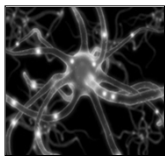
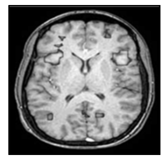
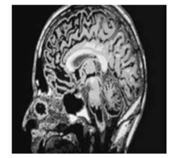
Mild Traumatic Brain Injury & Postconcussion Syndrome:

New Evidence Base for Evaluation and Management





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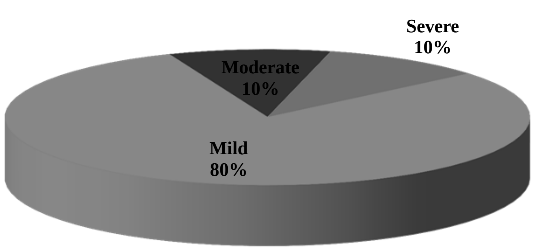
MEDICAL COLLEGE OF WISCONSIN

Concussion Research Consortium (CRC)

mTBI: What's all the Fuss About?

Hospitalizations Due to Head Injury



> 1 million mTBI ED visits per year

$100 billion/year in U.S

- 2.5-3.8 million mTBI estimated annually in U.S.
- True incidence unclear: 30-50% never receive medical attention
- Far fewer see a neurosurgeon, neurologist or *neuropsychologist*
- Subset with persistent symptoms and disability ("PCS")
- Costly public health issue in the billions of $
- Hot Buttons: **Sports, Military**

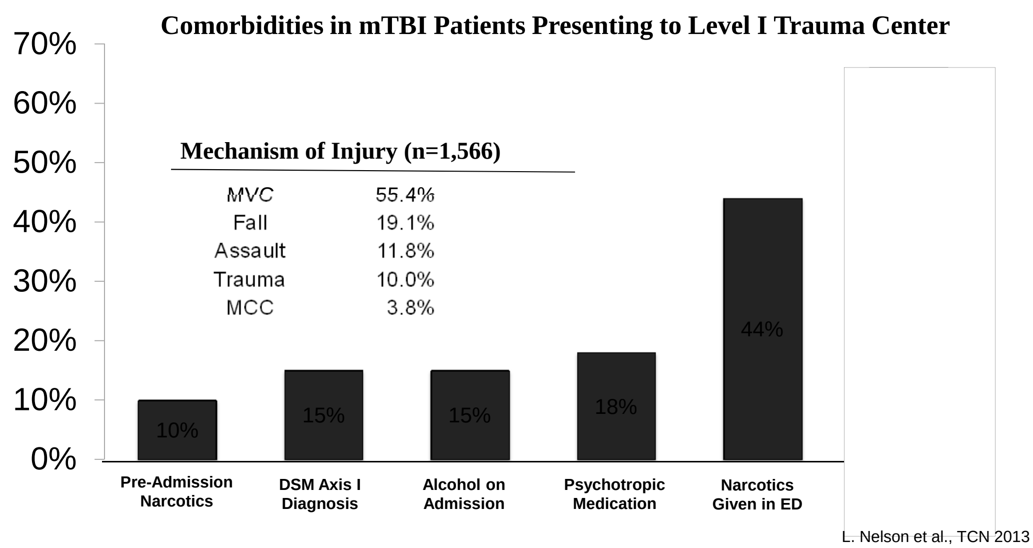
mTBI Disconnect:
Lowest Mortality, Major Clinical Challenge, *Least Science*

