The Physiology of Concussion

## ANS Function

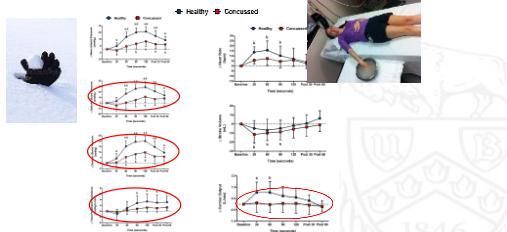
### The Autonomic ("automatic") Nervous System- responsible for exercise performance



Solid evidence of altered autonomic function after Concussion

Courtesy of Autonomic Dysfunction.com

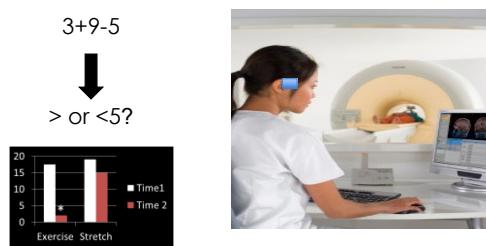
SNS function in College athletes within 1 week of SRC  
30 concussed v. 10 HC after Cold Water Immersion (30° C, 5.6 from injury) - Johnson BD et al JAT 2020



# The Physiology of Concussion

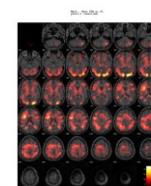
## Cerebral Blood Flow Regulation

CBF by fMRI during a Cognitive Task  
(Leddy et al. Jl Head Trauma Rehabil 2013)

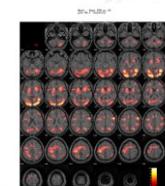


fMRI  
Cerebral Blood Flow (Leddy et al 2013)

PPCS after stretching- not recovered



Recovered after aerobic exercise = Control



## Assessing the Physiology of Concussion in the Office/Training Room

### Orthostatic and Exercise Intolerance

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19

- Arterial Baroreflex regulates cardiac output and peripheral vascular resistance to maintain cerebral perfusion during orthostatic stress.
- Post-concussion autonomic dysfunction appears to be an anatomical uncoupling or physiological reduction of neurotransmission between central autonomic centers and peripheral organs such as the heart and vasculature.

#### METHODS

- 10 collegiate athletes (20 y) after SRC compared with 10 matched controls.
- EKG and beat-to-beat systolic BP measured in seated upright position for 5 min within 48h of concussion and one week later (controls twice a week apart).

19

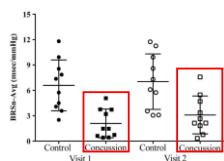
Jacobs School of Medicine and Biomedical Sciences  
University at Buffalo

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20

- **METHODS**
- 10 collegiate athletes (20 y) after SRC compared with 10 matched controls.
- EKG and beat-to-beat systolic BP measured in seated upright position for 5 min within 48h of concussion and one week later (controls twice a week apart).

### RESULTS AND CONCLUSIONS



- Broad reduction in resting BRS suggests that concussed athletes have reduced ability to buffer BP challenges for at least 1 week after injury.
- From a clinical perspective, concussed athletes often report feeling "light-headed" or "dizzy" upon standing or with exercise or weight training.
- This is the definition of **Orthostatic Intolerance (OI)**.

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21

21

The Buffalo Concussion Physical Exam (BCPE) and Exercise Testing for helping to establish physiological recovery after SRC



VIDEO OF BCPE available at [ubortho.com/services/concussion-management-center](http://ubortho.com/services/concussion-management-center)  
Under "Resources for Professionals"

22

Symptoms upon postural change and orthostatic hypotension in adolescents with concussion  
Haider MN et al. Brain Injury 2021

**Question:** what is prevalence of Orthostatic Intolerance (OI) in adolescents after sport-related concussion (SRC) vs. healthy controls?

**Participants:** Adolescents within 10 days of SRC (n = 297, 15 years, 59% male) were compared with age-, BMI- and sex-matched healthy controls (n = 214, 15 years, 58% male).

**Methods:** BP, heart rate, and complaints of lightheadedness/dizziness were measured after 2-min supine and 1-min standing.

Control Group was assessed once.

