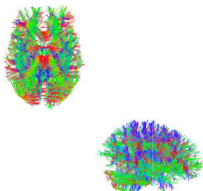


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Sacrificing for Glory: An Overview of Concussion in Sports.


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Assistant Professor
UAB Department of Neurology
Epilepsy Division

Conflicts of Interest/Funding

No financial disclosures related to this talk

US Patent #10,729,200 B2
EFS ID 24056598
International Application Number: PCT/US15/60227
Filed: November 11, 2015
Title: Protective Helmets Having Energy Absorbing Tethers
Blake Feltman, Dr. Dean Sicking, Dr. Thom Houston


Previous funding: NIH/NINDS: UAB Research and Education Program in Neurology, Neurosurgery, and Neuropathology **1R25 NS07918801** 2014- 2017 – completed



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Objectives

- Define concussion and the mechanisms of concussive injury
- Explore current diagnostic techniques of sports related concussion (SRC)
- Discuss modern/future preventative technology and post concussion treatment.



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What is concussion?



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Table Historical development of concussion

Author	Year	Term	Description	Effects
Rhazes	900	Comotio cerebri	Abnormal transient physiologic state without gross brain lesions	Transient
Avicenna	1020	Comotio cerebri	As per Rhazes definition	Transient
Landfrancus	1280	Comotio cerebri	Distinguished comotio (shaking) with no damage from comotio cerebri with structural damage	Transient
du Chauliac	1363	Comotio cerebri	Injury to the head without wounding of the brain or break of the skull	Transient
Brunschwig	1497	Comotio cerebri	Mild brain injury distinguished from penetrating brain injury	Transient
de Cuspi	1518	Comotio cerebri	Defined as brain injury without fracture or hemorrhage	Transient
Cotlier	1573	Comotio cerebri	Brain contusion causing impairment in memory, understanding, and judgement	Transient
Fabricius	1578	Comotio cerebri	Blow causing lethargy and vertigo	Transient
Pare	1579	Embranlement	Blow to the head causing symptoms	Variable
Quoyrat	1657	Comotio cerebri	Injury due to the "ebb and flow" of nervous tissue within the brain	Transient
Marchetti	1665	Concussion	"Alteration of the mind with privation of senses"	Transient

* Although Ambroise Pare reportedly spoke no Latin, his term *embranlement* may be translated as *to shake* in old French. When his books were translated into Latin, the terms *comotio cerebri* and *concussion* were variably used in place of *embranlement*. The term *concussion* is probably derived from the Latin verb *concussio* (to shake).

McCrory, Paul R., and Samuel F. Berkovic. "Concussion: the history of clinical and pathophysiological concepts and misconceptions." *Neurology* 57.12 (2001).

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TBI Classification – mTBI

Criteria for Closed Head Injury	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness	0-30 minutes	> 30 minutes and < 24 hours	> 24 hours
Alteration of consciousness / mental state	< =24 hours	> 24 hours	> 24 hours
Post-traumatic amnesia	< =24 hours	> 24 hours and < 7 days	> 7 days
Glasgow Coma Scale (best available score in first 24 hours)	13-15	9-12	3-8

Voss, Jameson D., et al. "Update on the epidemiology of concussion/mild traumatic brain injury." *Current pain and headache reports* 15.7 (2015): 32.

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Current evidenced based definition of concussion*

- a change in brain function,
- following a force to the head, which
- may be accompanied by temporary loss of consciousness (less than 30 minutes), but is
- identified in awake individuals, with
- measures of neurologic and cognitive dysfunction
- with normal brain imaging

NCAA Sport Science Institute: Diagnosis and Management of sports related concussion, best practices, 2017
Carney, Nantz, et al. "Concussion guidelines step 1: systematic review of prevalent indicators." *Neurosurgery* 75, suppl_1 (2014): S3-S15.



