

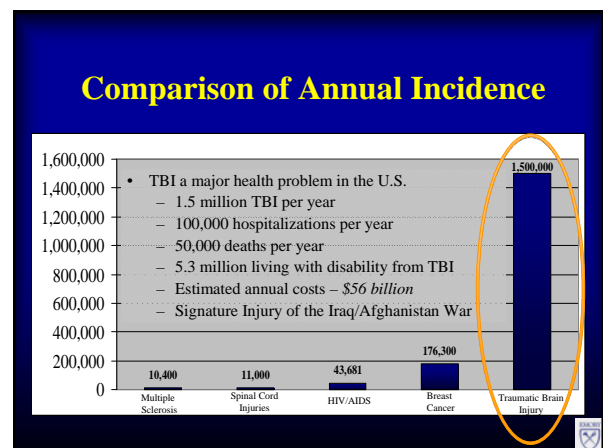
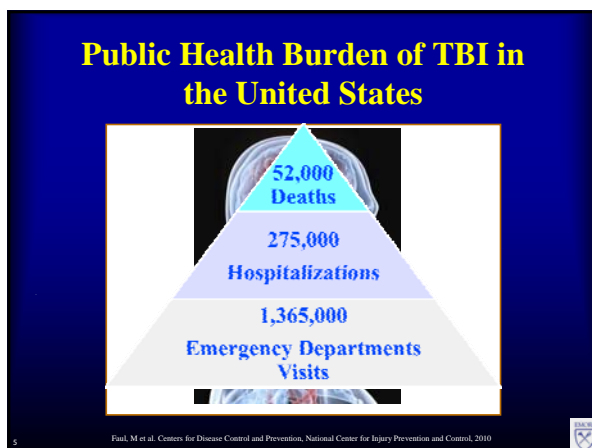


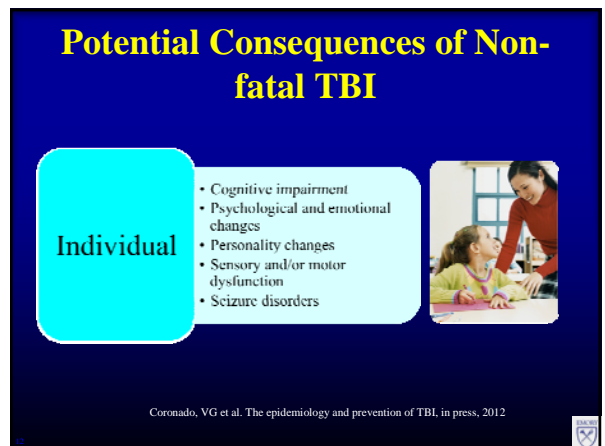
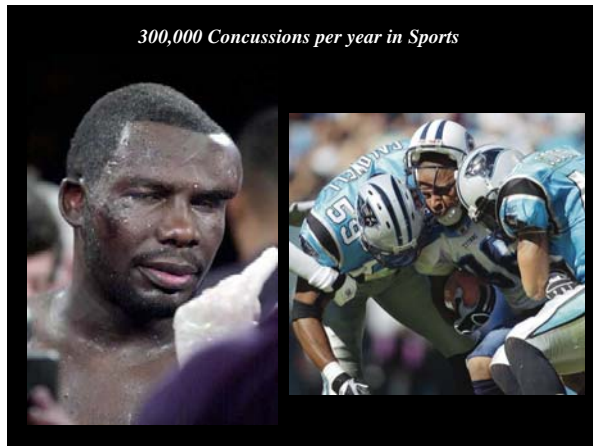
**COI**

**Zend Technologies®**  
 Inventor and stockholder  
 Startup company to further develop the DETECT™ Technology – a novel tool for detecting concussions

**BHR Pharma – Inventor of**  
 technology licensed from Emory to create path for progesterone technology to consumer. Eligible for Royalties through Emory University.

**“Every 15 seconds someone suffers a head injury.  
 Every five minutes a person becomes permanently disabled”**





**Family,  
Community,  
and Society**

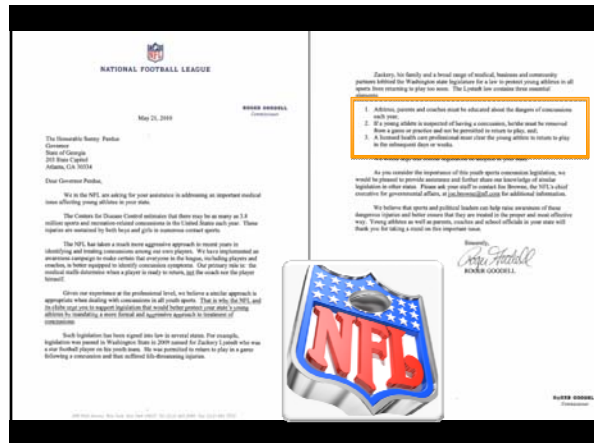
- Psychological stress
- Economic burden
- Productivity loss
- Need for supportive services



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Category	Cost (\$B)
Indirect	64.8
Medical	11.5
Direct (unlabeled)	23.7

14




“It takes very little energy to scramble an egg...”

