Neuropsychiatry of mild Traumatic Brain Injury(mTBI)/Concussion

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Learning Objectives

- To appreciate signs/symptoms of mTBI/concussion
- To understand neuropsychiatric diagnosis and formulation of mTBI/concussion
- To develop an understanding of other neuropsychiatric sequelae of mTBI/concussion
- To develop an approach to management of common neuropsychiatric sequelae of mTBI/concussion

PRE-QUIZ

Concussion/mTBI is a traumatic brain injury.

A. True
B. False

PRE-QUIZ

Concussion/mTBI is a traumatic brain injury.

A. <u>True</u>

B. False

PRE-QUIZ

What is the definition of a concussion/mTBI?

A. Loss of consciousness for <5 min after an impact to the head
B. A complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces
C. A structural brain injury caused by mild traumatic force that transiently decreases cerebral blood flow

PRE-QUIZ

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PRE-QUIZ

A concussion/mTBI be diagnosed on conventional CT or MRI?

A. True
B. False

PRE-QUIZ

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A. True

B. <u>False</u>

PRE-QUIZ

Which one of the following is correct regarding post-concussive syndrome?

A. Symptoms are always malingered
B. Psychiatric comorbidity can contribute to somatic and cognitive symptoms
C. Persistent concussive symptoms imply a diagnosis of chronic traumatic encephalopathy

PRE-QUIZ

Which one of the following is correct regarding post-concussive syndrome?

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C. Persistent concussive symptoms imply a diagnosis of chronic traumatic encephalopathy

WHAT IS A CONCUSSION?

- ***Traumatic brain injury*** *induced by* ***biomechanical forces***
- *Caused either by a* ***direct blow*** *to the* ***head OR elsewhere on the body*** *with an impulsive force transmitted to the head*
- *Results in* ***rapid onset of short-lived impairment of neurological function*** *that usually resolves spontaneously*
- ***Functional disturbance*** *rather than a structural injury*
- *Results in a* ***range of clinical signs and symptoms*** *that may or* ***may not involve loss of consciousness***
- *In some cases* ***symptoms may be prolonged***

Consensus statement on concussion in sport – 5th international conference, Berlin 2016

HOW DOES IT HAPPEN?

- Transmitting forces to the brain
  - Through injury to head, neck or body causing:
  - Sudden acceleration / deceleration forces
    - *No contact injury required*
  - Rotational forces-ie. Boxing
  - Generally disturbance of **function** rather than of brain structural injury *
- **NOT** necessarily due to bleeding or bruising in the brain
- **MAY** progress to more severe TBI in acute stage

*McCrory P et al. 2013; Signoretti S et al, 2011

mTBI versus concussion

- Synonymous acceptance of mTBI and concussion
- However not all mTBI are truly ‘concussive’
- Precise definition and diagnosis problematic:
  - Head injury/concussion/mTBI
    - Possible
    - Probable
    - Definite
  - Complicated mTBI vs Moderate TBI
  - Post-concussive syndrome

Signoretti et al. 2011

TBI severity classification

Sidebar 2: Indicators for Immediate Referral *(If a patient meets criteria for more than one category of severity, the higher severity level is assigned)*			
Criteria	**Mild**	**Moderate**	**Severe**
Structural Imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness (LOC)	0-30 min	>30 min and <24 hours	>24 hours
Alteration of Conciousness/ mental state (AOC)*	up to 24 hours	>24 hours; severity based on other criteria	
Posttraumatic Amnesia	0-1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (GCS) (best available score in 24 hours) **	13-15	9-12	<9

GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS. Ontario Neutrotrauma Foundation. May 2018.

Glasgow Coma Scale (GCS)

Feature	Response	Score
Best eye response	Open spontaneously	4
	Open to verbal command	3
	Open to pain	2
	No eye opening	1
Best verbal response	Orientated	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No verbal response	1
Best motor response	Obeys commands	6
	Localising pain	5
	Withdrawal from pain	4
	Flexion to pain	3
	Extension to pain	2
	No motor response	1

Glasgow Coma Scale and Score (NICE 2003)

Complicated mTBI

- 6-10 % of cases, May have:
  - Intracranial hemorrhage (ICH) or contusion on neuroimaging
  - Skull fracture
  - Lower GCS than would be expected
  - Focal neurological signs
- Functional outcomes more similar to moderate TBI patients
- If neurological deterioration of mTBI acutely or subacutely suspect evolving ICH and reassess TBI severity, investigations and management

Broshek et al.2015

WHO GETS A CONCUSSION/ mTBI?

- Most common form of traumatic brain injury and Neurological disorder
  - 70-90% of all TBI
- Reaching epidemic proportion :
  - ~ 148,000 in Ontario in 2013*
- Many undiagnosed
- Rate of death 0.2 % of those who visit emergency

*Bayley, M. & Zangeri, L. (2016). *Characterizing concussion in the province of Ontario*. Data obtained from the Institute of Clinical and Evaluative Sciences

WHO GETS A CONCUSSION?