Concussion Group was assessed twice.

- (1) initial visit (mean  $6.0 \pm 3$  days-since-injury) and
- (2) after clinical recovery (mean  $46.3 \pm 42$  days-since-injury).

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23

23

Symptoms upon postural change and orthostatic hypotension in adolescents with concussion  
Haider MN et al. Brain Injury 2021

#### Results

- Initial visit: Concussed reported feeling lightheaded/dizzy on postural change ~10x more often vs. Controls (37% vs 4%,  $p < .001$ ) but did not differ in meeting standard OH criteria (3% vs 5%,  $p = 0.32$ ).
- Experiencing symptoms did not correlate with meeting OH criteria but correlated with *abnormal VOR*.
- After clinical recovery: Concussed *did not differ* in experiencing lightheaded/dizziness on postural change vs. controls (4%,  $p = .65$ ).

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24

24

**Symptoms upon postural change and orthostatic hypotension in adolescents with concussion**  
Haider MN et al. Brain Injury 2021

**Conclusions**

- Adolescents commonly experience lightheaded/dizziness upon postural change after concussion but do not meet the standard criteria for OH.
- These symptoms may be due to altered Baroreflex sensitivity and/or vestibular impairment.
- Interpretation: a relatively smaller change in BP with standing causes a clinically important reduction in cerebral perfusion in the concussed brain, which is in a state of impaired cerebral autoregulation.
- Symptoms of OH resolve as the patient recovers.

## Systematic Evaluation of Exercise Tolerance after Concussion

### The Buffalo Concussion Treadmill and Bike Tests

**2016 Berlin CISG Strategy: restoration of “exercise tolerance” before unrestricted return to sport (RTS)**

Table 1 Graduated return-to-sport (RTS) strategy			
Stage	Aim	Activity	Goal of each step
Symptom-limited activity	Daily activities that do not provoke symptoms		Gradual reintroduction of work/school activities
Light aerobic exercise	Walking or stationary cycling at slow to moderate pace. No resistance training		Increase heart rate
Sport-specific exercise	Running or skating drills. No head impact activities		Add movement
Non-contact training drills	Harder training drills, e.g. passing drills. May start progressive resistance training		Exercise, coordination and increased thinking
Full contact practice	Following medical clearance, participate in normal training activities		Restore confidence and assess functional skills by coaching staff
Return to sport	Normal game play		

McCrory P et al. Consensus statement on concussion in sport—the 5th international conference on concussion in sport held in Berlin, October 2016. Br J Sports Med. 2017

**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.
- Introducing the Buffalo Concussion Bike Test (BCBT) (Haider et al Sports Health 2019)



BCTT is safe and reliable in PPCS  
(Loddy et al Clin J Sport Med 2010, 2011)



**Systematic Evaluation of Exercise Intolerance**

- Diagnosis and establishing recovery:** (Systematic Review and Meta analysis, Haider et al. J of Neurotrauma 2023).
  - If uncertain about diagnosis, exercise testing (e.g., the Buffalo Concussion Treadmill or Bike Tests) within 14 days of injury has excellent sensitivity (94.4% [90.8, 97.2]) to help rule in concussion.
  - and excellent specificity (94.6% [91.1, 97.3]) to help rule out concussion or establish physiological recovery from concussion (compared with expert clinical examination for diagnosis).
- Prognosis:** Casimatis et al. “Exercise Tolerance in Pediatric Concussion: An 8-Year Longitudinal Study” JHTR 2025 of 603 children/adolescents (6-18 y; mean age 13y). Significant predictors of prolonged concussion recovery:
  - delayed presentation time.
  - high initial symptom burden.
  - exercise intolerance at initial visit (all  $P < .001$ ).
- Treatment:** provides individual HR “exercise is medicine” dose for facilitating recovery.