**...and all our science is incapable of reversing that transaction."**

Dr. Richard Feynman  
Nobel Prize winning physicist

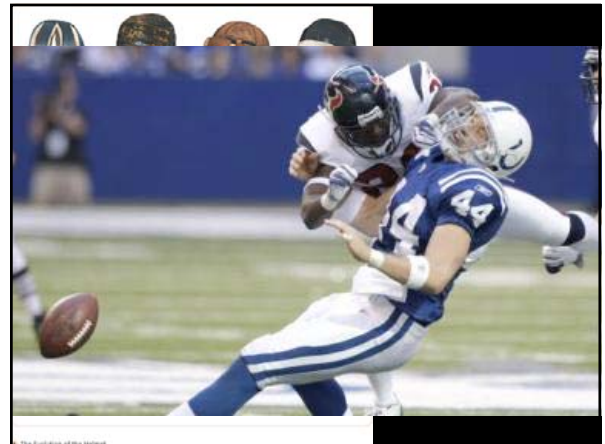
## Prevention: The Four E's



- E**ducation & Information
- E**nforcement & Regulation
- E**ngineering & Technology
- E**conomic Incentives

NTS-DTPC/JIA499 US-Africa Transportation



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## Children and Concussion

**School of hard knocks**

1 When a football player hits his head, the brain is shaken. 2 The shock waves travel through the brain. 3 The impact can cause tearing of the brain tissue.

**Symptoms:** Headache, Dizziness, Nausea, Vomiting, Blurred vision, Ringing in the ears, Loss of consciousness, Confusion.

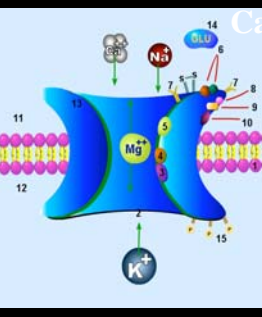
**Diagnosis:** Physical examination, History, Imaging (CT scan, MRI), Blood tests.

**Complications:** Seizures, Skull fractures, Brain swelling, Death.

**Prevention:** Proper technique, Helmets, Mouthguards, Concussion training.

**Nationally 135,000 ER visits for children ages 5-18 years annually**  
([www.cdc.gov/mmwr](http://www.cdc.gov/mmwr))

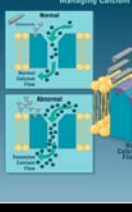
## Secondary Injury Neurotoxic




- Excitatory Amino Acids**
  - Glutamate, Glycine, others
- Critical Ions**
  - Calcium, Sodium, Magnesium

**Managing Calcium Flow Through the NMDA Receptor**

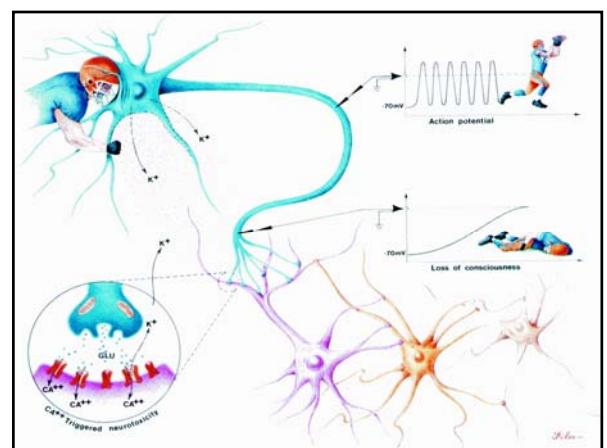
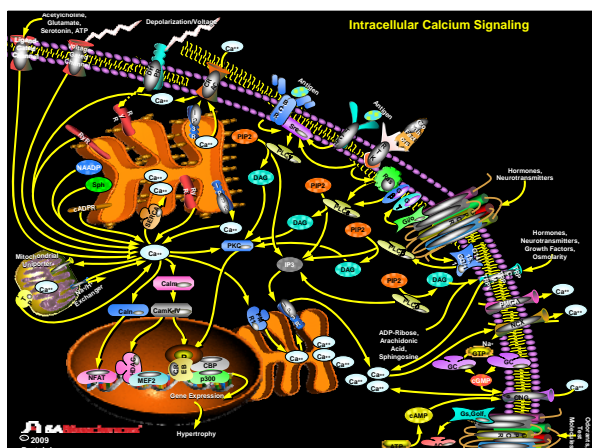
**Normal**