- Falls (30-38%)
- MVA (20-40%)
- Occupational (10%)
- Recreational (10%)-Individual risk of 20% per season in contact sports
- Assaults (5-17%)
- MVA more common in young, Falls more common in Elderly

(Feigin et al., 2013; Jennet & Frankovynsi, 1990)

Risk Factors for mTBI/Concussion

- Male
- High-Risk activities
- Lower socioeconomic status
- Lower cognitive reserve
- Substance Use
- ADHD
- History of previous mTBI/Concussion
- Other medical illness

Signs/Symptoms

Cognitive	Emotional	Somatic/Physical
Attention Concentration Disorientation Memory Recall In a 'Fog' Amnesia Executive dysfunction	Anxiety Depressed mood Irritability Lability Suicidal thoughts	Headache Dizziness Fatigue Sensitivity to light/sound Tinnitus LOC Incoordination Visual changes Sleep disturbance Seizures (less than 5% of mild to mod TBI)

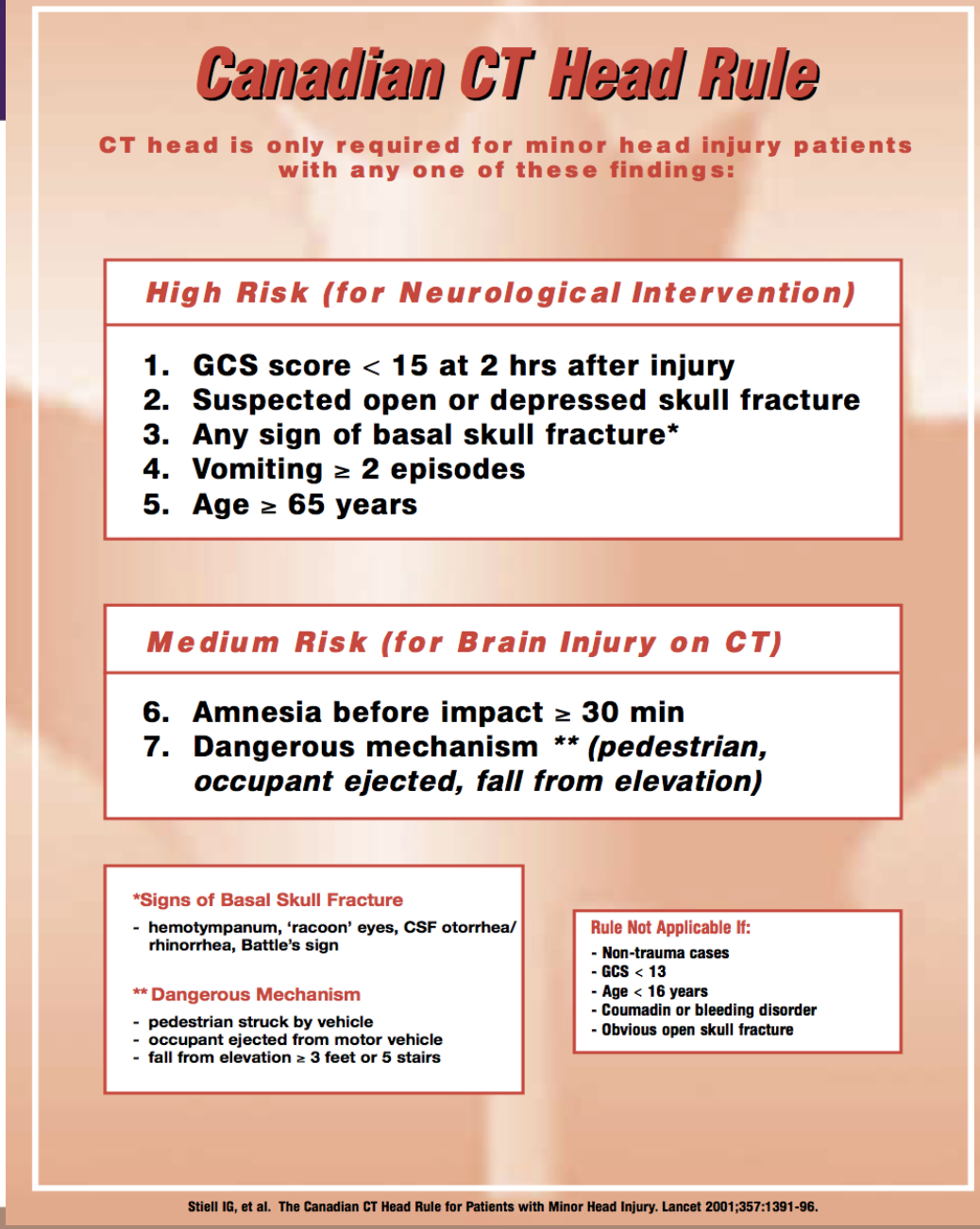
RED FLAGS

Sidebar 1: Indicators for Immediate Referral	
1. Progressively declining level of consciousness 2. Progressively declining neurological exam (Appendix 3.4) 3. Pupillary asymmetry 4. Seizures 5. Repeated vomiting 6. Neuroloigical deficit: motor or sensory	7. Double vision 8. Worsening headache 9. Connot recognize people or disoriented to place 10. Slurred speech 11. Unusual behavior

GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS. Ontario Neutrotrauma Foundation. May 2018.

