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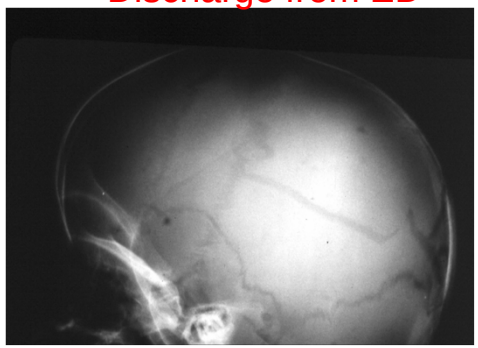
NewYork-Presbyterian
Phyllis and David Komansky
Center for Children's Health

Pediatric
Brain and Spine Center

Jeffrey Greenfield MD PhD

The Continuum

Linear skull Fracture in infants and toddlers
Discharge from ED



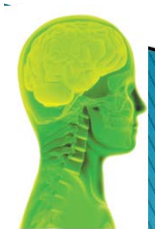
Everything
In Between

i.e. mild
Traumatic Brain Injury
(mTBI)

Severe TBI,
Admit Pediatric Neuro Intensive Care Unit

Sports Related head Trauma

- Incidence
- Continuum of mild-severe
- Proposed Mechanisms of Concussion
- Chronic Traumatic Encephalopathy
- Second Impact Syndrome
- Neurogenetic Aspects
- Concussion grading
- Sideline Assessment
- Neuropsychological Assessment
- Return-to-play decision making
- Team Medical Department
- Future Directions



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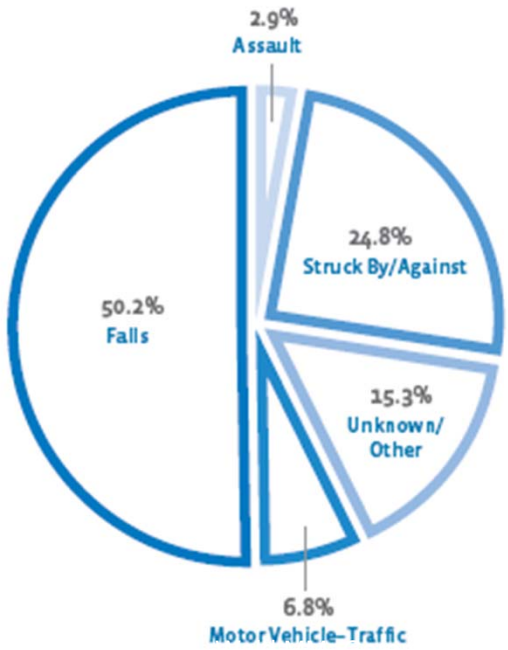
- Most common cause of death and disability in the young:
  - 1.7 million injuries, 52k deaths, 1.4 million ER visits
  - 30% of all injury-related deaths
  - 80k severe disabilities from sTBI
- Damage from combination of direct impact and rotational forces on axons
- Secondary injuries due to brain swelling and ischemia
- Incidence of concussion thought to be vastly underestimated
  - ~300k sports-related concussion with LOC annually
  - Represents only 8-19.2% of all sports-related concussion

FIGURE 6: Estimated Average Percentage of Annual Traumatic Brain Injury-Combined Emergency Department Visits, Hospitalizations, and Deaths Among Children 0 to 14 Years, by External Cause, United States, 2002–2006



Framing the problem

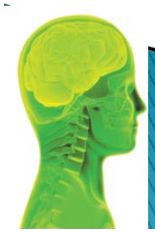
Subjective!!!

We are seeing more and more teens with post-concussion headaches (especially girls soccer); also those who need clearance to return-to-play. I give families the CDC handouts and use the Acute Concussion Evaluation (ACE) for return-to-school and return-to-play guidelines. Basically, they must have **NO** residual symptoms and perform graded exercises (including practice drills) without headaches.

Most teen athletes are seen by sports medicine and orthopedic physicians who serve as team physicians. ImPACT is useful, especially if baseline testing is done before injuries occur. The vendor does have normative data. Some of our schools are using it.

The brain is not a bone, ligament or tendon!!!

Basically have been leaving it up to parents



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- Pittsburgh Post-Concussion Scale
  - Basis of many assessment scales
- Sports Concussion Assessment Tool – 2
  - FIFA, IIHF, IOC, IRB
- Impact Test
- NCAA, NFL, NHL, MLB, NBA, MLS
- Newer testing

Lovell MR et al. Measurement of symptoms following sports-related concussion: reliability and normative data for the post-concussion scale. Appl Neuropsychol. 2006;13(3):166-74.