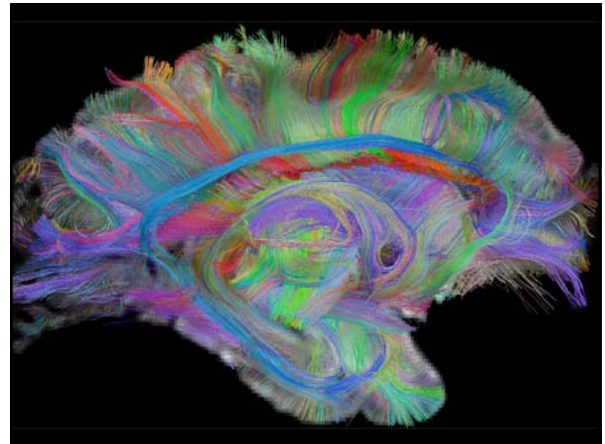
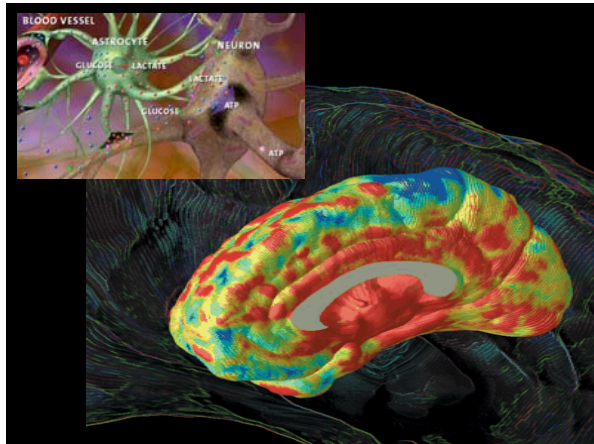


**Potential Treatments**



- Receptor Activation**
  - NMDA, AMPA, etc.





**DAI (Diffuse Axonal Injury)**  
The most important and most common pathology of mTBI/ concussion  
Difficult to detect, difficult to model

Evolution of Axonal Pathology

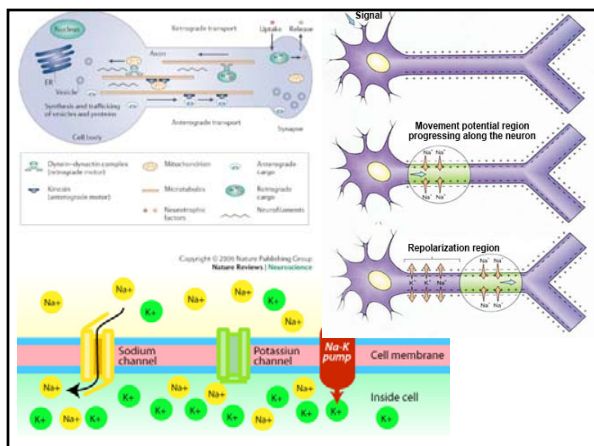
Terminal bulb

Periodic varicosities

Courtesy of Douglas Smith, MD - Department of Neurosurgery, Director of PENN's Center for Brain Injury and Repair, University of Pennsylvania

Mechanical failure of individual microtubules at multiple points along axons leads to axonal varicosities

The panels show electron micrographs of axons. Panel (a) shows a normal axon. Panel (b) shows a varicosity. Panel (c) shows a more pronounced varicosity. Panel (d) shows a severely dilated varicosity. Arrows point to the sites of microtubule failure.



**... Transport Interruption:**  
responsible for the formation of axonal varicosities

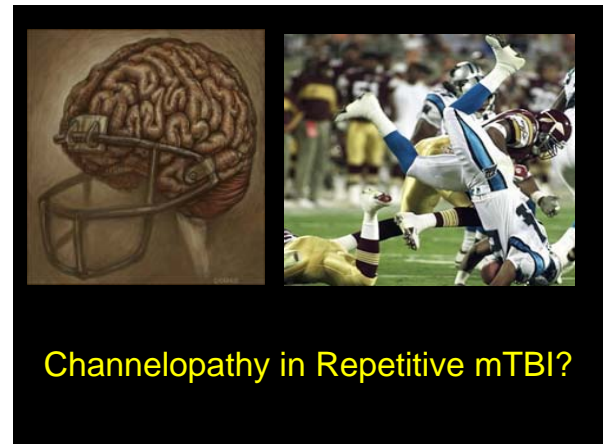
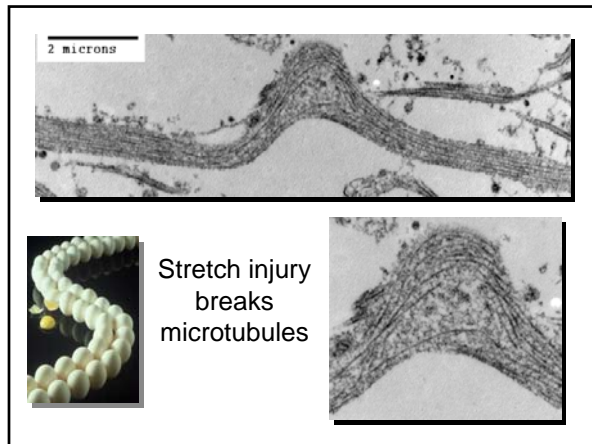
Primary mechanical breakage of individual microtubules – staggered between microtubules induces.....

The panels show the process of transport interruption and varicosity formation:
 

- a. Intact Axon (Pre-Injury):** Shows a normal axon with microtubules 1 and 2.
- b. Microtubule Breakage and Undulation Formation:** Shows the initial breakage of microtubules.
- c. Axon Relaxation:** Shows the axon relaxing after the breakage.
- d. Swelling Formation Due To Transport Interruption:** Shows the formation of a varicosity due to the interruption of transport.