Clinical Challenges in mTBI

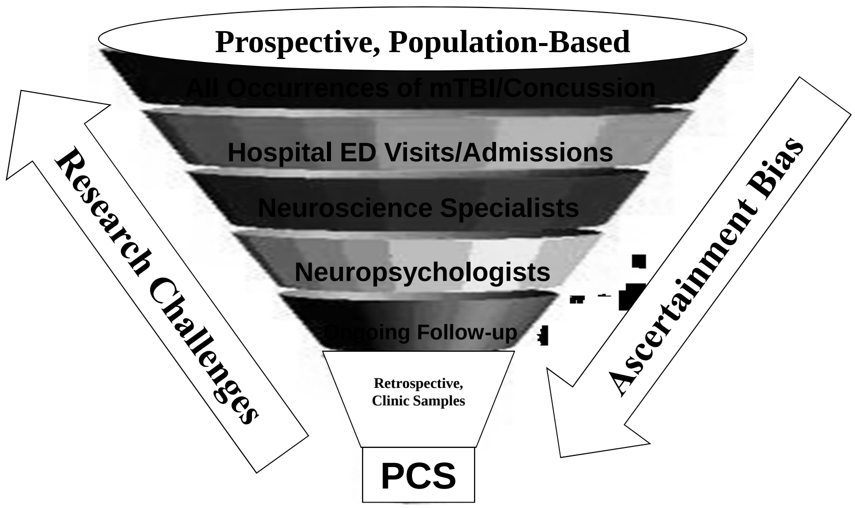
- Was the accident sufficient to cause the patient to sustain a traumatic brain injury?
- What are the effects of this injury on brain function?
- How long *should* it take for the patient to recover?
- Is the cause of their persistent symptoms "*organic*" or "*mental*"?

Historically, all hampered by lack of science

Challenges in mTBI Research:
One Reason It's So Hard



Research Challenges in mTBI: *The Denominator Problem*



Significant Impact on Epidemiology and Clinical Science of mTBI

Do As I Say…

"Dad, I want to be a scientist"

"That's great, honey. Just stay out of the weeds and pick something other than mTBI to study."

Alternative Paradigms for mTBI Research

***Sports Laboratory Assessment Model* (SLAM)**

Sports Concussion: mTBI Laboratory

(Barth, 2001)

- **Large sample at risk**
- **Defined Exposure Period**
- **Preinjury Baseline Measures**
- **Eye Witness Account: AIC's**
- **Immediate Assessment**
- **Serial Testing/Continuity**
- **Normal Controls**
- **Repetitive Concussion**
- **Chronic Exposure**
- **Longterm follow-up**

How Can We Inform the Broader Science of mTBI?

Lessons Learned

1. Wealth of data on acute **clinical effects and recovery** after SRC & mTBI.
2. Emerging research on acute **physiological effects and recovery** after SRC & mTBI.
3. Movement toward an **integrated, evidence-based neurobiopsychosocial model of mTBI** recovery.


AN INTEGRATED REVIEW OF RECOVERY AFTER MILD TRAUMATIC BRAIN INJURY (MTBI): IMPLICATIONS FOR CLINICAL MANAGEMENT

Michael McCrea[1,2], Grant L. Iverson[3,4], Thomas W. McAllister[5], Thomas A. Hammeke[2], Matthew R. Powell[1], William B. Barr[6], and James P. Kelly[7,8]

The Clinical Neuropsychologist, 22: 769–800, 2008

MANAGEMENT OF PEDIATRIC MILD TRAUMATIC BRAIN INJURY: A NEUROPSYCHOLOGICAL REVIEW FROM INJURY THROUGH RECOVERY

Michael W. Kirkwood[1], Keith Owen Yeates[2], H. Gerry Taylor[3], Christopher Randolph[4], Michael McCrea[5], and Vicki A. Anderson[6]

Keywords: Mild traumatic brain injury; Minor head injury; Concussion; Pediatrics; Treatment.

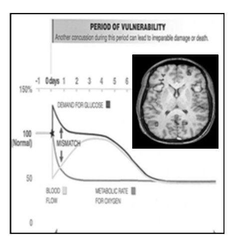
New Understanding of mTBI
Rethinking Postconcussion Syndrome

Scientific Advances in mTBI:
Acute Effects & Recovery

MECHANISM | **TRUE NATURUAL HISTORY**


Acute Effects and Recovery Time Following Concussion in Collegiate Football Players

The NCAA Concussion Study



Minimum Threshold: How much is enough to cause brain injury?