Symptom	None	Mild		Moderate		Severe	
Headache	0	1	2	3	4	5	6
Nausea	0	1	2	3	4	5	6
Vomiting	0	1	2	3	4	5	6
Balance Problems	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Fatigue	0	1	2	3	4	5	6
Trouble Falling Asleep	0	1	2	3	4	5	6
Sleeping More Than Usual	0	1	2	3	4	5	6
Sleeping Less Than Usual	0	1	2	3	4	5	6
Drowsiness	0	1	2	3	4	5	6
Sensitivity to Light	0	1	2	3	4	5	6
Sensitivity to Noise	0	1	2	3	4	5	6
Irritability	0	1	2	3	4	5	6
Sadness	0	1	2	3	4	5	6
Nervousness	0	1	2	3	4	5	6
Feeling More Emotional	0	1	2	3	4	5	6
Numbness or Tingling	0	1	2	3	4	5	6
Feeling Slowed Down	0	1	2	3	4	5	6
Feeling Mentally "Foggy"	0	1	2	3	4	5	6
Difficulty Concentrating	0	1	2	3	4	5	6
Difficulty Remembering	0	1	2	3	4	5	6
Visual Problems	0	1	2	3	4	5	6

Test Features

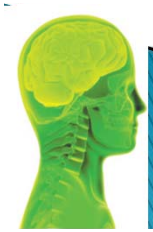
- Measures player symptoms
- Measures verbal and visual memory, processing speed and reaction time
- Reaction time measured to 1/100th of second
- Assists clinicians and athletic trainers in making difficult return-to-play decisions
- Provides reliable baseline test information
- Produces comprehensive report of test results
- Results can be e-mailed or faxed for fast consultation by a neuropsychologist
- Automatically stores data from repeat testing
- Testing is administered online for individuals or groups
- Compatible with PC and MAC

- ImPACT takes approximately 20 minutes to complete. The program measures multiple aspects of cognitive functioning in athletes, including:
  - Attention span
  - Working memory
  - Sustained and selective attention time
  - Response variability
  - Non-verbal problem solving
  - Reaction time

http://impacttest.com/about/background

- Gennarelli, T et al (1982) Annals of Neurology
  - ✓ Induced traumatic coma in 45 Primates
  - ✓ Accelerating the head w/o impact
  - ✓ Diffuse axonal injury related to amount of coronal head motion
- Adams, H (1982) Annals of Neurology
  - ✓ Analyzed 45 cases of diffuse axonal injury (DAI)

Acceleration De-Acceleration Rotation



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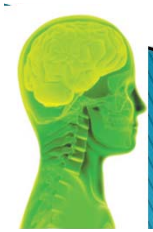
- Diagnostic Criteria: American Congress of Rehabilitation (1993). *Head Trauma Rehab.* Loss of Consciousness or Altered Mental Status or Posttraumatic Amnesia
- Lovell, M. (1999) Clin. *J. Sports Med.* LOC not correlated with Neuropsych Functioning in MTBI
- McCrea, M. (2002) *Neurosurgery.* Cognitive deficits related to PTA not LOC
- Collins, M. (2003) *Clin J Sports Med.* Presence of Amnesia not LOC predicts Symptoms and Neurocognitive deficits
- Erlanger, D. (2003) *J Neurosurgery.* LOC unrelated to duration of PCS

NO



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- Gronwall, D. (1975) *Lancet. S*econd concussion resulted in decreased processing speed and longer recovery time
- Gaetz, M. (2000) *Brain Injury.* Increased P300 change in ≥ 3 concussions
- Collins, M. (2002) *Neurosurgery.* Increased cognitive deficits in ≥ 3 concussions
- Guskiewicz, K. (2003) *JAMA.* NCAA Study increased time to PCS recovery in ≥ 3 concussions
- Iverson, G. (2006) *Brit J Sports Med.* HS & College Athletes, No effect with 1-2 prior concussions

YES

- APOE gene encodes a cholesterol carrying protein produced in the liver and the brain
- APOE human gene occurs in 3 allelic forms: ϵ2 ϵ3 ϵ4
- 6 possible genotypic combinations, 25 % populations has at least one copy of ϵ4
- APOE ϵ4 has been confirmed as a susceptibility factor for Alzheimer's

  Strittmatter, W, et al, *Proc Nat Acad Ssc* (1993)
  Tsuang, D, et al, *J Am Geriatr Soc* (1996)
- APOE ϵ has been associated with poor functional outcome from TBI

  Friedman, G, et al, *Neurology* (1999)
  Teasedale, G, *Lancet* (1997)

- Jordan, B., Relkin, N. et al (1997) JAMA
  - ✓ APOE genotype analysis of 30 active and retired boxers
  - ✓ 11-Normal, 12-Mild, 4-Moderate, 3-Severe Impairment
  - ✓ Boxers with low exposure $\leq$ 12 bouts=no or low impairment
  - ✓ Boxers with high exposure and $\geq$ 12 & ϵ4 copy=Severe Impairment
- Kutner, K. Jordan, B, Relkin, N., et al 2000 Neurosurgery
  - ✓ APOE genotype analysis of 53 active professional football players

    34: ϵ3/ϵ3 11: ϵ3/ϵ4 5: ϵ2/ϵ3 2: ϵ2/ϵ4
  - ✓ Players with a copy of ϵ4 and higher exposure $\geq$ 5 years = worse performance on
    - Speed of performance
    - Attention

- Term initially described by Schneider, R. (1973) *Head and neck injuries in football*