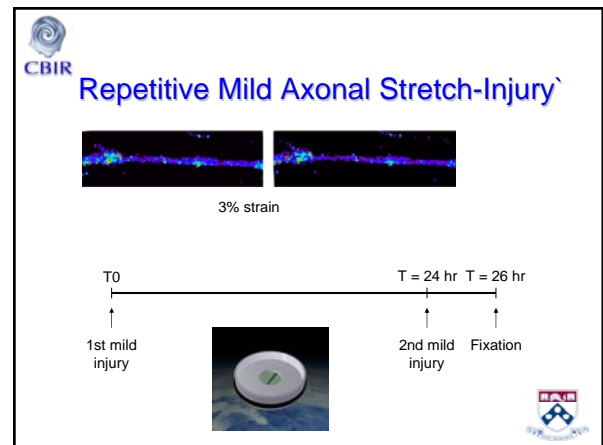
**Key:**

- Green circle: Cargo
- Blue line: Tubulin Dimer
- Red line: Microtubule 1
- Orange line: Microtubule 2



## Repetitive mTBI

"period of vulnerability", where another mild injury is thought to trigger a greatly exaggerated response



CBIR

Pre-2nd injury

Post -2nd injury

Repeat mild injury

Repeat mild injury + TTX

Mild TAI (below calcium influx threshold) predisposes axons to calcium influx with repeat exposure 24 hours later

CBIR

### NaCh immunoreactivity

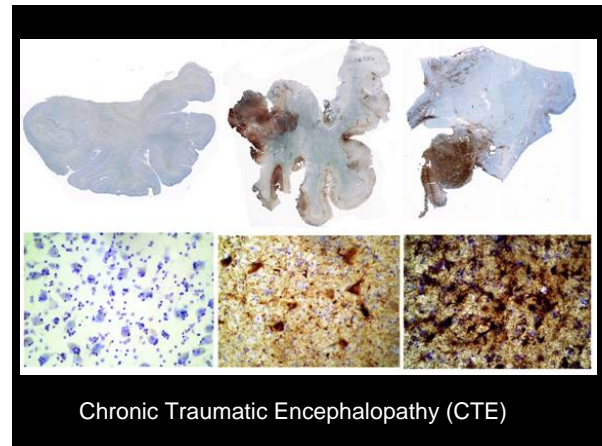
Pre-injury

1hr post-injury

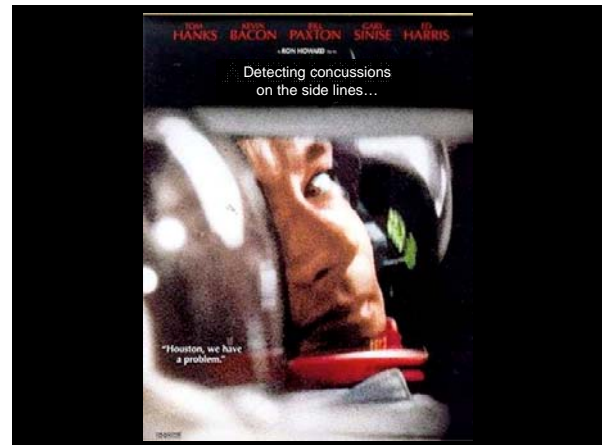
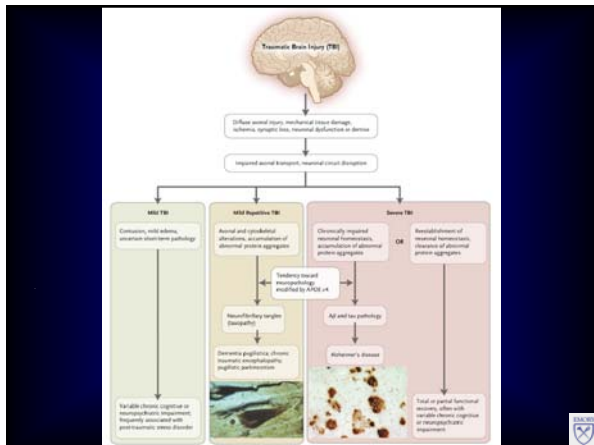
24hr post-injury

Posttraumatic increase in NaCh density = **NaChO?**





Chronic Traumatic Encephalopathy (CTE)



## The Need for Independent Evaluators on NFL Sidelines

Posted: October 20, 2011 by Dustin Fink in Athletic Training, Concussion Blog Original, Education, News Story, NFL Concussions, Return to Play

Tags: Sebold Reed, Mike Florio, Mike Vick, NFL Players Concussions, ProFootballTalk, Will Carroll

**“No area of sports medicine involves more clinical uncertainty and controversy than the treatment of concussion.”**

Melvin Field, MD

SIGNS OBSERVED BY COACHING STAFF	SYMPTOMS REPORTED BY ATHLETES
Appears dazed or stunned	Headache or “pressure” in head
Is confused about assignment or position	Nausea or vomiting
Forgets an instruction	Balance problems or dizziness
Is unsure of game, score, or opponent	Double or blurry vision
Moves clumsily	Sensitivity to light
Answers questions slowly	Sensitivity to noise
Loses consciousness ( <i>even briefly</i> )	Feeling sluggish, hazy, foggy, or groggy
Shows mood, behavior, or personality changes	Concentration or memory problems
Can't recall events <i>prior</i> to hit or fall	Confusion
Can't recall events <i>after</i> hit or fall	Just not “feeling right” or “feeling down”