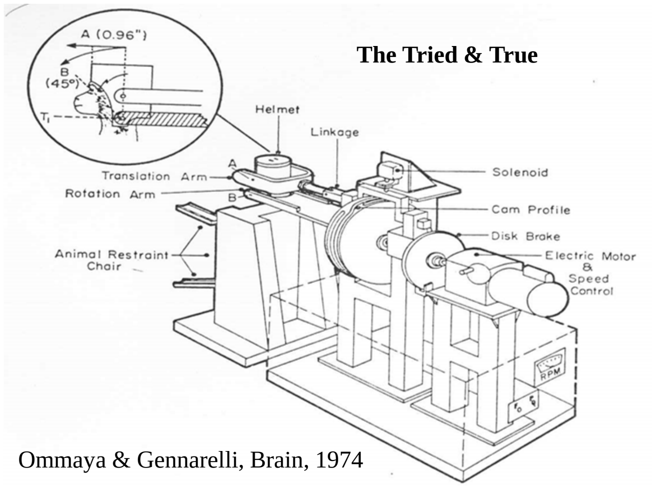
Clinical Recovery: How long does it take for sign & symptoms to recover?

Physiological Recovery: How long does the *brain* take to recover?

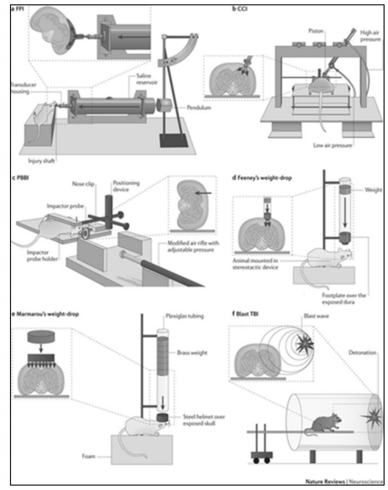
Driving Evidence Based Diagnosis, Assessment and Management

Biomechanics of TBI

The Tried & True



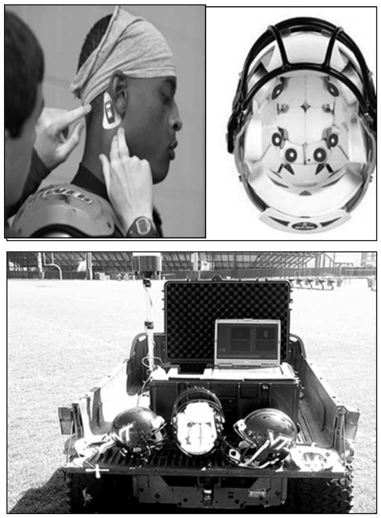
Ommaya & Gennarelli, Brain, 1974



Long Road of Clinical Translation

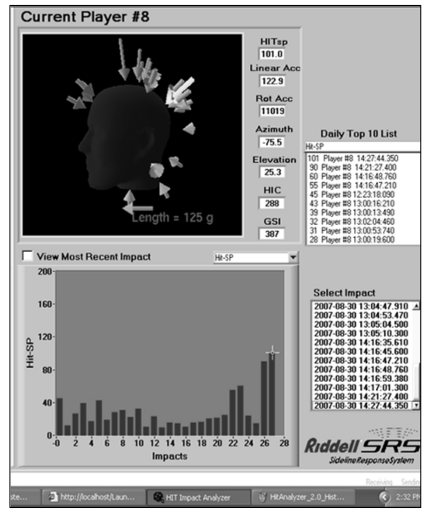
mTBI Laboratory!

Biomechanics of mTBI in Humans:
How Much is Enough to Cause Brain Injury?



Measure and record blows to the head:

- Impact location
- Impact magnitude
- Impact duration
- Linear and angular acceleration components
- Exact times of impacts
- Sync w/ video



HITS Studies: *Concussion Threshold*?


Guskiewicz et al, UNC

MORE THAN A “DING”

- > 250K impacts in 100 players
- 19 concussion with HITS
- Ave. impact of concussive events: **103g** (33) (<1% of NC impacts > 95g)
- Controlling for rotational acceleration, location of impact on the head, concussion:
  - 17x more likely if PLA $\geq$100g
  - 15x more likely if PRA > 5000r/sec2

Pellman et al: peak acceleration-concussion **98 g** (+/- 28), non-concuss 60 g (+/- 24)
Zhang (2004): Probability of MTBI – 25% at 66g, 50% at 82g, 80% at **106 g**
Brolinson (2006): Average peak acceleration **103.3 g** (range 56-118 g)

What Does That Mean in Real Life?