- Syndrome described by Saunders, R. (1984) *JAMA*
  - ✓ 19 yo Football player who sustained a head punch followed
  - ✓ 4 days later by minor head impact in football game
  - ✓ Occured as a result of second head injury
  - ✓ Athlete developed diffuse cerebral edema > brain herniation

- Alves & Polin (1996)
  Second Impact Syndrome may reflect:

  - ✓ Malignant Cerebral Edema due to disruption of cerebral
  - ✓ vascular dysregulation & consequent vascular congestion

- Cantu, R. (1998) Clin. Sports Med.
  - ✓ Review paper citing 17 cases of SIS
  - ✓ Due to second head injury occurring before symptoms first concussion resolves

- Punch Drunk Syndrome (Dementia Pugilistica)
  - ✓ Indentified in Boxer by Martland, H. (1928) *JAMA*
  - ✓ Described 38 year old retired boxer with: Advanced Parkinsonism, Ataxia, Pyramidal Tract Dysfunction

- Chronic Traumatic Encephalopathy in a NFL Player

- *Omalu, B. et al (2005) Neurosurgery*

  - ✓ Single Case Postmortem Study of retired 18 year veteran
  - ✓ Died suddenly to coronary atherosclerotic disease
  - ✓ E genotype was ϵ3/ϵ3 Retired 12 years
  - ✓ Many Diffuse Amyloid Plaques
  - ✓ Neurofibrillary tangles in neocortical areas
  - ✓ No cortical atrophy, contusion, hemorrhage, or infarcts

Functional MRI

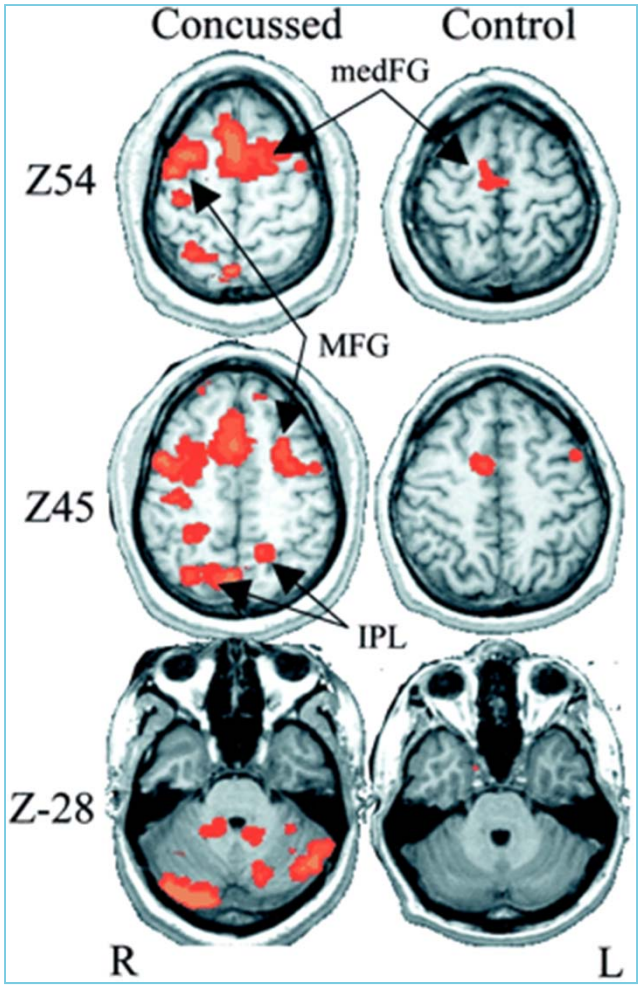
Jantzen, K., et al (2004) *Am J Neuroradiology*

✓8 college football players underwent fMRI preseason
- ✓ 4 of the players sustained mTBI

- ✓ All subjects showed ⇧ activation

✓Concussed players showed ⇧ activation on finger sequencing task

✓Increased activation in medial frontal gyrus, inferior parietal lobe, and
- ✓ Bilateral cerebellum