Sports Related Concussion

- Estimated 1.6 – 3.8 million sports related TBIs in the US each year. (Langlois et al.2006)
- Results in ~200,000 ED visits per year (CDC 2006)
- Men: highest incidence in football, ice hockey, and lacrosse, followed by soccer, rugby, and wrestling.
- Women – highest incidence in soccer > basketball > lacrosse

***Women - twice as likely to suffer concussions in similar sports compared to men**



Incidence by player position: *American Football*

Table 2 Incidence of concussion in football

	No. (%) of concussions	Injury risk (incidence proportion) per season	95% CI		Injury rate (incidence rate) per 100,000 athlete-exposures	95% CI	
Overall	239 (100)	8324	2.6	2.3, 3.0	1.3	676,274	35.3, 30.8, 39.8
Exposure type							
Games	148 (61.9)	—	—	—	77,767	190.3	159.7, 221.0
Practices	85 (35.6)	—	—	—	598,507	14.2	11.2, 17.2
Setting							
High school	197 (82.4)	7247	2.6	2.2, 3.0	1.4	566,063	34.8, 29.8, 39.7
College	42 (17.6)	1277	2.9	2.0, 3.8	1.9	110,212	38.1, 26.6, 49.6
Position ^d							
Defensive back	23 (9.6)	811	2.7	1.6, 3.8	2.4	65,327	35.2, 20.8, 49.6
Defensive lineman	26 (10.9)	1090	2.3	1.4, 3.2	2.3	87,072	26.9, 18.4, 41.3
Linebacker	29 (12.1)	909	2.8	1.7, 3.8	2.2	72,539	40.0, 25.4, 54.5
Offensive lineman	48 (20)	2051	2.2	1.6, 2.9	1.8	161,901	29.7, 21.3, 38.0
Quarterback	19 (7.9)	506	3.6	1.8, 5.2	2.7	39,737	47.8, 26.3, 69.3
Receiver	31 (13)	1264	2.4	1.5, 3.2	2.1	100,046	31.0, 20.1, 41.9
Running back	40 (16.7)	1135	3.3	2.2, 4.3	2.0	89,028	44.9, 31.6, 58.9
Special teams and kicker	5 (2.1)	230	2.2	0.3, 4.1	13.7	148,506	26.6, 13.3, 49.8
Tight end	13 (5.4)	487	2.7	1.2, 4.1	3.4	38,488	33.8, 15.4, 52.1

^aConfidence interval, CLL confidence limit rate

^bInjury risk is the average probability that an athlete will be concussed during a season

^cThere were six concussions (2%) in activities other than games and practices; position is undefined for these injuries

(Marshall et al, 2015)



Head Impacts, Women's soccer

	No. Head Impacts	Total Minutes Played	Head Impact Rate per 100 min per Player (95% CI)	Head Impact Rate Ratio (95% CI)		
Position				Mid.For.	Mid.Def.	Def.For.
Forward	295	4059	6.54 (5.79-7.29)			
Midfielder	513	5160	8.02 (7.33-8.71)	1.23 (1.07-1.41)	1.15 (1.03-1.30)	1.06 (0.93-1.22)
Defender	526	6810	8.90 (8.36-9.45)			
Year						
Fresh and Soph.	1099	10,518	9.40 (8.85-9.96)		2.77 (2.42-3.18)	
Junior and senior	236	6257	3.39 (2.96-3.83)			
Wide vs central						
Wide	754	8169	8.31 (7.71-8.90)		1.37 (1.23-1.52)	
Central	581	8608	6.08 (5.58-6.57)			

Mid., midfielders; For., forwards; Def., defenders; Fresh., freshmen; Soph., sophomore.

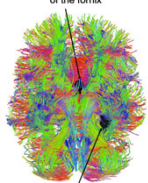
Pathophysiology

- *Neurotransmitter Dysregulation*
 - Glutamate release promotes K⁺ efflux, binding of NMDA receptors, causing hyperexcitability
- *Metabolic Mismatch*
 - Mitochondria can't keep up with demand – glycolysis and lactic acid production
- *Neuroinflammatory Changes*
 - Microglial infiltration locally – protective vs. damaging
- *Cerebral Blood Flow Changes*
 - Reduced vasoreactivity as a result of acute increases in CO₂ and increased nitric oxide production - worsened with exertion*
- *Axonal Injury*
 - Membrane swelling and possible rupture - leakage of ions and NTs

Steenerson, K, and Stirling, A.J., 2017. Pathophysiology of sports-related concussion. *Neurologic clinics*, 35(3), pp.403-408.

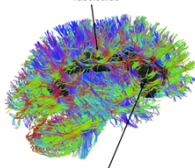
So where is the damage occurring?