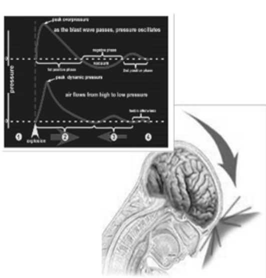
- 100 g PLA equivalent to 25 mph MVA into brick wall, striking head against dash (unhelmeted)
- Significant rotational acceleration component
- Highlights significance of head impacts in SRC (not so mild)
- Provides context for interpretation of injury mechanisms

Progress in mTBI Research:

Acute Effects & Recovery

INJURY MECHANISMS

TRUE NATURAL HISTORY OF RECOVERY



Threshold/Dynamics:
How much is enough
to cause brain injury?

Acute Effects and Recovery Time Following Concussion in Collegiate Football Players

The NCAA Concussion Study

Michael McCrea, PhD
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James A. Onate, PhD, ATC
Jingzhen Yang, MPH
James P. Kelly, MD

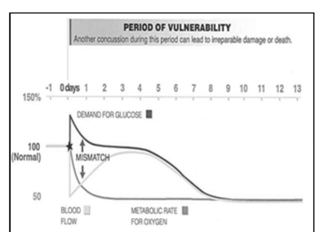
Context Lack of empirical data on recovery time following sport-related concussion hampers clinical decision making about return to play after injury.

Objective To prospectively measure immediate effects and natural recovery course relating to symptoms, cognitive functioning, and postural stability following sport-related concussion.

Design, Setting, and Participants Prospective cohort study of 1631 football players from 15 US colleges. All players underwent preseason baseline testing on concussion assessment measures in 1999, 2000, and 2001. Ninety-four players with concussion (based on American Academy of Neurology criteria) and 56 noninjured controls underwent assessment of symptoms, cognitive functioning, and postural stability immediately, 3 hours, and 1, 2, 3, 5, 7, and 90 days after injury.

Clinical Recovery:
How long does it take for
signs & symptoms to recover?

+



Giza & Hovda, 2010

Physiological Recovery:
How long does it take for the
brain to recover?

New Evidence Base to Guide Diagnosis, Assessment and Management

Acute Effects and Recovery Time Following Concussion in Collegiate Football Players

The NCAA Concussion Study

JAMA 2003; 290:2556-2563

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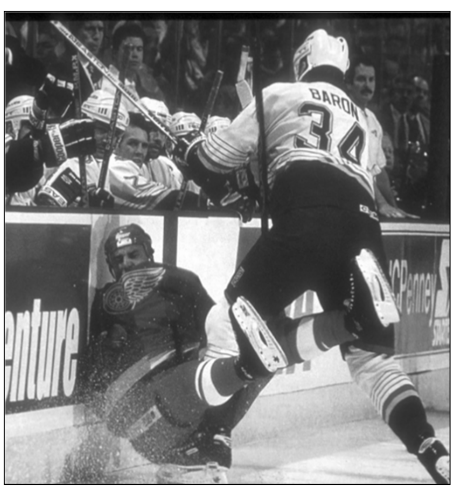
Over 25,000 Athlete Seasons, 1,500 Concussions Studied

Can we *measure* the acute effects of...