When to image

In Concussion/mTBI: Neuroimaging is usually unremarkable and not routinely indicated



Natural History of Recovery

- Disability worse on first 7-14 days
- Symptoms resolve within 1-3 months in most cases
- 15-20% may remain symptomatic beyond 6 months. Termed post-concussive syndrome/persistent post-concussive symptoms

Post-traumatic Headache (PTH)

- Most common mTBI symptom
- Typically improve days-weeks
- Migraine, tension type headaches, mixed & other
- Psychiatric disorders can also contribute to headaches in mTBI

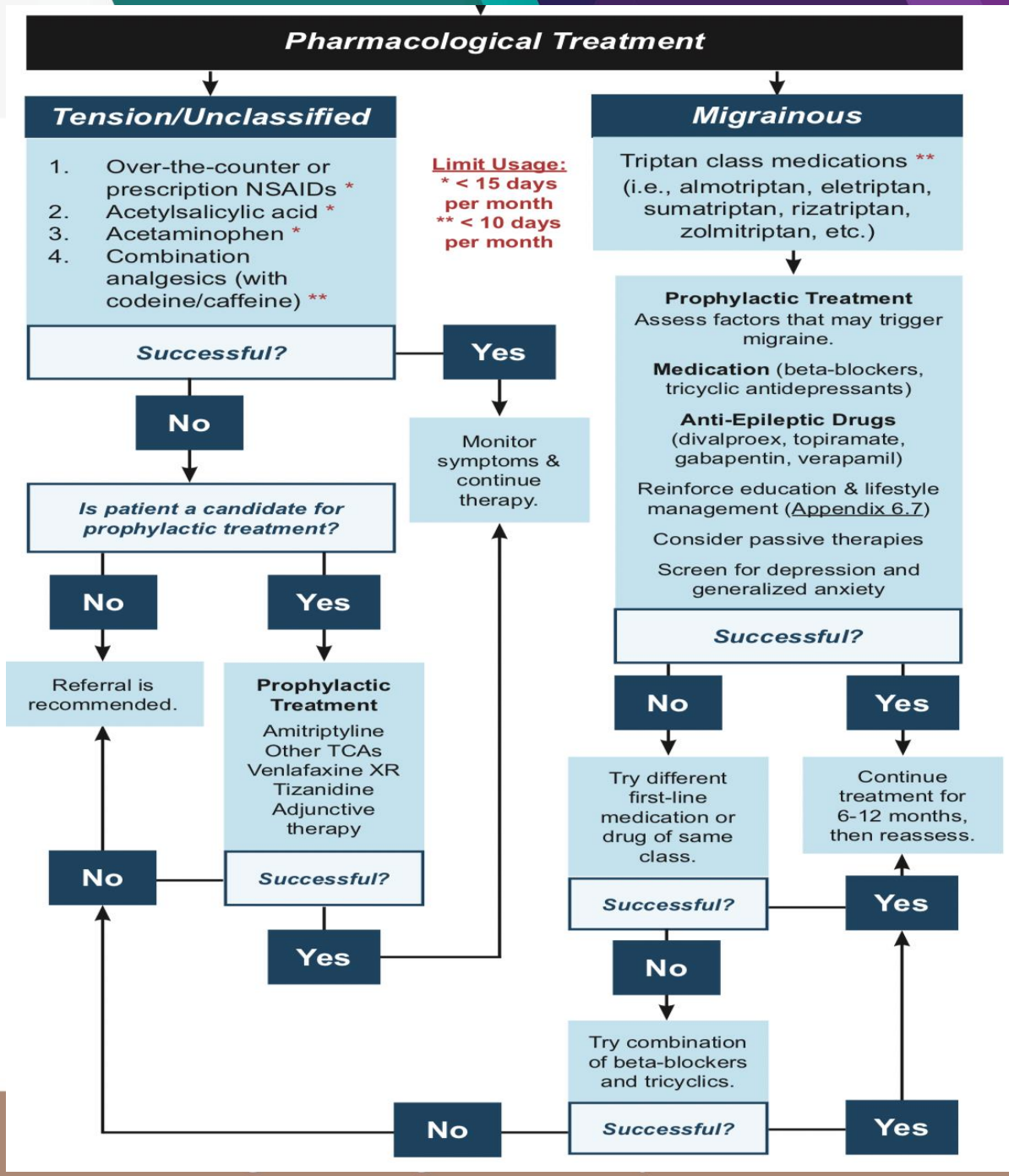
- ***Exacerbating factors:***
  - ***Stress***
  - ***Insomnia***
  - ***Lack of Aerobic Exercise***
  - ***Skipping Meals***
  - ***Dehydration***

Post-traumatic Headache

- Beware medication overuse headaches
  - 50% of people with 15+ headaches per month

Max Use 10 days per month	Max Use 15 days per month
-Combination Analgesics (with caffeine/codeine) -Triptans	-OTC or prescription NSAIDS -ASA -Acetaminophen