Decreased FA in the body and column of the fornix

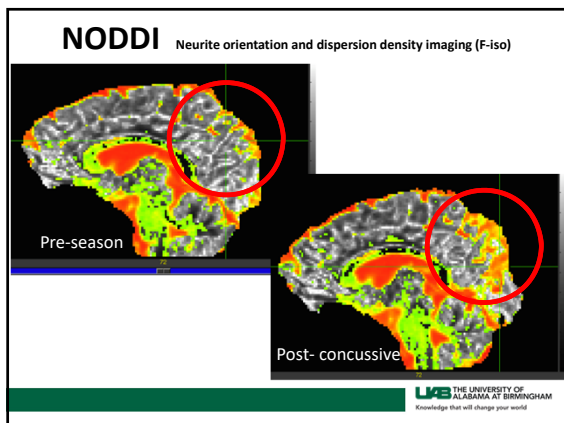


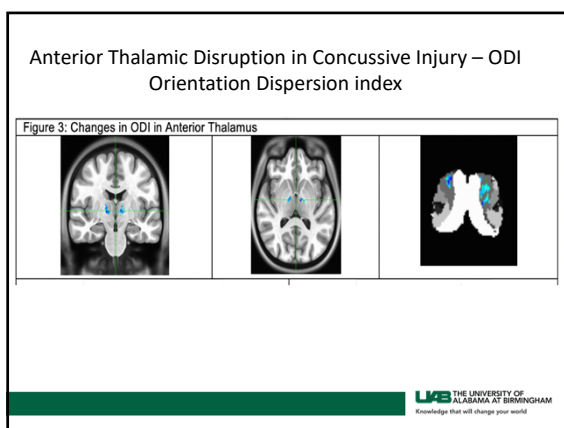
Decreased AD and MD in the posterior thalamic radiations

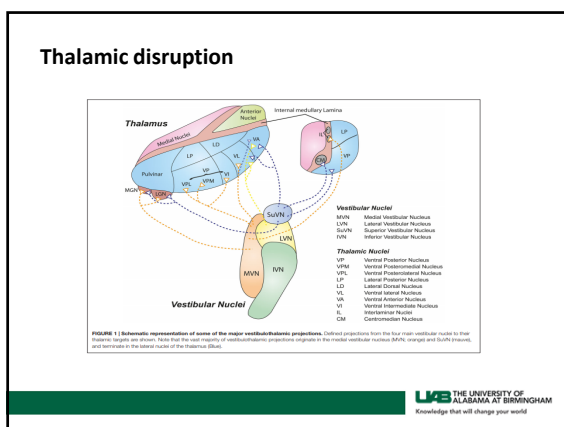
Decreased MD in the right superior fronto-occipital fasciculus



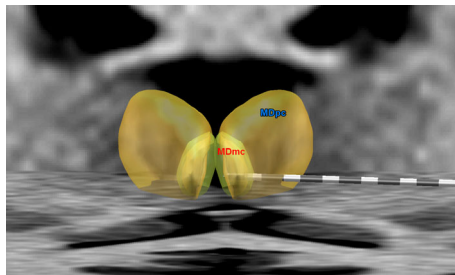
Decreased MD in the right anterior corona radiata







sEEG in Thalamus – Dr. Sindip Pati



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Diagnosis of SRC

- **Purely clinical** – patients either report symptoms or concussion is suspected by staff, medical personnel, or referees In event of lost of consciousness, **FIRST assess ABC's and examine for cervical spine injury**
- **Focal neuro deficits** – STAT ED evaluation with CT imaging
- **Sideline assessment** – includes standard physical/neuro exam with additional cognitive, balance and vestibulo-ocular testing

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Testing Protocols

- Maddocks Questions
- The Standardized Assessment of Concussion (SAC)
- King-Devick
- Balance Error Scoring System (BESS) or modified BESS.
- The Sport Concussion Assessment Tool (SCAT)
- NFL Sideline Concussion Assessment Tool