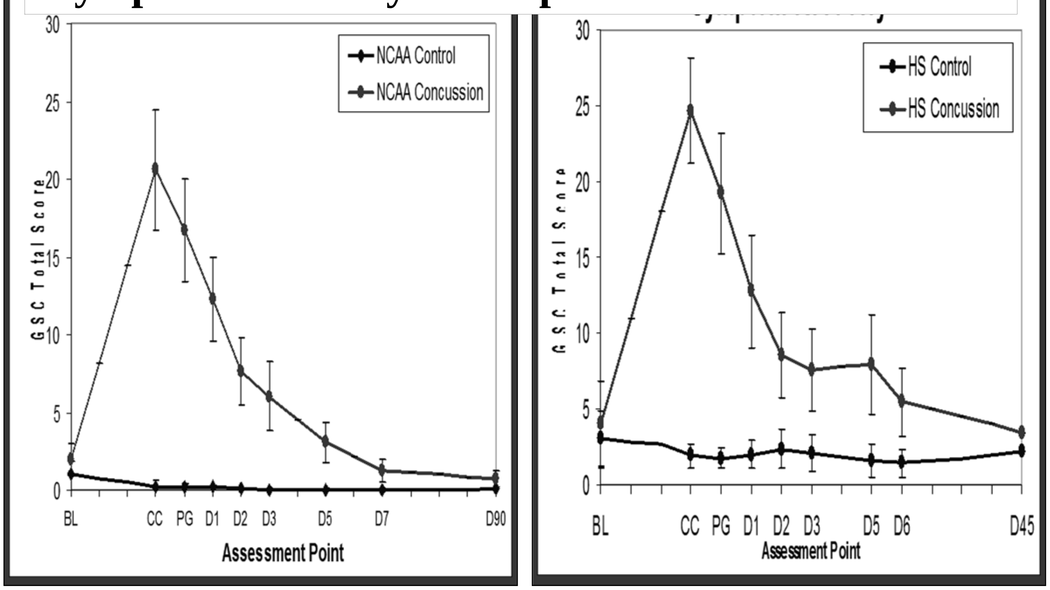


…What does early *recovery* look like?

Symptom Recovery After mTBI

Not tonight, honey, I have a concussion.

Symptom Recovery after Sport-Related Concussion



Higher score indicates more severe symptoms; error bars represent 95% CI

McCrea et al., JAMA 2003

How Long Does it Take to Recover?

Rate of Postinjury Recovery in HS and College Athletes (n=790)	**Total (%)**	**Cumulative Total (%)**
Rapid (< 1 day)	21.1	21.1
Gradual (> 1 day, < 7 days)	64.3	85.4
Prolonged (1 week – 1 month)	11.9	97.3
Persistent (> 1 month)	2.7	100.0

2013 (n=94): Mean Symptom Recovery **5.75 Days** (4.48)
90% Recover in 10 Days or Less, 2% > 30 days

Journal of the International Neuropsychological Society (2013), **19**, 22–33.

doi:10.1017/S1355617712000872

Incidence, Clinical Course, and Predictors of Prolonged Recovery Time Following Sport-Related Concussion in High School and College Athletes

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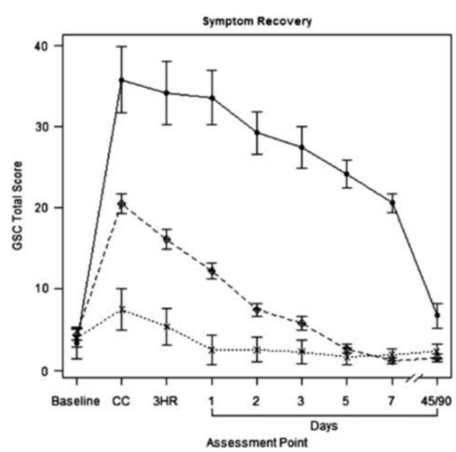
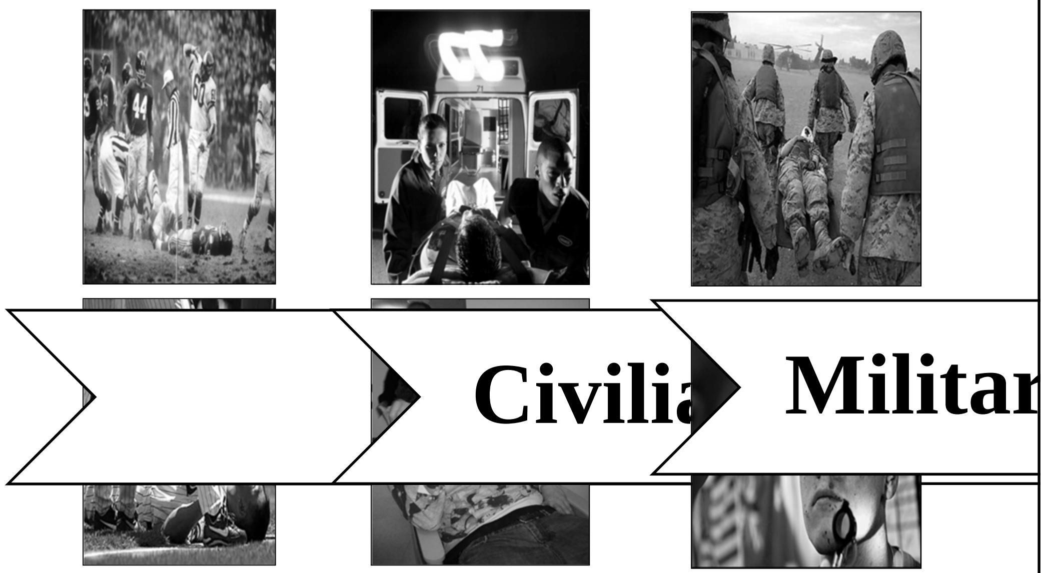
Abstract