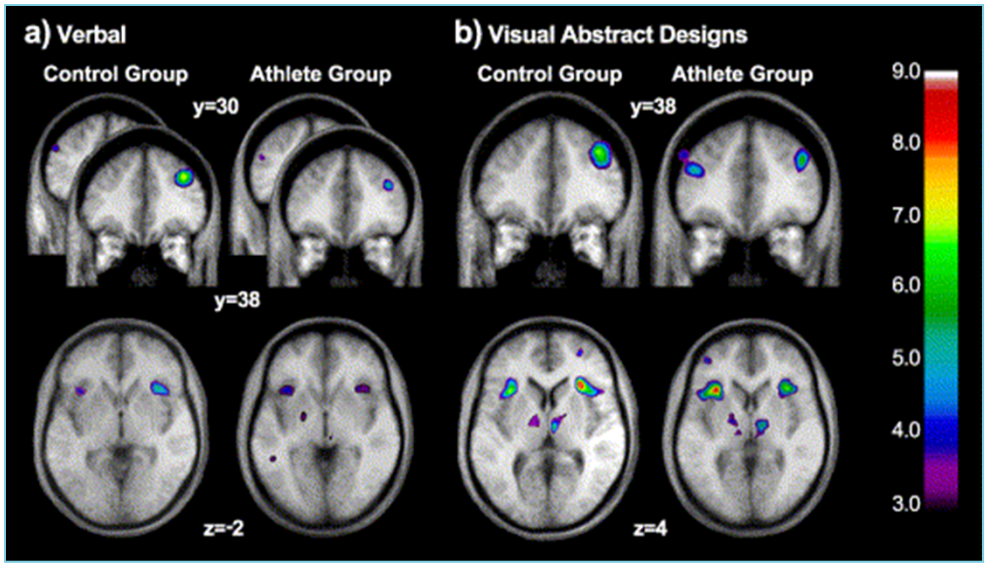


Functional MRI

Chen, J., et al (2004) Neuroimage

- ✓ Compared working memory in concussed & normal control subjects
- ✓All subjects showed strong activation in the mid-dorsolateral prefrontal cortex

- ✓Concussed athletes showed trend towards weaker activation I the right mid-dorsolateral cortex



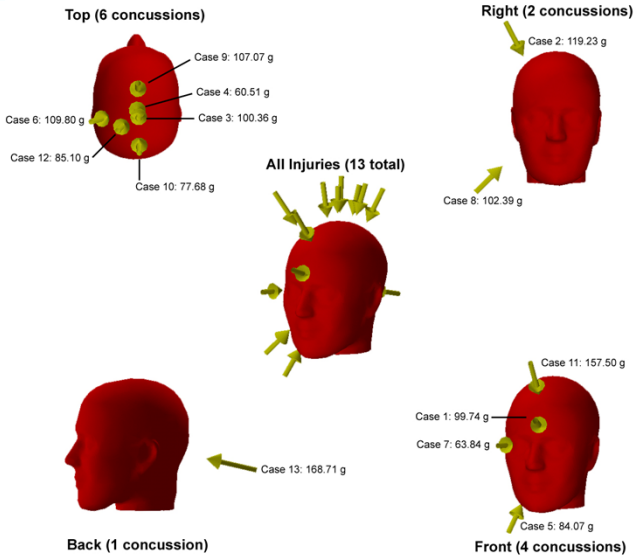
fMRI and Predicted Recovery

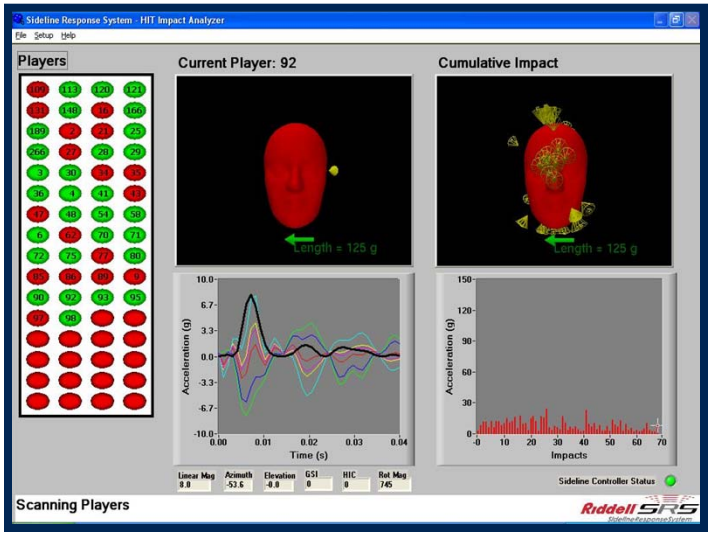
Lovell, M. et al (2007) Neurosurgery

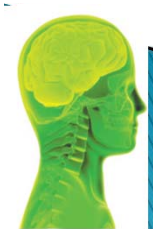
- High School and College Athletes
  - ✓ 28 Concussed Subjects and 13 age-matched controls
  - ✓ Baseline and Post-Concussion Impact Administered
  - ✓ fMRI with N-back task as measure of working memory
  - ✓fMRI administered within one week and following clinical recovery
- Athletes who demonstrated hyperactivation on fMRI at time of 1st scan had longer recovery period
- Higher activation in Posterior Parietal Cortex of concussed

Lovell, Marion, Pardini, Collins, Eddy, Becker, Field, and Boada (2001-2006)
RO1 HD 42386-05- NINDS

How can we protect our children better?







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Return to Play

On-Field Assessment

Triage ? Transport to Medical Facility

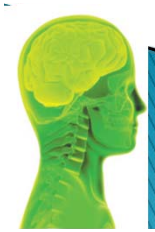
Sideline Assessment

? Return to Competition in same game

Concussion Management

? Return to in subsequent game

- Multiple Recommendations for Return-To-Play Exist
- *Not* Research-Based
  - ✓ Colorado (1990) *Colo. Med*
  - ✓ Cantu (1998) *Clin. Sports Med*
  - ✓ AAN (1997) *Neurology*



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Pocket SCAT2

Concussion should be suspected in the presence of **any one or more** of the following: symptoms (such as headache), or physical signs (such as unsteadiness), or impaired brain function (e.g. confusion) or abnormal behaviour.