Table 3 Sideline concussion evaluation tests

Test	Time to administer	Sensitivity	Specificity	False positives	False negatives
Symptom scores	2-3 min	68%			32%
Angelo (2003) 9-item		89%	100%	0%	11%
McCrea (2005) 17-item					
Maddocks (CSM 1999)	<1 min	32-75%	86-100%	29-68%	0-11%
SAC	5 min	94%	76%	24%	6%
Ban (2001)		80%	91%	9%	20%
McCrea (2005)	5 min				
BESS					
MACrew (2002)		34%	91%	66%	9%
Modified BESS	2-3 min	Unknown	Unknown	Unknown	Unknown
SAC + BESS	10 min	Unknown	Unknown	Unknown	Unknown
NFL Sideline Concussion Assessment Tool (SAC+modified BESS+Symptom score)	8-10 min	Unknown	Unknown	Unknown	Unknown
SCAT2 SAC+modified BESS+Glasgow coma scale+physical signs score+Maddocks's score+coordination exam	8-10 min	Unknown	Unknown	Unknown	Unknown

Harmon et al, 2013

*The sensitivity and specificity of the diagnosis of concussion may increase when combining multiple assessment tools. (Lau et al, 2011)

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SCAT 5 Testing

<https://scat5.cattonline.com>

- **Areas of Focus**
 - Orientation
 - Immediate and Delayed Recall
 - BESS (balance assessment)
 - VOMS (vestibulo-ocular assessment)
- *In acute sideline setting, SCAT 5 not typically used in comparison to prior tests*

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Emerging technologies - BrainScope™

Assess mild head injured patients in minutes

BrainScope is the only FDA cleared non-invasive medical device that objectively assesses head injured patients for both brain bleeds & concussions at point of care.
Demonstrated potential to reduce head CT in the ED by up to 80% 📊



FDA

- ✓ 8 FDA clearances
- ✓ 12 years of R&D
- ✓ 32 peer-reviewed publications
- ✓ 4,500+ subject evaluations

In the FDA validation study, the Brain Function Index (BFI) was demonstrated to scale with severity of functional impairment: as the BFI goes down, the level of functional impairment increases. The assessment is indicated for use on patients 18-85 years of age, within 72 hours of head injury, and GCS 13-15.

<https://www.brainscope.com>

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Eye Tracking Metrics – FDA approved March 2022 for aid in concussion diagnosis.

OCULOGICA

PUBLICATIONS NEWS ABOUT US REQUEST A DEMO



EyeBOX Concussion Assessment

Gain Objective Insights

EyeBOX is FDA cleared to aid specifically in the diagnosis of concussion by measuring abnormalities in eye movements. It's sensitive to eye movements and takes less than 5 minutes.

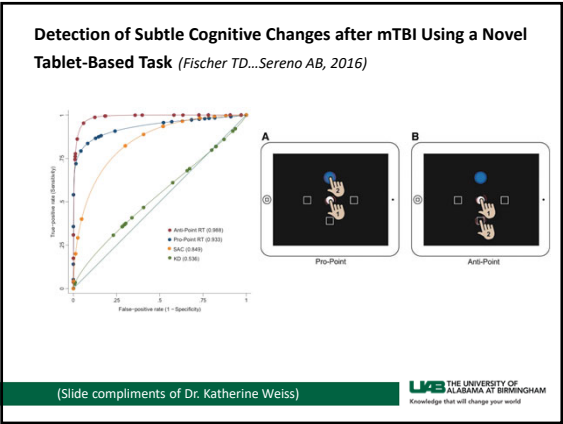
Communicate Clearly

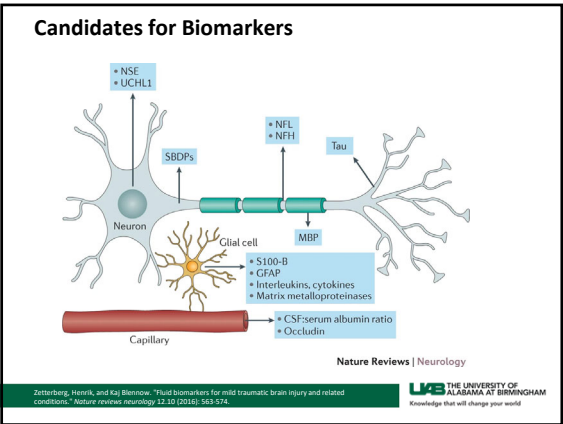
The EyeBOX report is delivered instantly and helps you communicate clearly with patients, their family, and other providers.

Increase Consistency

Our innovative patented optical technology to assess concussion more consistently across patients and across providers in your organization. EyeBOX has been the subject of 11 peer-reviewed studies.