- Avoid Narcotics
- Consider prophylactic therapy if frequent and disabling (Beta-blockers, Antiepileptics , TCA's, SNRI's and many others, consider comorbidities to reduce polypharmacy)*



Headache

- Tension/Other vs Migrainous
- OTC
- Prophylactic
- Abortive

GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS.
Ontario Neutrotrauma Foundation. May 201

Sleep Disturbance

- 50% + of mTBI
- Initially hypersomnic
- Insomnia in subacute/chronic
- Poor prognostic factor at 1 year post injury
- Screen for depression, anxiety, PTSD, pain
- Can be driver of subjective cognitive dysfunction, other somatic symptoms in mTBI

mTBI & Sleep Treatment

- Cognitive Behavioral Therapy/Mindfulness
- Melatonin
- Magnesium/Zinc supplementation
- Trazodone
- ‘Z’ class drugs*
- Tricyclic antidepressants*
- Mirtazapine
- Prazosin if PTSD related nightmares
- Avoid Benzodiazepines*

Fatigue in mTBI

- 30% of mTBI
- Multifactorial
  - Insomnia
  - Pain
  - Iatrogenic
    - Ie. Medication
    - Prolonged prescribed rest
  - Cognitive
  - Psychological/Psychiatric
  - Social Stressors
  - Deconditioning*
- If present, poor prognostic factor
- Can persist 5 years post injury

11.3* A

After a brief period of rest during the acute phase (24–48 hours) after injury, patients can be encouraged to become gradually and progressively more active as tolerated (i.e., activity level should not bring on or worsen their symptoms).

INJURY & PERSISTENT SYMPTOMS. Ontario Neutrotrauma Foundation. May 2018.

Fatigue in mTBI treatment

- Exercise
- Light therapy
- Cognitive Behavioral Therapy (CBT)
- Mindfulness
- Modafinil
- Methylphenidate
  - Caution regarding rebound fatigue
  - Caution re: anxiety

Dizziness/Balance in mTBI

- Most commonly from benign paroxysmal positional vertigo (BPPV)
- DDX:
  - Migraines
  - Medications
  - Other vestibular cause
  - Treatment:
    - ENT/multidisciplinary team
    - Vestibular Rehabilitation
    - Epley maneuver on Dix-Hallpike + patients
  - ***Anxiety is Common***
    - *Can be primary reason for dizziness*
    - *'functional overlay' in magnifying or perpetuating underlying physical symptoms*

mTBI and Cognition

- Changes in cerebral metabolic activity and perfusion can occur acutely
  - Attention/Concentration
  - Processing speed
  - Memory
  - Executive Function
  - Other
- Cognitive recovery in 1 week- 6 months
- Cognition should not worsen over time from single mild injury alone
  - ***15% + experience persistent cognitive symptoms***

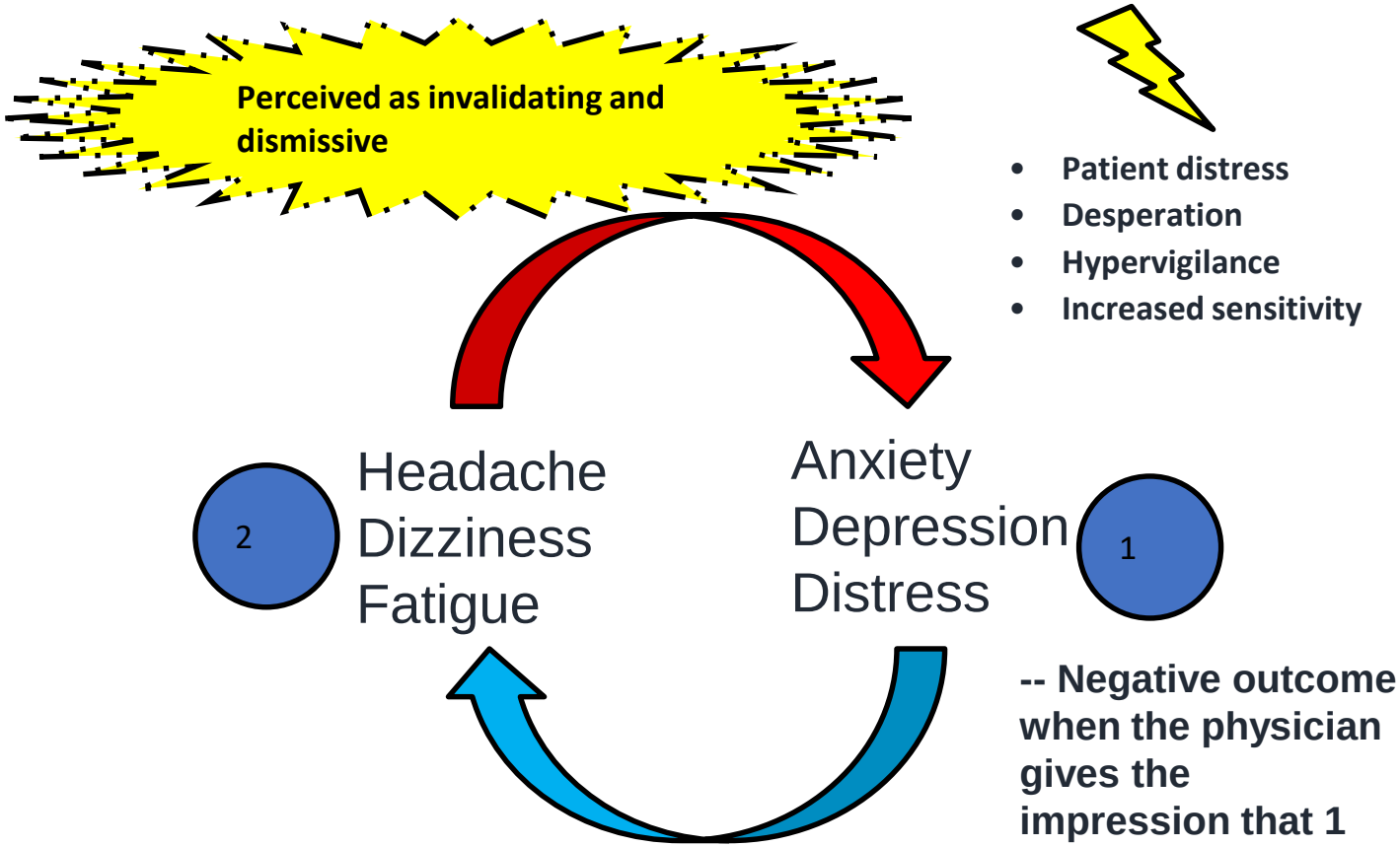
mTBI persistent or worsening cognitive symptoms