Physical	Cognitive	Emotional	Sleep
<ul style="list-style-type: none"> <li>Headache</li> <li>Nausea</li> <li>Vomiting</li> <li>Balance problems</li> <li>Dizziness</li> <li>Visual problems</li> <li>Fatigue</li> <li>Sensitivity to light</li> <li>Sensitivity to noise</li> <li>Numbness/ Tingling</li> <li>Dazed or stunned</li> </ul>	<ul style="list-style-type: none"> <li>Feeling mentally "foggy"</li> <li>Feeling slowed down</li> <li>Difficulty concentrating</li> <li>Difficulty remembering</li> <li>Forgetful of recent information or conversations</li> <li>Confused about recent events</li> <li>Answers questions slowly</li> <li>Repeats questions</li> </ul>	<ul style="list-style-type: none"> <li>Irritability</li> <li>Sadness</li> <li>More emotional</li> <li>Nervousness</li> </ul>	<ul style="list-style-type: none"> <li>Drowsiness</li> <li>Sleeping less than usual</li> <li>Sleeping more than usual</li> <li>Trouble falling asleep</li> </ul>

## Maddock's Questions

- Where are we playing?
- Which team are we playing today?
- Who is your opponent presently?
- Which quarter is it?
- How far into the quarter is it?
- Which team scored last?
- Which team did we play last?
- Did we win our last match?



## Concussions & Sports

Concussion:  
trauma-induced alteration in mental status

Confusion and amnesia are key



## Diagnosing

- Recognition difficult
  - Variety of signs and symptoms
  - Signs can be subtle
  - Athletes reluctant to report
  - Awareness of problem limited among health professionals
  - No specific diagnostic tool



1) ORIENTATION:

Month: \_\_\_\_\_ 0 1

Date: \_\_\_\_\_ 0 1

Day of week: \_\_\_\_\_ 0 1

Year: \_\_\_\_\_ 0 1

Time (within 1 hr): \_\_\_\_\_ 0 1

Orientation Total Score \_\_\_\_\_ / 5

2) IMMEDIATE MEMORY: (all 3 trials are completed regardless of score on trial 1 & 2; total score equals sum across all 3 trials)

List	Trial 1	Trial 2	Trial 3
Word 1	0 1	0 1	0 1
Word 2	0 1	0 1	0 1
Word 3	0 1	0 1	0 1
Word 4	0 1	0 1	0 1
Word 5	0 1	0 1	0 1
Total			

Immediate Memory Total Score \_\_\_\_\_ / 15  
(Note: Subject is not informed of delayed recall testing of memory)

3) CONCENTRATION:

Digit Backward (If correct, go to next string length. If incorrect, read trial 2. Stop after incorrect on both trials.)

4-9-3 \_\_\_\_\_ 0 1

3-8-1-4 \_\_\_\_\_ 0 1

6-2-9-7-1 \_\_\_\_\_ 0 1

7-1-8-4-6-2 \_\_\_\_\_ 0 1

5-5-9-1-4-8 \_\_\_\_\_ 0 1

Months in Reverse Order: (entire sequence correct for 1 point)

Dec-Nov-Oct-Sep-Aug-Jul \_\_\_\_\_ 0 1

Jun-May-Apr-Mar-Feb-Jan \_\_\_\_\_ 0 1

Concentration Total Score \_\_\_\_\_ / 5

4) DELAYED RECALL:

Word 1 \_\_\_\_\_ 0 1

Word 2 \_\_\_\_\_ 0 1

Word 3 \_\_\_\_\_ 0 1

Word 4 \_\_\_\_\_ 0 1

Word 5 \_\_\_\_\_ 0 1

Delayed Recall Total Score \_\_\_\_\_ / 5

EXERCUTIONAL MANEUVERS (when appropriate):

5 jumping jacks \_\_\_\_\_ 0 1

5 sit-ups \_\_\_\_\_ 0 1

5 push-ups \_\_\_\_\_ 0 1

5 knee bends \_\_\_\_\_ 0 1

SUMMARY OF TOTAL SCORES:

ORIENTATION \_\_\_\_\_ / 5

IMMEDIATE MEMORY \_\_\_\_\_ / 15

CONCENTRATION \_\_\_\_\_ / 5

DELAYED RECALL \_\_\_\_\_ / 5

OVERALL TOTAL SCORE \_\_\_\_\_ / 30

NEUROLOGIC SCREENING:

Loss of Consciousness: (occurrence, duration) \_\_\_\_\_

Retrograde & Posttraumatic Amnesia: (recollection of events pre- and post-injury) \_\_\_\_\_