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Prevention – Do rule changes help?

TABLE 1
Raw Concussion Counts by Play Type in Pac-12 Football Games, 2016-2019*

	2016		2017		2018		2019		All Years	
	No.	% Total	No.	% Total	No.	% Total	No.	% Total	No.	% Total
All plays	43	100.0	63	100.0	53	100.0	54	100.0	213	100.0
Targeting	1	2.3	5	7.9	5	9.4	4	7.4	15	7.0
Upphail	1	2.3	4	6.3	9	16.9	4	7.4	18	8.5
Overturned	0	0.0	1	1.6	2	3.8	0	0.0	3	1.4
All other plays	42	97.7	58	92.1	48	90.6	50	92.6	198	92.9

*Pac-12, Pacific-12 Conference.

TABLE 2
Concussion Incidence in Pac-12 Football Games, 2016-2019*

	2016		2017		2018		2019		All Years	
	No. of Incidents per 1000 Plays	% of Incidents per 1000 Plays	No. of Incidents per 1000 Plays	% of Incidents per 1000 Plays	No. of Incidents per 1000 Plays	% of Incidents per 1000 Plays	No. of Incidents per 1000 Plays	% of Incidents per 1000 Plays	No. of Incidents per 1000 Plays	% of Incidents per 1000 Plays
All plays	17.431	9.5	17.046	9.7	16.862	9.1	17.331	9.1	68.670	9.1
Targeting	22	45.5	41	122.0	44	113.6	34	117.6	141	106.4
Upphail	16	62.5	30	133.3	24	125.0	15	106.7	85	141.2
Overturned	6	0.0	11	90.9	39	108.0	19	0.0	56	53.6
All other plays	17.409	9.4	17.005	9.4	16.818	9.9	17.297	9.9	68.509	9.9

*Pac-12, Pacific-12 Conference.

The risk of sustaining a concussion during collegiate American football was 37 times higher during a targeting play than nontargeting plays, reflecting the importance of eliminating targeting to decrease concussions.

Aukerman, Douglas F., et al. "Risk of concussion after a targeting foul in collegiate American football." *Orthopaedic journal of sports medicine* 10.2 (2022): 23259671221074055.

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Technology



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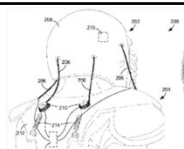
Dummy Smashing



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Helmet with energy absorbing tethers - US

Patent #: 10,729,200 B2



- Reduce rotational accelerations during impact without sacrificing normal range of motion during normal play.
- Potential intervention window between 600 rad/sec² - 1700 rad/sec².
- Must react within 5-10 milliseconds of impact initiation.
- Prelim results show reduced linear impact forces when shoulder pads are fixed to the body of the ATD

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So what about persistent symptoms? - Post Concussion Syndrome (PCS)



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Definition of PCS

- History of concussion
- Greater than one ICD-10/DSM IV symptom for at least 14 days – 1 month.

Headache
Dizziness
Fatigue
Irritability
Sleep problems
Concentration problems
Memory problems
Problems tolerating stress/emotion/alcohol
Affect changes, anxiety, or depression
Changes in personality
Apathy
Impaired cognitive function

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Post concussion headache treatment - adults

Table 6.— Change in Headache Frequency After Starting Specific Prophylactic Medications

	Baseline (Days/Month)	Follow-up (Days/Month)	Change (%) (Days/Month)	Paired t- test	Responders
Any prophylactic	17.11 ± 9.21	14.45 ± 10.28	-2.66 (-15.5%)	P = .009	35/100 (35%)
TCA (n = 48)	14.7 ± 8.61	12.9 ± 9.12	-1.8 (-12.2%)	P = .23	14/48 (29%)
TPM (n = 29)	19.4 ± 8.96	14.9 ± 10.3	-4.5 (-23.2%)	P = .02	14/29 (48%)
Propranolol (n = 18)	19.3 ± 10.0	16.1 ± 12.1	-3.2 (-16.6%)	P = .22	6/18 (33%)
Valproate (n = 13)	19.5 ± 10.0	20.8 ± 13.1	1.3 (6.7%)	P = .83	1/5 (20%)

TCA = tricyclic antidepressant; TPM = topiramate.