- Medical reassessment
- Education to reduce misattribution of symptoms to original injury that now may be due to other factors (not just psychiatric factors)
- Graduated reintegration to previous level of function
- Be aware of Iatrogenic factors that perpetuate symptoms
  - unnecessary medical workup/referrals
  - controversial or excessive use of treatments

******Physical/cognitive/emotional deconditioning secondary to well-intentioned healthcare professionals prescribing protracted cognitive and physical rest******

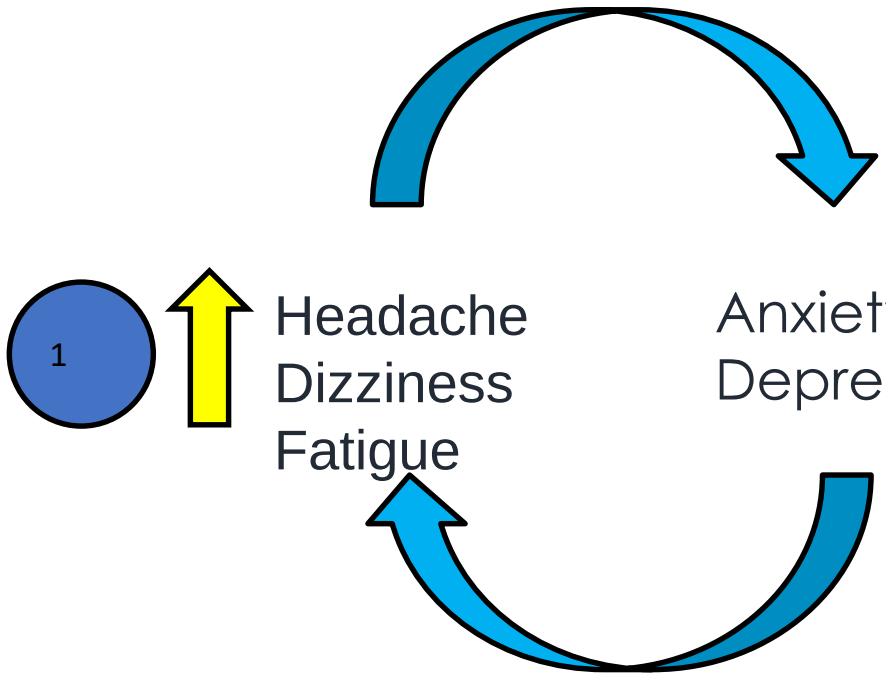
Broshek et al.2015

Common Approach To Discussing Psychological Factors that may contribute to Physical Symptoms



