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

Public Health Burden of TBI in the United States

- 52,000 Deaths
- 275,000 Hospitalizations
- 1,365,000 Emergency Departments Visits

Comparison of Annual Incidence

- TBI a major health problem in the U.S.
  - 1.5 million TBI per year
  - 100,000 hospitalizations per year
  - 50,000 deaths per year
  - 5.3 million living with disability from TBI
  - Estimated annual costs – $56 billion
  - Signature Injury of the Iraq/Afghanistan War
300,000 Concussions per year in Sports

Teen Sports Concussions in the News

Nathan Stiles
Spring Hill Kansas High School Senior Nathan Stiles collapsed on the sideline just before halftime of his last football game. He died later at the hospital.

Nathan Stiles (1993-2010)
17-year-old captain and homecoming king

Potential Consequences of Non-fatal TBI

- Cognitive impairment
- Psychological and emotional changes
- Personality changes
- Sensory and/or motor dysfunction
- Seizure disorders

Corriveau, VJ et al. The epidemiology and prevention of TBI, in press, 2012

Comparison of Annual Incidence

Potential Consequences of Non-fatal TBI

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

Coronado, VG et al. The epidemiology and prevention of TBI, in press, 2012

Estimated Economic Costs of TBI
$76.3 Billion in 2010

Medical $11.5B
Indirect $64.8B

Coronado, VG et al. The epidemiology and prevention of TBI, in press, 2012

“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

Education & Information
Enforcement & Regulation
Engineering & Technology
Economic Incentives
Children and Concussion

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

Secondary Injury Neurotoxic

- Excitatory Amino Acids
  - Glutamate, Glycine, others
- Critical Ions
  - Calcium, Sodium, Magnesium
- Receptor Activation
  - NMDA, AMPA, etc.

Intracellular Calcium Signaling

- Hormones, Neurotransmitters, Growth Factors, Osmolarity
- Light, Odorants, Test Molecules
- ADP-Ribose, Arachidonic Acid, Sphingosine
Evolution of Axonal Pathology

Terminal bulb

Periodic varicosities

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

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

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

... Transport Interruption:
responsible for the formation of axonal varicosities
Repetitive mTBI

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

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

Posttraumatic increase in NaCh density = NaChO?
Chronic Traumatic Encephalopathy (CTE)

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

Melvin Field, MD
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

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

**History**

- Incredible need
  - Current state of the art for sidelines concussion testing exceedingly poor
- Over 6 years of research at Georgia Tech and Emory & 3 major clinical studies
  - Immersiveness study
  - 20/20 clinical study
  - 405 subject validation study
- Focus: mTBI (sports) & MCI
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

Technology

Hardware
- Noise and Light attenuation
- Portable
- Ease of use

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

Device components

<table>
<thead>
<tr>
<th>Component</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultra-mobile computer</td>
<td>Data storage and program interface</td>
</tr>
<tr>
<td>Head mounted display containing virtual reality glasses, visual isolation, and passive noise reduction headphones</td>
<td>Visual and auditory immersion</td>
</tr>
<tr>
<td>Handheld controller</td>
<td>Input Device for answering questions</td>
</tr>
</tbody>
</table>

DETECT
Display Enhanced Testing for Concussions and mTBI

ZENDA TECHNOLOGIES
- 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.

**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™**

<table>
<thead>
<tr>
<th>DETECT</th>
<th>“Standard” NP testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short (5-7 minutes)</td>
<td>Long (1 – 2 hours)</td>
</tr>
<tr>
<td>Immersive (independent of environment)</td>
<td>Requires quiet testing room</td>
</tr>
<tr>
<td>Portable</td>
<td>Facility dependent</td>
</tr>
<tr>
<td>Objective (independent of examiner)</td>
<td>Requires trained examiner to administer</td>
</tr>
<tr>
<td>Simple (yes no buttons)</td>
<td>Complex</td>
</tr>
<tr>
<td>Cool!</td>
<td>Not Cool!</td>
</tr>
</tbody>
</table>

DETECT MCI 20:20 Study

Wesley Woods Neurology Clinic
Results

Multivariable Analysis

Stepwise Forward Backward

Model Selection Procedure

C-index

DETECT MCI
400 Patient Study

Wesley Woods Geriatrics

Preliminary Results
(GT Football 2005-2006)

Response Time Analysis

Baseline Post-Injury

Player Averages

Baseline: Concussed players vs. non-injured players during game
Post-Injury: Injured players recorded slower response times, with differences substantially greater than controls

Results on large (400 patient) study

Preliminary Results
(GT Football 2005-2006)

2006 Concussion Tests

Arrows Faces

Test Results

Baseline Post-Injury
Head Impact Telemetry System or HIT
Riddell and Symbex

It's Better to Miss One Game Than the Whole Season

CDC
Do’s and Don’ts with a Concussion

Cognitive Rest

- Do not attend school or work.
- Do not drive.
- Do not play video games.
- Do not watch TV.
- Do not read.
- Do not use your phone.

Core Principle #1 – Education

- "On a yearly basis, a concussion and head injury information sheet shall be signed and returned by the youth athlete and the athlete’s parent and/or guardian prior to the youth athlete’s initiating practice or competition.”
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.