Erickson, Jay C. "Treatment outcomes of chronic post-traumatic headaches after mild head trauma in US soldiers: An observational study." *Headache: The Journal of Head and Face Pain* 51.6 (2011): 933-944.

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Other interventions

- Botox
- Greater occipital nerve blocks
- Trigger point injections
- Physical therapy (cervicogenic) – NSGY/imaging
- Amantadine 100 mg BID x 2 months
- CGRP agents – mixed response so far, Ajovy, Emgality
- Lyrica, Propranolol, Depakote, Gabapentin, Cymbalta – all mixed effects.

Visual testing - UAB Optometry, Dr. Katherine Weise – mTBEye Clinic

- Vision testing includes well-established clinical measures of accommodation, vergence, and ocular motility
- Most common diagnoses are Convergence Insufficiency (CI), Accommodative Insufficiency (AI), and Saccadic dysfunction (SD)
- May predict prolonged recovery
- Dysfunction may exacerbate other clinical symptoms



Vestibular Rehab

TABLE 2. Mean (SD) of Outcome Measures at Times of Initial Evaluation and Discharge

Outcome Measure	Pre-treatment	Post-treatment	F Test, P Value
Dizziness severity (41 children, 21 adults)	21 (22)	12 (18)	$F_{1,60} = 11.4, <.001^a$
ABC Scale (41 children, 21 adults)	64 (27)	84 (17)	$F_{1,60} = 31.5, <.001^a$
DGI (42 children, 27 adults)	49 (21)	30 (22)	$F_{1,69} = 45.5, <.001^a$
DGI (30 children, 18 adults)	20 (13)	23 (13)	$F_{1,48} = 42.6, <.001^a$
FOA (39 children, 18 adults)	22 (15)	28 (15)	$F_{1,57} = 42.6, <.001^a$
Gait speed (29 children, 17 adults)	1.02 (0.28)	1.28 (0.23)	$F_{1,46} = 38.3, <.001^a$
TUG (22 children, 16 adults)	9.7 (2.5)	7.8 (3.8)	$F_{1,38} = 27.8, <.001^a$
FTSIS (20 children, 16 adults)	131 (68)	97 (5)	$F_{1,36} = 15.8, <.001^a$
SOT (composite) (13 children, 9 adults)	48 (19)	71 (13)	$F_{1,20} = 36.8, <.001^a$
SOT condition 1 (13 children, 9 adults)	83 (13)	92 (9)	$F_{1,18} = 7.2, .019^a$
SOT condition 2 (13 children, 9 adults)	76 (18)	86 (9)	$F_{1,18} = 5.3, .037^a$
SOT condition 3 (13 children, 9 adults)	71 (21)	87 (9)	$F_{1,18} = 7.8, .012^a$
SOT condition 4 (13 children, 9 adults)	44 (28)	80 (9)	$F_{1,18} = 27.2, <.001^a$
SOT condition 5 (13 children, 9 adults)	29 (24)	51 (15)	$F_{1,18} = 21.6, <.001^a$
SOT condition 6 (13 children, 9 adults)	29 (21)	60 (15)	$F_{1,18} = 32.6, <.001^a$

^a $p < .05$. Abbreviations: SD, standard deviation; ABC Scale, Activities-specific Balance Confidence Scale; DGI, Dizziness Handicap Inventory; DGI, Dynamic Gait Index; FOA, Functional Gait Assessment; TUG, Timed Up and Go; FTSIS, Five Times sit to stand; SOT, Sensory Organization Test.

TABLE 3. Mean (SD) for the Significant Interaction Effect ($P < .05$) Between Age Group and Treatment on Dizziness Severity and SOT Scores

Outcome Measure	Children		Adults	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Dizziness severity (41 children, 21 adults)	20 (22)	7 (11)	21 (20)	20 (20)
SOT condition 1 (13 children, 9 adults)	79 (18)	82 (5)	81 (13)	91 (8)
SOT condition 2 (13 children, 9 adults)	72 (21)	89 (5)	83 (11)	83 (11)

Abbreviations: SD, standard deviation; SOT, Sensory Organization Test.