Strength: \_\_\_\_\_

Sensation: \_\_\_\_\_

Coordination: \_\_\_\_\_

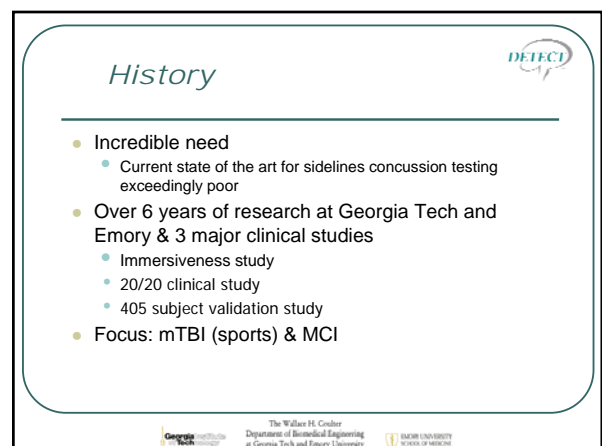
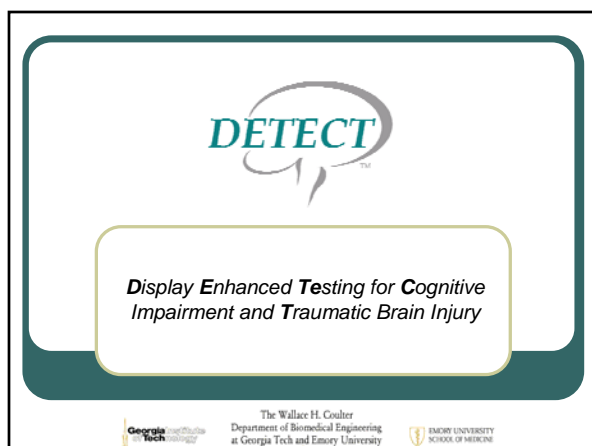
## Standardized Assessment of Concussion (SAC)


- Simple - no expertise needed
- 5 minutes to administer
- Preseason score for comparison
- Pocket sized cards



## SAC


- Questionable reliability on the field
- Can't replace clinical judgment or real neuropsych testing
- Sensitivity remains to be proven







## DETECT™

- Novel, portable, immersive platform for rapid neuropsychological testing to assess cognitive function:
  - mild traumatic brain injury (mTBI) / concussion
  - mild cognitive impairment (MCI) / early Alzheimer's





The Wallace H. Coulter  
 Department of Biomedical Engineering  
 at Georgia Tech and Emory University





## Technology





### Hardware


- Noise and Light attenuation
- Portable
- Ease of use

### Software

- 7 minutes
- Measures response time, processing speed, working memory, other cognitive scales



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 Department of Biomedical Engineering  
 at Georgia Tech and Emory University





## Device components




Component	Function
Ultra mobile computer	Data storage and program interface
Head mounted display containing visual reality glasses, visual isolation, and passive noise reduction headphones	Visual and auditory immersion
Handheld controller	Input Device for answering questions



The Wallace H. Coulter  
 Department of Biomedical Engineering  
 at Georgia Tech and Emory University





## Device components





The Wallace H. Coulter  
 Department of Biomedical Engineering  
 at Georgia Tech and Emory University



# DETECT

## Display Enhanced Testing for Concussions and mTBI





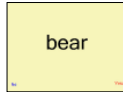


## ZENDA TECHNOLOGIES

- Completed pilot
- Completed GT TBI exploratory study
- Completed 20-20 study in MCI
- Completed 400 patient study MCI
- Submitting STTR and VA study for TBI



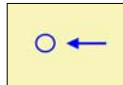
## DETECT™ Neuropsychological Tasks:



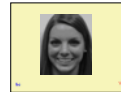
**Selective Reminding** - Subjects are asked to remember a group of 12 words. They are then shown 24 words and asked to respond when one from the original list is recognized.



**Simple and Complex** - Subjects are asked to respond to a stimulus with 1 to 3 characteristics: shape, color, and internal line orientation. Correctness and mean reaction time are recorded.



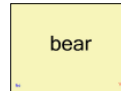
**Go No Go** - Subjects are asked to respond to a stimulus with 2 characteristics: shape and orientation. If the arrow is blue, they are to select the side that the arrow is pointing. If the arrow is red, they are to select the side opposite from where it is pointing.



**1 Back** - Subjects are asked to remember a face and decide if the next face is the same as the one shown previously. This test continues with over 30 faces.



**2 Back** - Subjects are asked to remember a face. Then a second face is shown followed by a third. They are asked to remember if the third face is the same as the first one. This test continues with over 30 faces.



**Delayed Selective Reminding** - Subjects are asked to remember the original group of 12 words.



## Domains Tested

- Verbal memory (selective reminding)
- Visual Memory
- Delayed memory (selective reminding)
- Executive Function
- Working Memory
- Reaction time
- Attention & vigilance



## Advantages of DETECT™

DETECT	"Standard" NP testing
Short (5-7 minutes)	Long (1 – 2 hours)
Immersive (independent of environment)	Requires quiet testing room
Portable	Facility dependent
Objective (independent of examiner)	Requires trained examiner to administer
Simple (yes no buttons)	Complex
Cool!	Not Cool!