Sport-related concussion (SRC) is typically followed by clinical recovery within days, but reports of prolonged symptoms are common. We investigated the incidence of prolonged recovery in a large cohort ($n = 18,531$) of athlete seasons over a 10-year period. A total of 570 athletes with concussion (3.1%) and 166 controls who underwent pre-injury baseline assessments of symptoms, neurocognitive functioning and balance were re-assessed immediately, 3 hr, and 1, 2, 3, 5, 7, and 45 or 90 days after concussion. Concussed athletes were stratified into typical (within 7 days) or prolonged (> 7 days) recovery groups based on symptom recovery time. Ten percent of athletes ($n = 57$) had a prolonged symptom recovery, which was also associated with lengthier recovery on neurocognitive testing ($p < .001$). At 45–90 days post-injury, the prolonged recovery group reported elevated symptoms, without deficits on cognitive or balance testing. Prolonged recovery was associated with unconsciousness [odds ratio (OR), 4.15; 95% confidence interval (CI) 2.12–8.15], posttraumatic amnesia (OR, 1.81; 95% CI, 1.00–3.28), and more severe acute symptoms ($p < .0001$). These results suggest that a small percentage of athletes may experience symptoms and functional impairments beyond the typical window of recovery after SRC, and that prolonged recovery is associated with acute indicators of more severe injury. (*JINS*, 2013, *19*, 22–33)



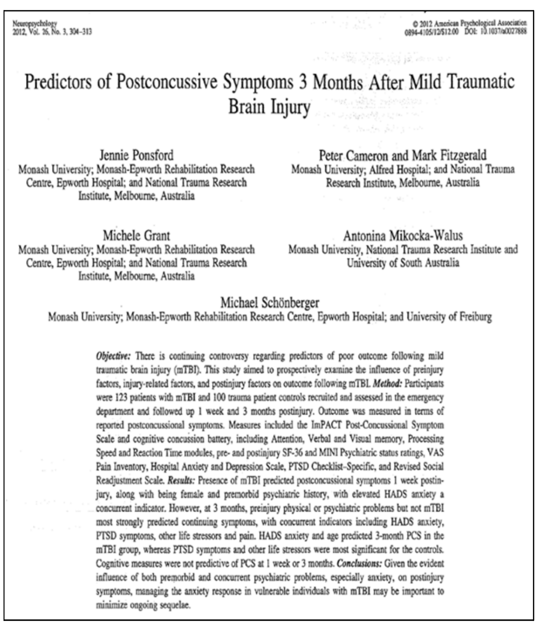
- 10% take > 7 days to recover
- Acute severity predicts recovery
- 2.5% symptomatic > 45 days
- No impairment on objective measures at Day 45 relative to BL

Translational Research?



How Do the Findings Apply to Other Populations at Risk of mTBI?