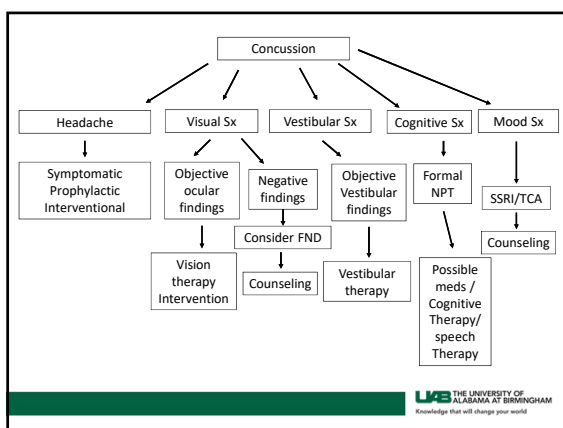
Alsaheien, Bara A., et al. "Vestibular rehabilitation for dizziness and balance disorders after concussion." *Journal of Neurologic Physical Therapy* 34.2 (2010): 87-93.

Emotional disturbance

- Sertraline, citalopram, and methylphenidate are effective for post-TBI depression
- Methylphenidate was also found to be effective for attention deficits after mTBI
- Anxiety disorders and PTSD are significant contributors to prolonged symptoms and should be treated aggressively according to existing clinical guidelines
- There are few studies to guide the pharmacological treatment of irritability after mTBI, although SSRIs are generally tried first, before mood stabilizers

Quinn, Devin K., et al. "Prolonged postconcussive symptoms." *American journal of psychiatry* 175.2 (2018): 103-111.
 Huang, Chi-Hsien, et al. "Methylphenidate on cognitive improvement in patients with traumatic brain injury: a meta-analysis." *Current neuropharmacology* 14.3 (2016): 272-281.
 Salter, Katherine L., et al. "Pharmacotherapy for depression posttraumatic brain injury: a meta-analysis." *Journal of head trauma rehabilitation* 31.4 (2016): E21-E32.

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Treatment - Overview

- Successful treatment of PCS involves a “detailed multimodal clinical assessment”
 - early post-concussion management, with
 - assessment and recognition of early complications
 - education about symptoms and expectations for recovery
 - recommendations for activity modifications
 - close follow up
- This comprehensive approach minimizes risk of early symptoms evolving into late phase symptoms

Dwyer, Bridget, and Douglas L. Katz. "Postconcussion syndrome." *Handbook of clinical neurology*. Vol. 158. Elsevier, 2018. 163-178.

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Return to Play – Individualized

Exercise step	Functional exercise at each step	Goal of each step
1. Symptom-limited activity	Daily activities that do 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, coordination, 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 play/sport	Normal game play.	

Harmon et al, 2013

Echemendia, Ruben J., et al. "The sport concussion assessment tool 5th edition (SCAT5): background and rationale." *British journal of sports medicine* 51.11 (2017): 848-850.

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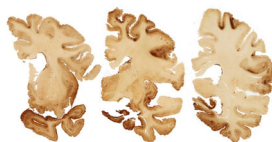
Return to School

Mental Activity	Activity at each step	Goal of each step
1. Daily activities that do not give the athlete symptoms	Typical activities that the athlete does during the day as long as they do not increase symptoms (e.g. reading, texting, screen time). Start with 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 school-work. 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 school activities until a full day can be tolerated.	Return to full academic activities and catch up on missed work.

Echemendia, Ruben J., et al. "The sport concussion assessment tool 5th edition (SCAT5): background and rationale." *British journal of sports medicine* 51.11 (2017): 848-850.

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Chronic
Traumatic
Encephalopathy
(CTE)



- Abnormal aggregation of aberrantly phosphorylated **tau proteins** following long term exposure to repetitive mTBIs.
- Pathology shows NFTs throughout the frontal, temporal, and insular cortices; diencephalon; brainstem; cerebellar dentate nucleus; and spinal cord, especially at the depths of sulci and around blood vessels.
- Profiles of tau tangles purified from boxer CTE brains and AD brains are indistinguishable (*Dekosky et al, 2013*)
- No imaging modality is available currently for diagnosis.

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Summary

- SRC is a significant public health concern in the United States and around the world.
- Early diagnosis is essential to prevent further damage of brain tissue and allow for proper recovery time
- Prevention / mitigation of impact forces are important areas of ongoing research
- Early treatment and identification of persistent symptoms helps hasten recovery

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