1. Symptoms

Presence of any of the following signs & symptoms may suggest a concussion.

- Loss of consciousness
- Seizure or convulsion
- Amnesia
- Headache
- "Pressure in head"
- Neck Pain
- Nausea or vomiting
- Dizziness
- Blurred vision
- Balance problems
- Sensitivity to light
- Sensitivity to noise
- Feeling slowed down
- Feeling like "in a fog"
- "Don't feel right"
- Difficulty concentrating
- Difficulty remembering
- Fatigue or low energy
- Confusion
- Drowsiness
- More emotional
- Irritability
- Sadness
- Nervous or anxious

2. Memory function

Failure to answer all questions correctly may suggest a concussion.

"At what venue are we at today?"
"Which half is it now?"
"Who scored last in this game?"
"What team did you play last week/game?"
"Did your team win the last game?"

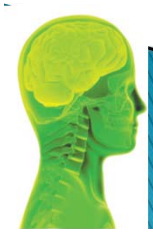
3. Balance testing

Instructions for tandem stance

*"Now stand heel-to-toe with your **non-dominant** foot in back. Your weight should be evenly distributed across both feet. You should try to maintain stability for 20 seconds with your hands on your hips and your eyes closed. I will be counting the number of times you move out of this position. If you stumble out of this position, open your eyes and return to the start position and continue balancing. I will start timing when you are set and have closed your eyes."*

Observe the athlete for 20 seconds. If they make more than 5 errors (such as lift their hands off their hips; open their eyes; lift their forefoot or heel; step, stumble, or fall; or remain out of the start position for more that 5 seconds) then this may suggest a concussion.

Any athlete with a suspected concussion should be IMMEDIATELY REMOVED FROM PLAY, urgently assessed medically, should not be left alone and should not drive a motor vehicle.



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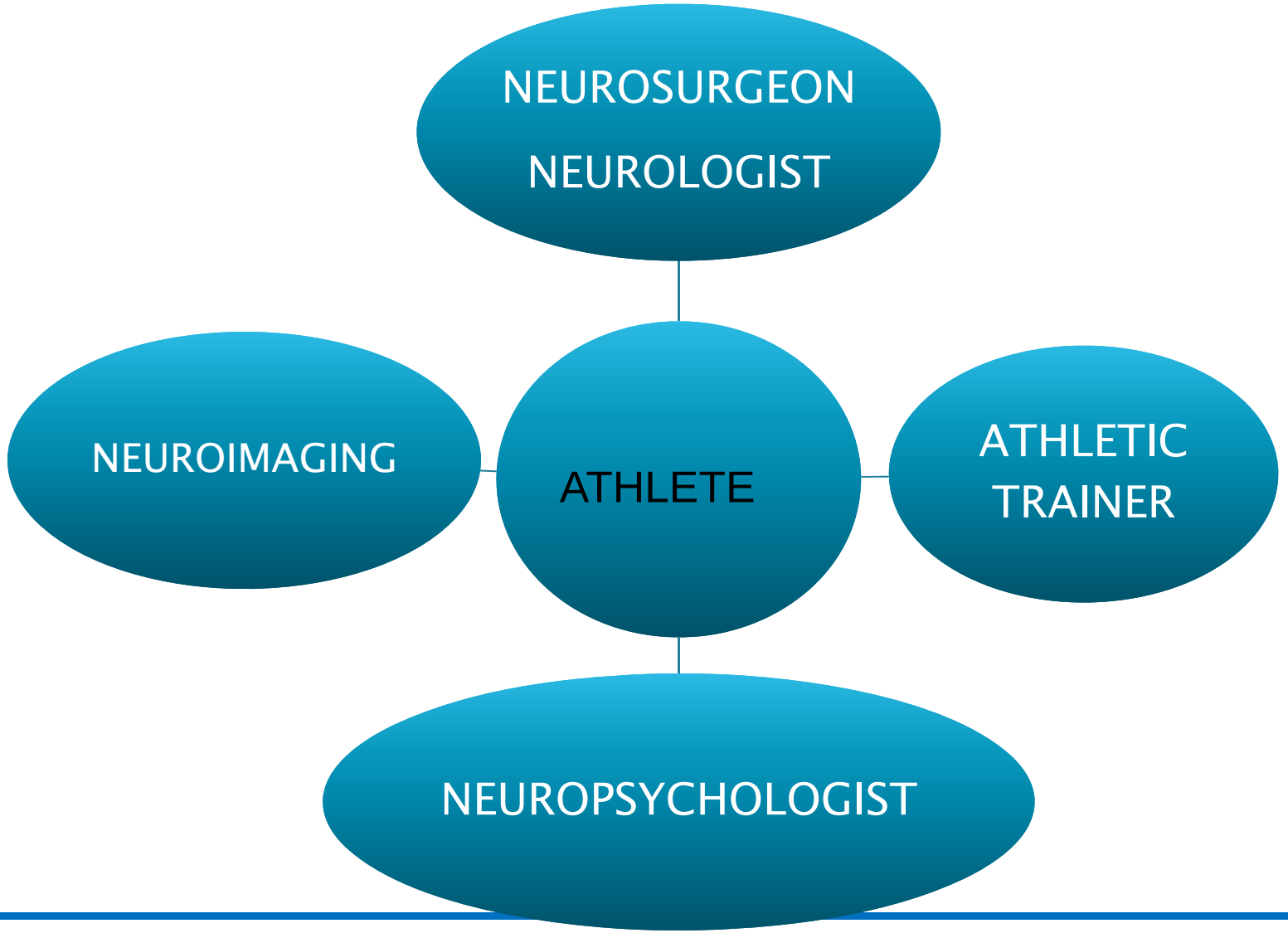
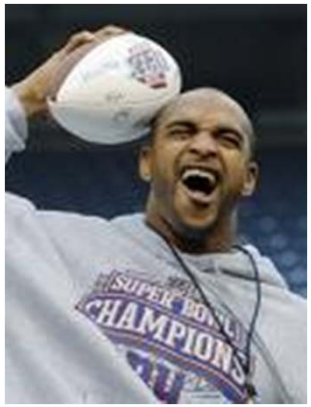
- Provides accurate assessment of cognitive functioning following mTBI
- Provides additional diagnostic information in mTBI in which basic neurological examination and neuroimaging is usually non-contributory
- *Baseline assessment* is utilized in order to reduce type I & II errors