Adapted from Gerretsen P

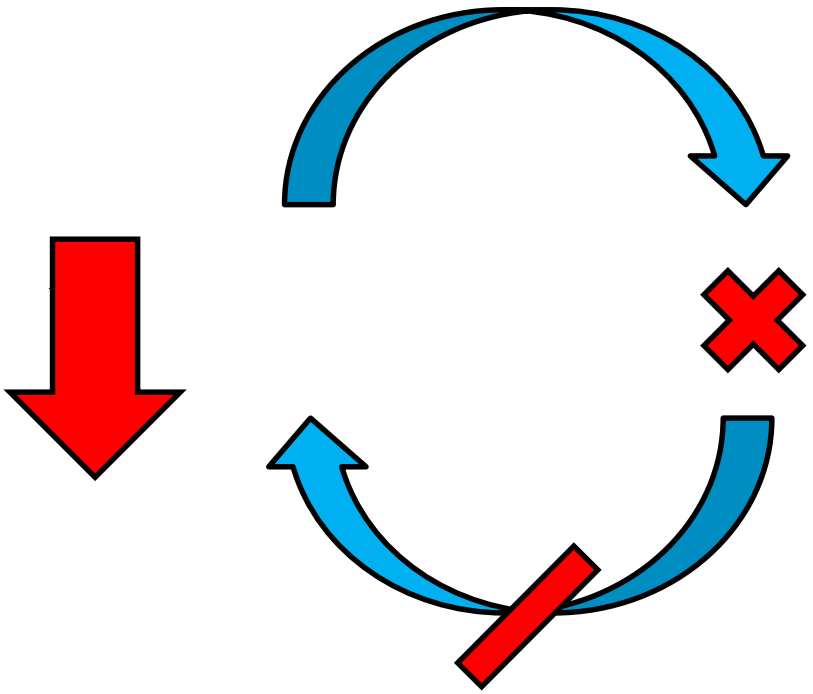
Bidirectional Brain-Body Interaction



- **Fear of falls**
- **Fear of reinjury**

- **Isolation**
- **Depressed mood**
- **Anhedonia**
- **Avoidant behaviors**
- **Deconditioning**

Bidirectional Brain-Body Interaction



- Fear of falls
- Fear of reinjury

- Isolation
- Depressed mood
- Anhedonia
- Avoidant behaviors
- Deconditioning

Neuropsychiaty & mTBI/concussion

- **MAJOR ISSUE!**
  - Major Depressive Disorder
  - PTSD
  - Phobias
  - Generalized Anxiety
  - Somatoform disorders
  - Substance Use Disorder
- **'Vicious Cycle'**
  - **Bidirectional relation of injury/physical symptoms and psychiatric symptoms**

Acute mTBI/concussion Neuropsychiatry

- Irritability, Labile mood, Apathy, Anxiety
  - Transient early acute concussive symptoms vs. primary psychiatric disorder
  - Prompt treatment if symptoms persist or worsen

- Mental status at time of injury important to know
  - Rule out exacerbation of pre-existing psychiatric condition
    - Special Ψ populations in mTBI
      - ADHD
      - Substance Use Disorders
      - Personality Disorders
      - Factitious Disorders/Malingering

Neuropsychiatry & mTBI/concussion

- Neurobiological impact of injury

- Psychiatric Diagnoses preceding/following
- Psychosocial stressors of injury
  - Inability to work/function/play
  - Workplace injury/Legal proceedings
    - BEWARE MALINGERED SYMPTOMS
    - Workplace stressors at time of injury?

mTBI ⋔ Treatment

- Treatment of medical comorbidities
- Lifestyle & Goal management training
- Cognitive Behavioral Therapy/Mindfulness
- Medications:
  - Start low and go slow
  - One change at a time
- Antidepressants
  - Best evidence Sertraline & Citalopram for anxiety and depression in mTBI
  - Can improve cognition, somatic symptom burden, mood, anxiety, irritability, and improve level of overall function

- ***Other agents equally useful depending on clinical presentation***

mTBI ⏚ Treatment

- BE AWARE:
  - Increased sensitivity to cognitive side effects of anticholinergic agents
    - ie. Amitriptyline for headache management
    - Dimenhydrinate for nausea
  - Risk of seizures 1.5x that of general population
    - Special attention to TCA's, Bupropion, antipsychotics
  - Benzodiazepines
    - Not appropriate as first line therapy or for long term use
    - Risk of dependence, falls, reinjury and cognitive side effects
    - ***HOWEVER, short term use can be helpful in SOME patients***

Post-Concussive Syndrome (PCS)
"The Miserable Minority"

- Cognitive/Emotional/Physical symptoms similar to those of original injury that persist beyond 3-6 months
  - 15-20% of concussion patients.

- Controversial Cause:
  - Cerebral dysfunction vs. psychiatric vs. other medical cause
  - Generally multifactorial

- By definition symptoms should not worsen from a single concussion/mTBI over time
  - However, many PCS do report worsening or fluctuating symptoms over time

Broshek et al.2015; Oldenburg et al. 2018; Iverson & Lange, 2003; GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS. Ontario Neutotrauma Foundation. May 2018.