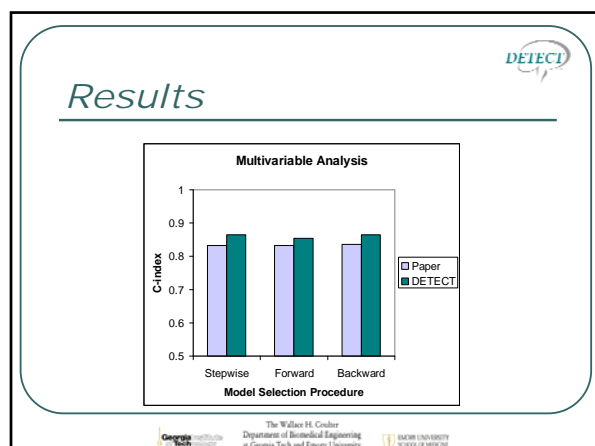


DETECT ★	Traditional NPT Testing	Computer Based Testing	Common Screens MiniCog, MMSE
•Short (10 min.) ★	•Long (1 – 2 hrs.)	•Long (15 – 30 min.)	•Short (5 min.) ★
•Can be administered anywhere ★	•Requires noise-free room	•Requires noise-free room	•Common exam room ★
•Does not require physician to deliver or score ★	•Requires physician	•Does not require physician to deliver or score ★	•Requires physician
•Simple to take ★	•Laborious	•Requires keyboard skills ★	•Simple ★
•Objective ★	•Subjective	•Objective ★	•Subjective

## DETECT MCI 20:20 Study

Wesley Woods Neurology Clinic

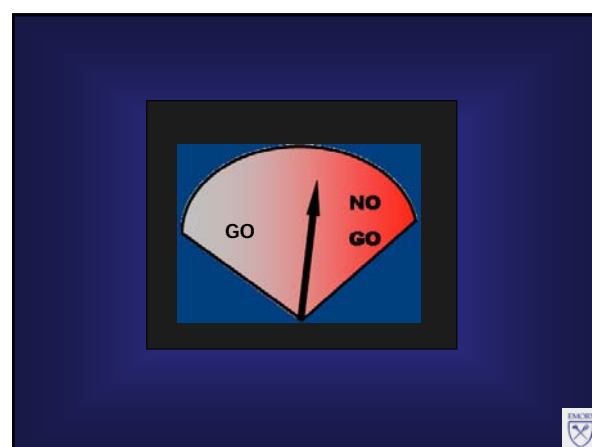
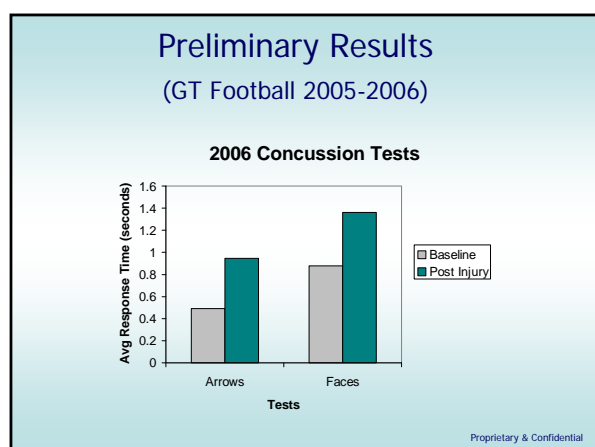
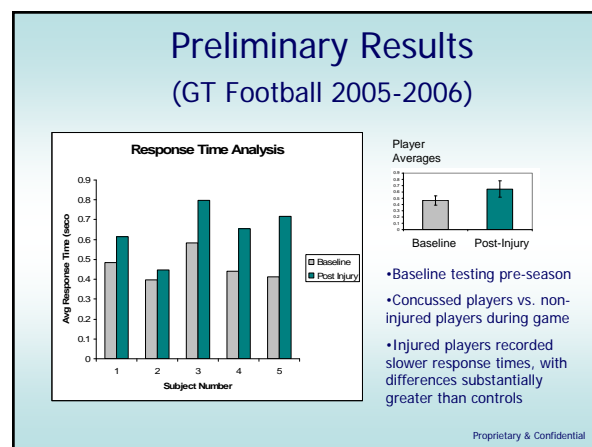
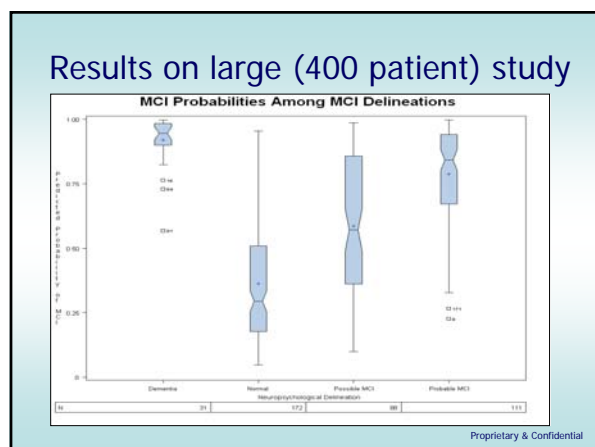