Type I Error: False Positive

Type II Error: False Negative


NEUROSURGEON
NEUROLOGIST
NEUROIMAGING
ATHLETE
ATHLETIC TRAINER
NEUROPSYCHOLOGIST



HEAD INJURY PROTOCOL

Initiated 1995 1st team in NFL

Sideline Assessment (SCC)

Baseline Examination

Post Concussion Assessment

Return to Baseline

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COGNITIVE AND NEUROBIOLOGICAL RESEARCH CONSORTIUM IN TRAUMATIC BRAIN INJURY (CNRC-TBI)

Weill Medical College of Cornell University – New York Presbyterian Hospital,
University of California at Berkeley, University of California at San Francisco

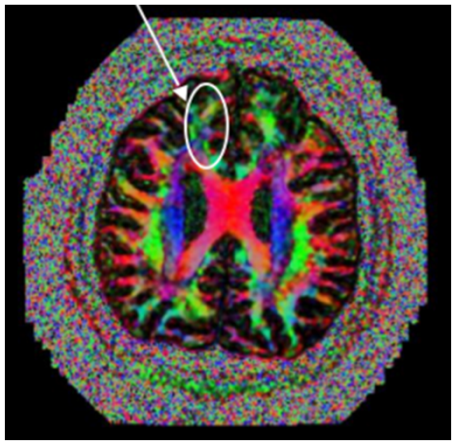
Network Coordination –Brain Trauma Foundation, New York, NY.

Cornell-New York Presbyterian*
- Jamshid Ghajar – TBI expert/Neurosurgery PI
- Bruce McCandliss – Attentional function/Sackler Institute/Psychiatry
- Steve Flanagan – TBI expert/Rehabilitation medicine
- Nicholas Schiff – Conscious states/Neurology
- Philip Stieg – Neurosurgery Chair/Neurosurgery
- Minah Suh – Neurophysiologist /Neurosurgery
- Robert Zimmerman – Neuroradiology/Radiology

Pediatric*
Steven Weinstein – Pediatric Neurology
Jeffrey Greenfield – Pediatric Neurosurgery
Ken Perrine – Pediatric Neuropsychology

UC-Berkeley
- Mark D'Esposito – Neuroimaging/Neuroscience
- Richard Ivry – Cerebellar Function/Neuroscience
- Robert Knight – Frontal Lobe/Attentional Function/Neuroscience

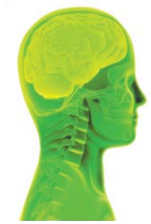
UC-San Francisco*
- Geoffrey Manley – TBI expert/Neurosurgery
- Pratik Mukherjee – DTI expert/Radiology



We hypothesize long white matter tract injury from mild and moderate TBI, visualized by MRI diffusion tensor imaging, causes cognitive deficits.

Anterior tracts subserving anticipatory timing are preferentially damaged and the locus and severity of tract injury accounts for persistent symptoms

** Designated level-one trauma facilities – see appendix for descriptions.*



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The Predictive Brain State: Timing Deficiency in Traumatic Brain Injury?

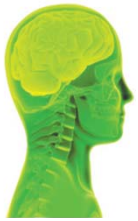
Jamshid Ghajar, MD, PhD, Richard B. Ivry, PhD, and the Cognitive and Neurobiological Research Consortium

Attention and memory deficits observed in traumatic brain injury (TBI) are postulated to result from the shearing of white matter connections between the prefrontal cortex, parietal lobe, and cerebellum that are critical in the generation, maintenance, and precise timing of anticipatory neural activity.

These fiber tracts are part of a neural network that generates predictions of future states and events, processes that are required for optimal performance on attention and working memory tasks.