**Why consider Exercise to improve Concussion Physiology?**

Concussion and deconditioning adverse effects	Exercise beneficial effects
<ul style="list-style-type: none"> <li>• Autonomic Nervous System</li> <li>• Cerebral Blood Flow</li> <li>• Neuroplasticity</li> <li>• Psychological</li> <li>• Sleep</li> </ul>	<ul style="list-style-type: none"> <li>→ Improves ANS balance and <math>\text{CO}_2</math> sensitivity</li> <li>→ Improves CBF regulation</li> <li>→ Upregulates BDNF genes</li> <li>→ Improves Mood</li> <li>→ Improves sleep</li> </ul>

## WE CAN TREAT ACUTE CONCUSSION AND PPCS

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

## WITH EXERTION TESTING (Leddy et al. Exercise is Medicine for Concussion. CSMR 2018)

- Establish the diagnosis by systemic evaluation of exercise tolerance
- Sub max symptom-limited threshold on the treadmill or bike
- Sub-threshold exercise prescription ("Exercise is Medicine")
  - 90% of HRT on BCTT = training target HR.
  - HR monitor is **KEY** to prevent athlete from under or over-exertion.
  - 20 min/day minimum at target HR, not including warmup/cool down.
    - \*Stop at **symptom exacerbation** (>2 point increase from pre-exercise resting value on a 0-10 point scale). So, can exceed 20 min.
  - Bike first, then running, 6-7 d/wk.
  - Increase target HR 5-10 bpm every 3 to 7 days (or re-test).**
  - ≥ 80% age-predicted max HR x 20 min without symptoms for 2 days= "Cardiovascular and Cerebrovascular Physiological Recovery"



32

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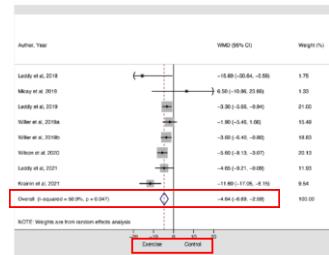
Rest and exercise early after sport-related concussion: a systematic review and meta-analysis

John J Leddy <sup>1</sup>, Joel S Burma <sup>2</sup>, Clodagh M Toomey <sup>3</sup>, Alix Hayden <sup>4</sup>, Gavin A Davis <sup>5</sup>, Franz E Babil <sup>6</sup>, Isabelle Gagnon <sup>7,8</sup>, Christopher C Giza <sup>9,10</sup>, Brad G Kurowski <sup>11</sup>, Noah D Silverberg <sup>12</sup>, Barry Weller <sup>13</sup>, Paul E Ronksley <sup>14</sup>, Kathryn J Schneider <sup>15</sup>

To cite: Leddy JJ, Burma JS, Toomey CM, et al. Br J Sports Med. 2023;57:762-770.

## Forest Plot of early PA and Prescribed Aerobic Exercise Treatment on Recovery

## Meta-analysis



- Sub-symptom threshold aerobic exercise treatment (based on formal exercise testing) should be prescribed to adolescents as soon as 2 days after SRC, which facilitates recovery by a mean of -4.64 days (95% CI -6.69, -2.59).

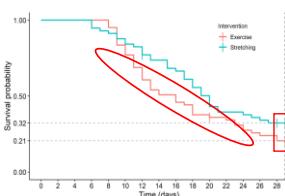
- Grading of Recommendations, Assessment, Development and Evaluations (GRADE) recommendation is **high**.

33

34

Early targeted heart rate aerobic exercise versus placebo stretching for sport-related concussion in adolescents: a randomised-controlled trial

McCrory P, Meeuwisse W, Dvorak J, et al. Early targeted heart rate aerobic exercise versus placebo stretching for sport-related concussion in adolescents: a randomised-controlled trial. Lancet Child & Adolescent Medicine 2021

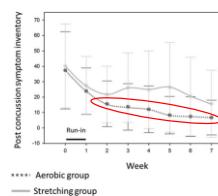


AMSSM CRN Grant  
Lancet Child & Adolescent Medicine 2021

- PPCS: 21% AEx vs 32% Stex.
- ITT: controlling for sex, site, and mean daily exercise time, the Hazard Ratio for PPCS=0.52 corresponding to a **48% reduction in PPCS incidence for AEx** ( $p=0.039$ )

## 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 ( $P = .044$ ).

35

36

## Exercise Prescription in Concussion: Effective Methods for Recovery

## Without Systematic Exertion Testing



37

Practical Management: Prescribing Sub-symptom Threshold Aerobic Exercise for Sport-Related Concussion in the Outpatient Setting  
Bezherano et al. CJS 2020

50% of age-appropriate maximum HR (220-age)  
for 15-20 minutes and systematically advance the training HR according to the degree of symptom exacerbation experienced during the prior exercise bout.