Civilian Symptom Recovery



Neuropsychology
2012, Vol. 26, No. 3, 304–313
0894-4105/12/$12.00 DOI: 10.1037/a0027888

Predictors of Postconcussive Symptoms 3 Months After Mild Traumatic Brain Injury

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Peter Cameron and Mark Fitzgerald
Monash University; Alfred Hospital; and National Trauma Research Institute, Melbourne, Australia

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Michael Schönberger
Monash University; Monash-Epworth Rehabilitation Research Centre, Epworth Hospital; and University of Freiburg

Objective: There is continuing controversy regarding predictors of poor outcome following mild traumatic brain injury (mTBI). This study aimed to prospectively examine the influence of preinjury factors, injury-related factors, and postinjury factors on outcome following mTBI. ***Method:*** Participants were 123 patients with mTBI and 100 trauma patient controls recruited and assessed in the emergency department and followed up 1 week and 3 months postinjury. Outcome was measured in terms of reported postconcussional symptoms. Measures included the ImPACT Post-Concussional Symptom Scale and cognitive concussion battery, including Attention, Verbal and Visual memory, Processing Speed and Reaction Time modules, pre- and postinjury SF-36 and MINI Psychiatric status ratings, VAS Pain Inventory, Hospital Anxiety and Depression Scale, PTSD Checklist–Specific, and Revised Social Readjustment Scale. ***Results:*** Presence of mTBI predicted postconcussional symptoms 1 week postinjury, along with being female and premorbid psychiatric history, with elevated HADS anxiety a concurrent indicator. However, at 3 months, preinjury physical or psychiatric problems but not mTBI most strongly predicted continuing symptoms, with concurrent indicators including HADS anxiety, PTSD symptoms, other life stressors and pain. HADS anxiety and age predicted 3-month PCS in the mTBI group, whereas PTSD symptoms and other life stressors were most significant for the controls. Cognitive measures were not predictive of PCS at 1 week or 3 months. ***Conclusions:*** Given the evident influence of both premorbid and concurrent psychiatric problems, especially anxiety, on postinjury symptoms, managing the anxiety response in vulnerable individuals with mTBI may be important to minimize ongoing sequelae.

- Prospective study of 123 mTBI patients, 100 TC's
- Evaluated in ED, follow-up at 7 days, 3 mos
- PCS scale and cognitive testing, SF-36, MINI Psychiatric screening, HADS, PTSD CL
- Elevated PCS scores in mTBI group at Day 7, not different from TCs at 3 mos
- PCS at 3 mos predicted by preinjury physical problems and concurrent psychosocial factors, not by mTBI
- Cognitive measures not predictive of PCS at 7 days or 3 mos

The Clinical Neuropsychologist, 2011, 25 (5), 702 715
http://www.psypress.com/tcn
ISSN: 1385-4046 print/1744-4144 online
DOI: 10.1080/13854046.2011.566892

Psychology Press
Taylor & Francis Group

CE Symptom Complaints Following Reports of Blast Versus Non-Blast Mild TBI: Does Mechanism of Injury Matter?

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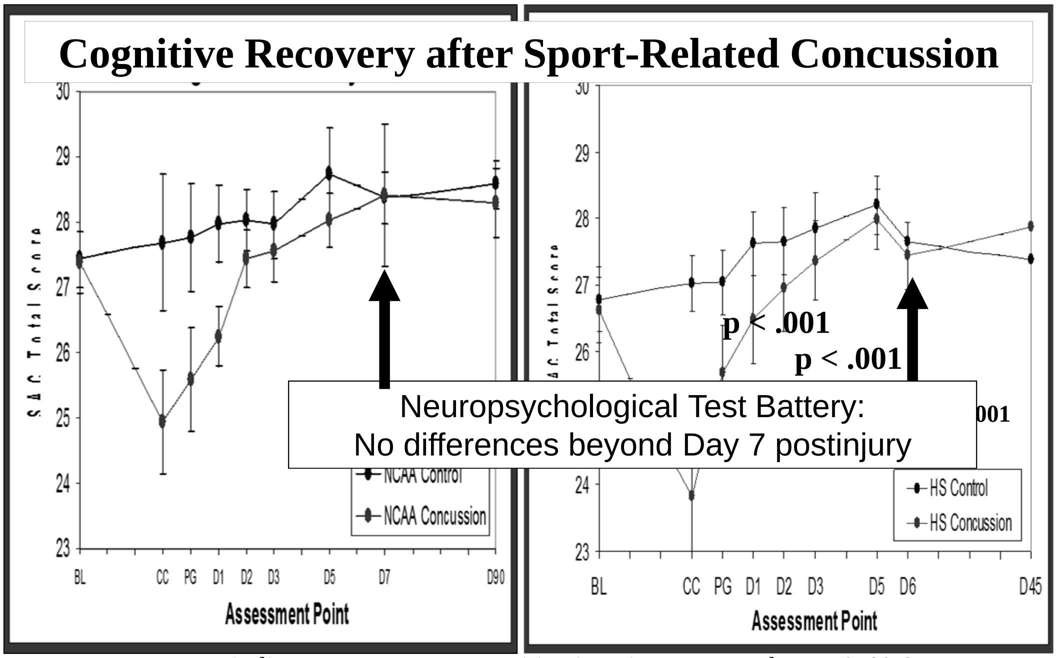
Patients with a reported history of mild traumatic brain injury (mild TBI) due to blast ($n-298$) or non-blast ($n-92$) mechanisms were asked to complete the Neurobehavioral Symptom Inventory (NSI) and the Post-traumatic Stress Disorder Checklist (PCL). Mechanism of injury did not account for a significant amount of variance in post-concussion symptom reporting overall, nor did severity of mild TBI (i.e., brief loss of consciousness versus only an alteration of consciousness). Symptom reporting was greater in those injured more than 1 month ago compared to those injured less than 1 month ago and in those reporting higher levels versus lower levels of PTSD symptoms. When examining specific symptoms, the only symptom that significantly varied between groups was hearing difficulty (with the blast-injured group reporting more severe difficulty with hearing). Findings suggest that greater symptom reporting is most strongly related to emotional distress.