DDX- Persistent Post-Concussion Syndrome

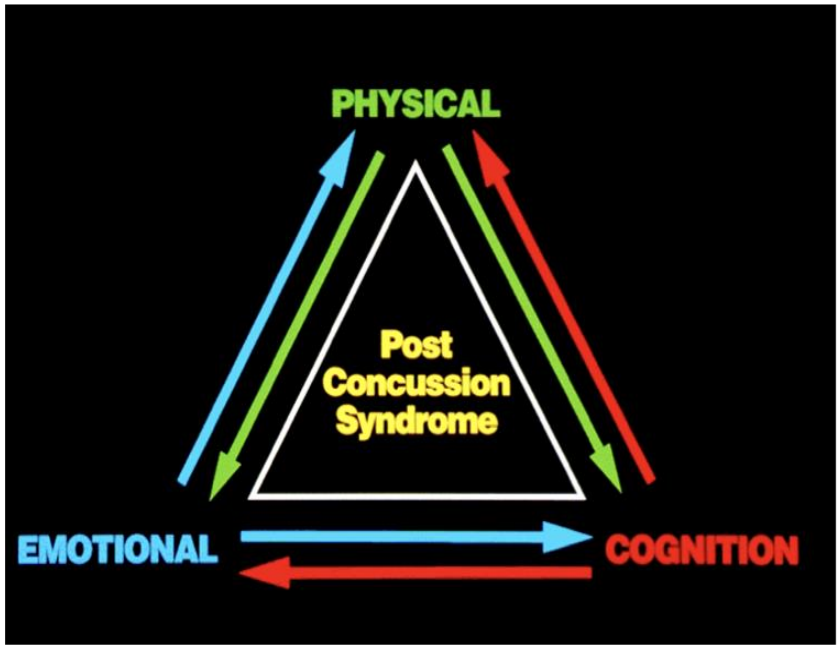
Major depressive disorder
Generalized anxiety disorder
Post-traumatic stress disorder (PTSD)
Chronic pain syndrome
Cervical strain/whiplash associated disorder
Substance abuse or polypharmacy
Somatic symptom disorder
Factitious disorder
Malingering
Post-traumatic headache
Post-traumatic dizziness
Fibromyalgia syndrome (secondary)
Primary sleep disorder: e.g., obstructive sleep apnea

GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS. Ontario Neutotrauma Foundation. May 2018.

Post-Concussion Syndrome

- Concussion-> Disrupted Cognition -> Psychological Distress/Anxiety->Anxiety Related Cognitive Symptoms-> More Anxiety and Avoidance-> Depression/Deconditioning-> Depression Related Cognitive Symptoms->

- **Psychological cognitive overlay may accumulate becoming more disabling than that from the original physical injury**



Broshek et al.2015

Post-Concussion Syndrome Associated With:

INTRINSIC FACTORS	EXTRINSIC FACTORS
High Expectations of Self High Harm-Avoidance Embitterment/Suspiciousness Depression/Anxiety Trauma history Symptom Preoccupation Personality traits/disorders: *Histrionic* *Narcissistic* *Obsessive Compulsive*	External pressure at work/school/sport Prescribed/protracted rest Litigation/Insurance ?Non-Deliberate vs. Deliberate Exaggeration?

Broshek et al.2015; Oldenburg et al. 2018; Iverson & Lange, 2003; Garden et al., 2010, Losoi et al, 2015

When are symptoms of PCS truly gone?

NOTE: Endorsement of 'PCS like' symptoms common in the ***absence of brain injury*** in the general population

- 60% of healthy participants meet criteria for PCS in absence of injury
- Severity of original TBI does not necessarily predict PCS symptom burden

TABLE 1
Percentage of BC-PSI Post-Concussion Symptom Endorsement: Frequency Ratings for All Levels of Intensity ($n = 96$)

Post-concussion symptoms	%
Headaches	81.3
Dizziness	52.1
Nausea	53.2
Fatigue	81.3
Noise sensitive	34.4
Irritability	78.1
Feeling sad	70.1
Nervous or tense	76.0
Temper problems	58.3
Poor concentration	73.4
Memory problems	56.3
Difficulty reading	36.5
Poor sleep	68.8

Note. BC-PSI = British Columbia Post-Concussion Symptom Inventory.

Adapted from: Garden & Sullivan, 2010, Wijenberg et al. 2017

"Good-old-days" Recall bias in PCS

- "...experience of any negative event, be it accident or illness, head injury or non-head-injury, may be required for one to focus on the past as 'better' than one's current state, for one to think about the 'good old days' prior to the negative event"

  Gundstad & Suhr, 2001

- "given that PCS symptoms are relatively non-specific, any negative event may result in report of more current PCS symptoms and fewer PCS symptoms in the past"

  Gundstad & Suhr 2004

RETURN TO ACTIVITY in mTBI history
'if some rest if good, more is better?'

- Advocacy for bed rest in 1920's/1930's after mTBI and many other medical conditions
- 2002 RCT challenges dogma of prescribed rest (de Krujik et al. 2002)
- 'Rest Until Asymptomatic' endorsed in Consensus Statements on Concussion into the 2000's based on expert opinion
- 2016 Canadian Consensus Statement on Concussion in sport recommends gradual re-introduction of activity after a 24-48 hour period of initial rest
- 2017 systematic review confirms a brief 24-48 hour period of cognitive and physical rest followed by gradual increase in activity at subsymptom threshold with submaximal initial exercise beneficial in mTBI (Schneider KJ et al., 2017)
- 2019 study shows little evidence of de-implementation of prescribed prolonged rest and worsened productivity in those advised to rest by a health care practitioner (Silverberg and Otamendi, 2019)

GRADUATED RETURN TO SCHOOL

Stage	Aim	Activity	Goal of each step
1	Daily activities at home that do not give the student-athlete symptoms	Typical activities during the day as long as they do not increase symptoms (i.e. reading, texting, screen time). Start at 5-15 minutes at a time and gradually build up.	Gradual return to typical activities
2	School activities	Homework, reading or other cognitive activities outside of the classroom.	Increase tolerance to cognitive work.
3	Return to school part-time	Gradual introduction of schoolwork. May need to start with a partial school day or with increased breaks during the day.	Increase academic activities.
4	Return to school full-time	Gradually progress.	Return to full academic activities and catch up on missed school work.