37



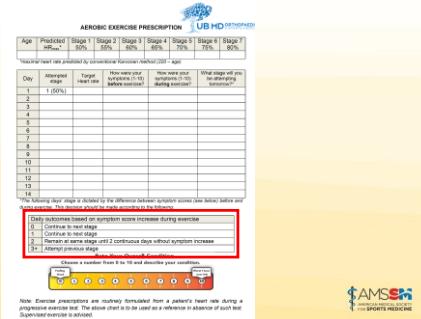
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38

Practical Management: A Standardized Aerobic Exercise Program for Adolescents with Concussion in the Absence of Graded Exercise Testing  
Chizuk H et al CJS 2023

Data-driven, standardized aerobic exercise treatment program

RISING TO THE CHALLENGE



39



40

40

Practical Management: A Standardized Aerobic Exercise Program for Adolescents with Concussion in the Absence of Graded Exercise Testing  
Chizuk H et al CJS 2023

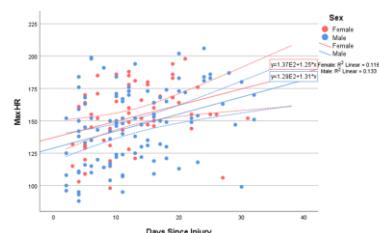
- Data combined from 2 studies\* of adolescent athletes with SRC within 10 days of injury and *had exertion testing*.
- Sex and days since injury**, but not age, affected the HRt of adolescents after SRC.
- Exercise recommendations limited to first 4 weeks because a concussion that lasts 28 days or longer typically requires a multimodal treatment approach (e.g., vestibular, vision, cognitive, psychological treatments, etc.) in addition to aerobic exercise.

\*Chizuk HM. Sex differences in the Buffalo Concussion Treadmill Test in adolescents with acute sport-related concussion. J Sci Med Sport. 2021; Leddy et al Lancet Child & Adolescent Health 2021.



41

Derivation of training target HRs: effect of days from injury and of sex.



41



42

42

## Training Target HRs for time from injury for each sex

	Mean HR Prescription
<b>Females</b>	
Week One	116 - 119
Week Two	124 - 127
Week Three	132 - 135
Week Four	141 - 144
<b>Males</b>	
Week One	123 - 126
Week Two	131 - 134
Week Three	140 - 143
Week Four	147 - 150



## AEROBIC EXERCISE PRESCRIPTION

Your health care provider has given you a prescription for light aerobic exercise. It is very important that you exercise according to your prescription and follow the instructions very carefully. You can progress slowly and increase the amount of exercise as you feel comfortable. You can jog, walk, swim, or cycle, but it is important to avoid a lot of neck motion during exercise. If you are experiencing balance difficulties, avoid exercises that require good balance (for example, bicycling).

Exercise at a target heart rate (HR). Start with a target HR of 60% of your heart rate (HR) resting, for a minimum of 20 minutes at the target HR. Followed by a gradual cool-down. Aim to complete at least 20 minutes of exercise at least 5 days a week. You can exercise for more than 20 minutes on a given day, provided your symptoms do not worsen. You may need to take breaks (by more than 20 minutes) if you feel fatigued compared with your pre-exercise resting value.

**Warning:** While you may increase the amount of time you choose to exercise, please do not increase the exercise target HR intensity without consulting your provider.

## Heart Rate Prescription for Concussed Adolescents (13-18 years)

	Mean HR Prescription
<b>Females</b>	
Week One	116 - 119
Week Two	124 - 127
Week Three	132 - 135
Week Four	141 - 144
<b>Males</b>	
Week One	123 - 126
Week Two	131 - 134
Week Three	140 - 143
Week Four	147 - 150

**Weekly Exercise Calendar**

Name \_\_\_\_\_ Age \_\_\_\_\_ Sex \_\_\_\_\_

Rx \_\_\_\_\_ BHR for \_\_\_\_\_ minutes \_\_\_\_\_ days per week

**Week of:**

Day	Aerobic Exercise	Time	Max HR	RPE	Symptoms Pre-Exercise	Symptoms Post-Exercise
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

When rating your RPE, use 0-10 scale: 0 = light activity, 10 = maximum effort activity. When rating your symptoms, use 0-10 scale: 0 = no symptoms, 10 = worse than ever felt.