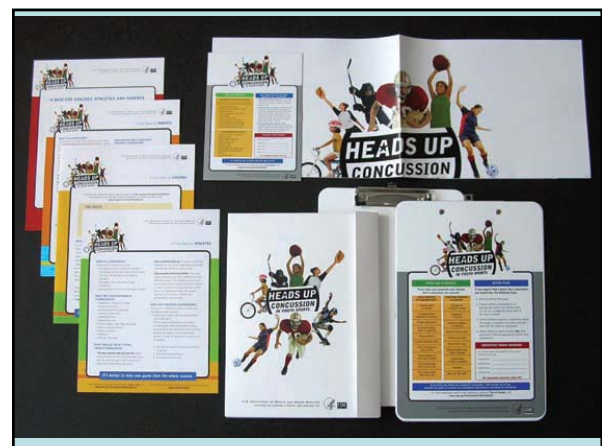
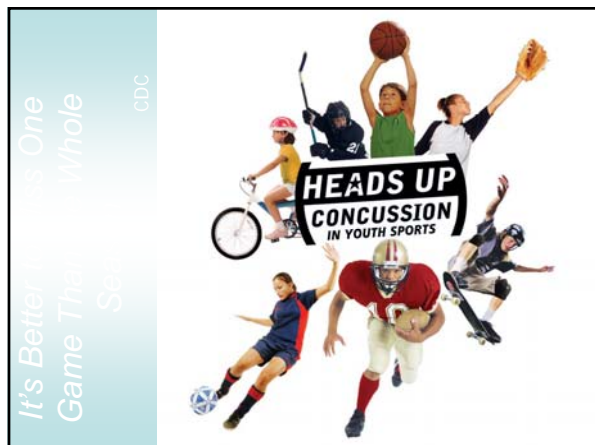
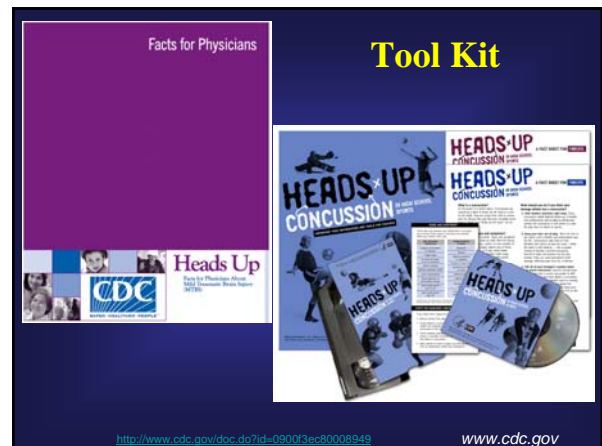
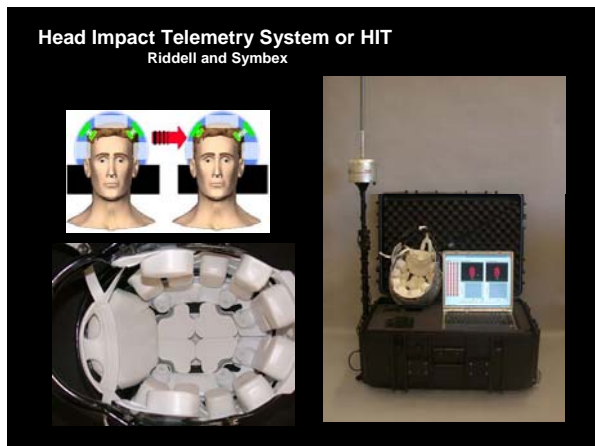


## DETECT MCI 400 Patient Study

### Wesley Woods Geriatrics

The Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University  
Georgia Tech  
EMORY UNIVERSITY SCHOOL OF MEDICINE









## Core Principle #2 – Removal

- “A youth athlete who is suspected of sustaining a concussion or head injury in a practice or game shall be removed from competition at that time.”

## Core Principle #3 – Return to Play

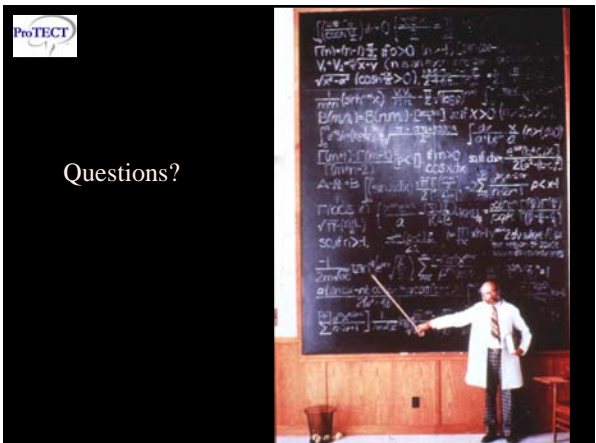
- “A youth athlete who has been removed from play may not return to play until the athlete is evaluated by a licensed health care provider trained in the evaluation and management of concussion and receives written clearance to return to play from that health care provider...”

## Why A Law Is Necessary

- Education, awareness and information are essential, but insufficient without more
- Laws mandate behavior change
- Without laws, standards are slow to develop. The lessons learned are not reinforced.



NATIONAL FOOTBALL LEAGUE



Questions?