Preparatory neural activity normally allows the efficient integration of sensory information with goal-based representations. It is postulated that an impairment in the generation of this activity in traumatic brain injury (TBI) leads to performance variability as the brain shifts from a predictive to reactive mode. This dysfunction may constitute a fundamental defect in TBI as well as other attention disorders, causing working memory deficits, distractibility, a loss of goal-oriented behavior, and decreased awareness.

The authors discuss the role of this anticipatory neural system for understanding the varied symptoms and potential rehabilitation interventions for TBI.



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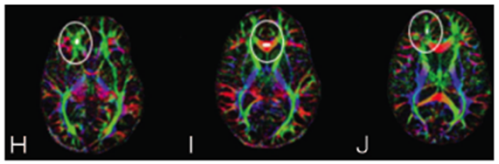
White Matter Shear: Decreased Attention



Published February 13, 2008 as 10.3174/ajnr.A0970

ORIGINAL RESEARCH

Extent of Microstructural White Matter Injury in Postconcussive Syndrome Correlates with Impaired Cognitive Reaction Time: A 3T Diffusion Tensor Imaging Study of Mild Traumatic Brain Injury

S.N. Niogi
P. Mukherjee
J. Ghajar
C. Johnson
R.A. Kolster
R. Sarkar
H. Lee
M.R. Meeker
R.D. Zimmerman
G.T. Manley
B.D. McCandliss

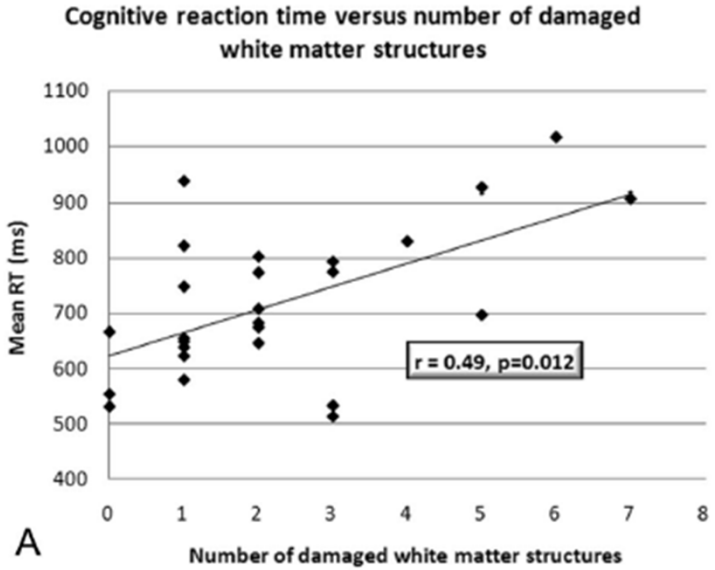
BACKGROUND AND PURPOSE: Diffusion tensor imaging (DTI) may be a useful index of microstructural changes implicated in diffuse axonal injury (DAI) linked to persistent postconcussive symptoms, especially in mild traumatic brain injury (TBI), for which conventional MR imaging techniques may lack sensitivity. We hypothesized that for mild TBI, DTI measures of DAI would correlate with impairments in reaction time, whereas the number of focal lesions on conventional 3T MR imaging would not.

MATERIALS AND METHODS: Thirty-four adult patients with mild TBI with persistent symptoms were assessed for DAI by quantifying traumatic microhemorrhages detected on a conventional set of T2*-weighted gradient-echo images and by DTI measures of fractional anisotropy (FA) within a set of a priori regions of interest. FA values 2.5 SDs below the region average, based on a group of 26 healthy control adults, were coded as exhibiting DAI.

RESULTS: DTI measures revealed several predominant regions of damage including the anterior corona radiata (41% of the patients), uncinate fasciculus (29%), genu of the corpus callosum (21%), inferior longitudinal fasciculus (21%), and cingulum bundle (18%). The number of damaged white matter structures as quantified by DTI was significantly correlated with mean reaction time on a simple cognitive task ($r = 0.49$, $P = .012$). In contradistinction, the number of traumatic microhemorrhages was uncorrelated with reaction time ($r = -0.08$, $P = .71$).

CONCLUSION: Microstructural white matter lesions detected by DTI correlate with persistent cognitive deficits in mild TBI, even in populations in which conventional measures do not. DTI measures may thus contribute additional diagnostic information related to DAI.