When rating your symptoms, use 0-10 scale: 0 = no symptoms, 10 = worse than ever felt.

**Notes:**

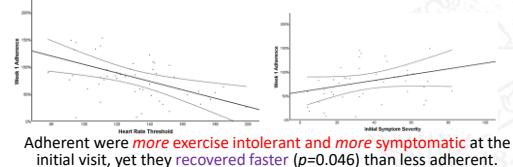
If you experience an increase in your current concussion-related symptoms (e.g. headache, nausea, vomiting, dizziness, etc.) during exercise, stop exercising and return to the pre-exercise resting value (baseline). If you experience an increase in your symptoms when compared with your pre-exercise resting value (baseline), please stop exercising for the day and try again when your symptoms return to the pre-exercise level. The increase in severity of any symptoms should be added to your total score, and the appearance of any new symptoms adds to the symptom score by 1. You can typically tolerate an increase in the RPE by 1-2 units. If you experience an increase in your RPE or a new symptom, stop exercising and return to the pre-exercise resting value. If you experience an increase in your concussion-related symptoms during exercise, stop and contact your provider.

**Rate Your Overall Condition:**

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

## Is Early Aerobic Exercise effective regardless of clinical severity?

Adolescents with Sport-Related Concussion who Adhere to Aerobic Exercise Prescriptions Recover Faster (Chizuk HM et al. MSSE 2022)



## REST AND EXERCISE- AMSTERDAM 2022

- Strict rest until the complete resolution of concussion-related symptoms is **not beneficial for SRC**.
- Relative (not strict) rest, which includes ADLs and reduced screen time, is indicated immediately and for up to the first 2 days after injury.
- Individuals can return to light-intensity physical activity (PA), such as walking that does not more than mildly exacerbate symptoms, during the initial 24–48 hours, while avoiding the risk of contact, collision or fall.
- Individuals can systematically advance their exercise intensity based on the degree of symptom exacerbation experienced during the prior bout of aerobic exercise.
- Reduced screen use in the first 48 hours after injury is warranted but may not be effective beyond that.

## REST AND EXERCISE-

- HCPs with access to exercise treatment within a sub-symptom threshold (HRt) that does not exacerbate during the exercise.
- Sub-symptom threshold aerobic exercise treatment can be progressed systematically based on repeat exercise testing (every few days to every week).
- Athletes may continue/advance the duration and intensity of PA or prescribed aerobic exercise provided there is no more than mild and brief (<1 hour) exacerbation of concussion-related symptoms.
- \*Mild symptom exacerbation during PA, prescribed aerobic exercise treatment or during cognitive activity is typically brief (under an hour) and **does not delay recovery**.



Table 2. Return to sport (RTS) strategy			
STEP	EXERCISE STRATEGY	ACTIVITY AT EACH STEP	GOAL
1	Symptom-limited activity	Daily activities that do not exacerbate symptoms (e.g., walking)	Gradual reintroduction of work/school
2	Aerobic exercise 2A - Light (up approx. 55% maxHR*) then 2B - Moderate (up to approx. 70% maxHR*)	Stationary cycling or walking at slow to medium pace. Moderate light resistance training that does not result in more than mild and brief exacerbation of concussion symptoms	Increase heart rate
3	Individual sport-specific exercise  NOTE: if sport-specific involves risk of head impact, medical determination should occur prior to step 3.	Sport-specific training away from the team environment (e.g. running, change of direction and/or individual sport drills) away from the team environment  No activities at risk of head impact	Add movement, change of direction
Steps 4-6: after resolution of any new symptoms, abnormalities in cognitive function, and clinical findings related to the current concussion			

Amsterdam RTS Strategy

Stages 1-3 are therapeutic

4	Non-contact training drills	Exercise to high intensity including more challenging training drills (e.g., passing drills, multiplayer training) Can integrate into team environment	Resume usual intensity of exercise, coordination, and increased thinking
5	Full contact practice	Participate in normal training activities	Restore confidence and assess functional skills by coaching staff
6	Return to sport	Normal game play	

maxHR=age-predicted maximal Heart Rate (included in supplementary table)