Canadian Guideline on Concussion in Sport
Adapted from Consensus statement on concussion in sport –5th international conference, Berlin 2016

Return to School (Post-Secondary)

- ASYMPTOMATIC:
  - Return to school as tolerated
- SYMPTOMATIC:
  - **1-2 weeks:** no school if debilitated
  - Academic accommodations office for support
  - Medical follow up
  - **2 weeks:**
    - Gradual return to school
  - **4 weeks post-injury:**
    - **If still symptomatic reassess and consider other comorbidities**
    - **Review accommodations**
    - **Consider temporary withdrawal from program if negative consequences to grades or participation expected**

GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS. Ontario Neutrotrauma Foundation. May 2018.

Table 3.2. Graduated Return-to-Sport Strategy

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

NOTE: An initial period of 24–48 hours of both relative physical rest and cognitive rest is recommended before beginning the RTS progression.
There should be at least 24 hours (or longer) for each step of the progression. If any symptoms worsen during exercise, the athlete should go back to the previous step.
Resistance training should be added only in the later stages (stage 3 or 4 at the earliest). If symptoms are persistent (e.g., more than 10–14 days in adults or more than 1 month in children), the athlete should be referred to a healthcare professional who is experienced in the management of concussion.

Adapted from *McCrory P, Meeuwisse W, Dvořák J, et al. Consensus statement on concussion in sport. Br J Sports Med 2017;51:838-847*

GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS. Ontario Neutrotrauma Foundation. May 2018.

The Four Ps can help you gradually increase your activity after a concussion.[3]

Prioritize	• Decide what activities are most important to you and what you are able to do, based on how you feel. • Make these activities a priority.
Plan	• Plan what activities you will do, when you will do them, how you will do them, and where you will do them. • Do activities that require more energy at times in the day when you feel best. • Plan rest breaks into your day as you progress toward full return to activity.
Pace	• It may take you longer to complete activities after a concussion. • Break up long or difficult tasks so that you are not doing too much at once.
Position	• Environments that are noisy, are busy, or require a lot of physical effort, like too much standing, will use more energy. • Be thoughtful about *where* you do an activity. Start with quiet places that have few distractions.

Modifed from : Reed N, et al., Arch Phys Med Rehabil. 2019 Apr;100(4):789-791.

SECOND IMPACT SYNDROME (SIS)

- Concussed brain cells vulnerable to reinjury within a close temporal window
  - Second 'non-lethal' injury in a short time can cause these cells to die
- 2 'non-lethal' injuries in close proximity can cause catastrophic injury
  - Malignant brain swelling
  - Increased intracranial pressure
  - Erratic cerebral perfusion
- POTENTIALLY FATAL

Signoretti S et al., 2011

CHRONIC TRAUMATIC ENCEPHALOPATHY (CTE)

- Proposed to be a progressive neurodegenerative/ neurocognitive disorder as a late effect of repetitive head trauma
  - Typically pro-athletes/military personnel
  - 8-10 years after repetitive brain injury
  - *Dementia Pugilistica* (Punch Drunk Syndrome)->CTE
  - **There remains controversy**
- Symptoms may include personality change, depression, anxiety, impulsivity, aggression, memory difficulty, parkinsonism and suicidality
  - Many other reasons these symptoms may occur before or after injury

Randolph C, 2018; Zuckerman et al., 2018

CTE:

NEUROPATHOLOGICAL diagnosis postmortem (Tauopathy)

CANNOT DIAGNOSE CTE IN LIVING PATIENTS:

- Lack of clear clinical profile
  - Many possible explanations for reported symptoms
  - No definitive biomarkers
  - Neuropathological findings not consistent in symptomatic versus not
- Iatrogenic Fear and Anxiety
  - May be seen as 'Death Sentence'
  - Irreversible psychological harm possible in absence of definitive standards to diagnose and prognosticate

Randolph C, 2018; Zuckerman et al., 2018

Key Messages

- Concussion/mTBI is common
- Concussion is a CLINICAL diagnosis and imaging is **not** required in the absence of red flags
- Signs and symptoms are typically short-lived, but may persist in some cases
    - Bidirectional relationship of somatic/psychological symptoms
    - Consider other medical and psychiatric causes
- Encourage gentle activity and gradual return to function instead of prescribed protracted rest
- Caution re: Secondary Impact Syndrome
- CTE is controversial and is a post-mortem diagnosis

Questions?

References

- GUIDELINE FOR CONCUSSION/MILD TRAUMATIC BRAIN INJURY & PERSISTENT SYMPTOMS. Ontario Neutrotrauma Foundation. May 2018.

  www.onf.org

- CANADIAN GUIDELINE ON CONCUSSION IN SPORT| PARACHUTE

  www.parachutecanada.org