This work was supported by a collaborative grant from the James S. McDonnell Foundation to the Brain Trauma Foundation



A

RESULTS

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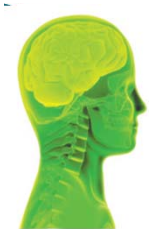

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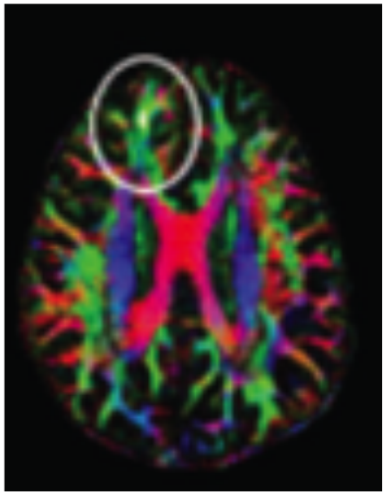
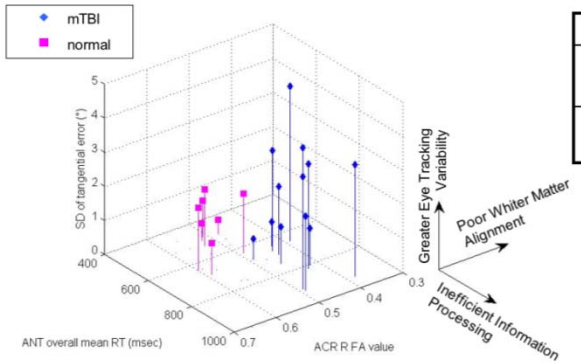
Pediatric Brain and Spine Center

EYE-TRAC DoD TBI Technology Award 2008-2012

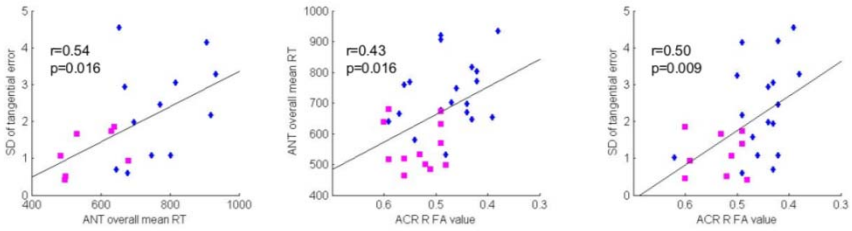




Correlation with FA - ACR R

	r	p
SD Tang Err	0.50 (0.44)	0.009 (0.06)
ANT Mean RT	0.43* (0.41)	0.016 (0.08)

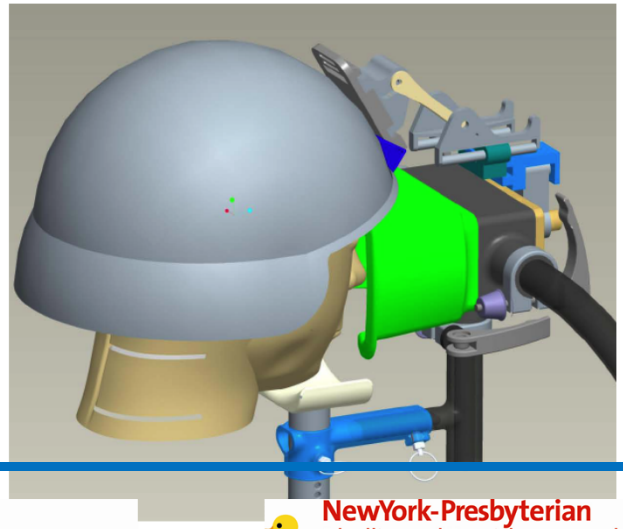
( ) - r and p values derived from the subjects who were tested with ***both*** eye tracking and ANT
* An outlier >2SDs removed

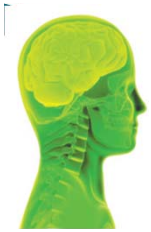


-Significant correlations between eye tracking variability (SD) and FA score (white matter integrity) of right anterior white matter tract (ACR R)- anterior portion of attention network

- Correlation between integrity of anterior white matter tract in TBI AND normals- normal subjects with poor attention have poor integrity in ACR R.

-Significant correlation of eye tracking and mean reaction time on Attention Network Task- a standard computer based test of attention





Weill Cornell Medical College

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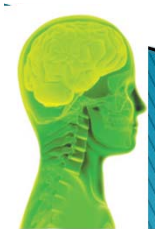
Pediatric Concussion Clinic
212-746-2378

Every child with a head injury—no matter how minor it may seem-- needs to be evaluated by a physician *experienced in diagnosing and treating concussions*, even if the child says he or she is feeling fine.

- All suspected concussions should be evaluated by a physician trained in concussion-assessment
- All symptomatic patients should be withheld from participation
- All symptomatic patients should be referred to a specialist for evaluation and management
- No previously symptomatic patient should return to sports activities until cleared by a neurologist or neurosurgeon



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- Pediatric concussion management services may include:
- Medical history and neurologic exam
- Screening ImPACT (Immediate Post-Concussion Testing and Cognitive Testing) exam
- Pre-Season Testing
- Review of any prior neuroimaging studies
- Imaging tests, including CT scan, MRI and DTI (Diffusion Tensor Imaging)
- EEG analysis
- Development of an appropriate care plan
- Close monitoring and tracking of clinical changes
- Neuropsychological testing and counseling as necessary
- Arrangement for academic accommodation
- Medical clearance for safe return to play, academics and other activities
- Follow-up studies as needed, until full recovery observed

Research

Smooth eye tracking,
Attention and information processing studies
Sophisticated and sensitive type of MRI called diffusion tensor imaging (DTI).