Stages 4-6 reintroduce contact risk

Amsterdam RTS Strategy

## Amsterdam RTS Strategy

- Athletes may begin Step 1 (i.e., symptom-limited activity) within 24 hours of injury, with progression through each subsequent step **typically** taking a minimum of 24 hours.
- Athletes may be moved into the later stages that involve risk of head impact (steps 4-6 and step 3 if there is any risk of head impact with sport-specific activity) following authorization by the HCP and *after resolution of any new symptoms, abnormalities in cognitive function, and clinical findings related to the current concussion.*

## Amsterdam RTS Strategy

- If more than mild exacerbation of symptoms occurs during **Steps 1-3**, the athlete should *stop and attempt to exercise the next day.*
- If more than mild symptom exacerbation occurs during **Steps 4-6**, the athlete should *return to Step 3 to establish full resolution of symptoms with exertion before engaging in at-risk activities.*
- Written determination of readiness to RTS should be provided by a healthcare professional before unrestricted RTS as directed by local laws and/or sporting regulations.

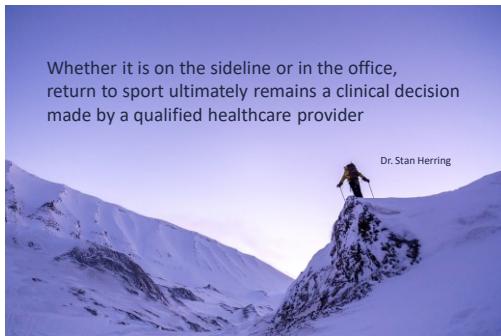
## Amsterdam RTS Strategy

- Expect a minimum of 1 week to complete the full rehabilitation strategy, but *typical unrestricted RTS can take up to one-month post-SRC.*
- Athletes having difficulty progressing through the RTS strategy or with symptoms and signs that are not progressively recovering *beyond the first 2-4 weeks* may benefit from rehabilitation and/or involvement of a multidisciplinary team of HCP experienced in managing SRC.
- Athletes should be *fully back to school* without academic supports *before* RTS.

## Signs and symptoms of Concussion/mTBI

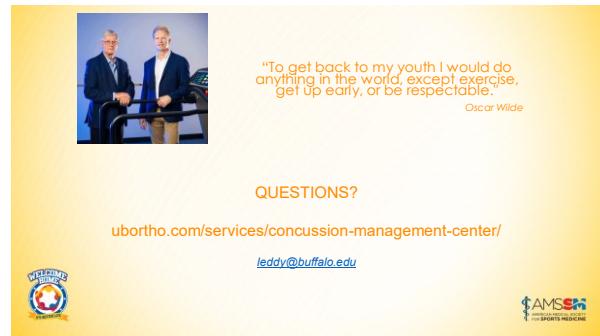
\*Must appear within 72 hours of injury

Domains	Symptoms	Signs
<b>Cognitive</b>	Confusion Feeling "In a fog" or "Zoned Out" Inability to focus	Anterograde amnesia Retrograde amnesia Loss of consciousness Disorientation Delayed verbal and motor responses Vacant state Slurred/incoherent speech
<b>Somatic</b>	Headache <b>Orthostatic Intolerance</b> Visual disturbances Photophobia, blurry double vision Nausea Vomiting	Balance disruption <b>Exercise Intolerance</b> Abnormal near point convergence
<b>Affective</b>	Emotional lability Irritability Fatigue Sleepiness Sadness	Acts irritable Flat affect
<b>Sleep Disturbances</b>	Trouble falling asleep Sleeping more than usual Sleeping less than usual	Excessive drowsiness



Whether it is on the sideline or in the office,  
return to sport ultimately remains a clinical decision  
made by a qualified healthcare provider

61



"To get back to my youth I would do  
anything in the world, except exercise,  
get up early, or be respectable."  
Oscar Wilde

QUESTIONS?

[ubortho.com/services/concussion-management-center/](http://ubortho.com/services/concussion-management-center/)

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

62