Symptoms after Military mTBI

- 298 blast, 92 non-blast mTBI patients
- NSI and PCL administered
- Symptoms higher in mTBI < 1 mo ago vs. > 1 mo ago, and with higher PTSD sx's
- PCS not predicted by mechanism or acute characteristics of mTBI
- Symptom reporting most strongly associated with emotional distress

Is Symptom Recovery Really *Recovery:* Performance-Based mTBI Assessment

Cognitive Recovery after Sport-Related Concussion



Lower score indicates more severe cognitive impairment; error bars = 95% CI

McCrea et al., JAMA 2003

Journal of the International Neuropsychological Society (2005), **11**, 345–357.

DOI: 10.1017/S1355617705050411

The neuropsychological impact of sports-related concussion: A meta-analysis

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Abstract

There is increasing interest in the potential neuropsychological impact of sports-related concussion. A meta-analysis of the relevant literature was conducted to determine the impact of sports-related concussion across six cognitive domains. The analysis was based on 21 studies involving 790 cases of concussion and 2014 control cases. The overall effect of concussion ($d = 0.49$) was comparable to the effect found in the non-sports-related mild traumatic brain injury population ($d = 0.54$; Belanger et al., 2005). Using sports-concussed participants with a history of prior head injury appears to inflate the effect sizes associated with the current sports-related concussion. Acute effects (within 24 hr of injury) of concussion were greatest for delayed memory, memory acquisition, and global cognitive functioning ($d = 1.00$, 1.03, and 1.42, respectively). However, no residual neuropsychological impairments were found when testing was completed beyond 7 days postinjury. These findings were moderated by cognitive domain and comparison group (control group *versus* preconcussion self-control). Specifically, delayed memory in studies utilizing a control group remained problematic at 7 days. The implications and limitations of these findings are discussed. (*JINS*, 2005, *11*, 345–357.)

Keywords: Brain concussion, Head injury, Mild concussion, Sequelae, Traumatic brain injury, Football, Soccer

INTRODUCTION

Sports-related concussion occurs with some frequency. Among high school athletes, for instance, 5.5% of all injuries are concussions with an estimated 62,816 new cases of concussion annually (Powell & Barber-Foss, 1999). Football accounts for 63% of these injuries. The rate of concussion is similarly high in professional sports with an estimated .41 concussions per National Football League game (Pellman et al., 2004).

Sports-related concussion has gained increasing attention in the neuropsychology literature. Early work by Barth and colleagues (Barth et al., 1983; Rimel et al., 1981) in the 1980s set the stage for a plethora of empirical investigation into the neuropsychological impact of concussion in sports and the resolution of cognitive sequelae over time. In addition, other researchers have suggested the possibility that repeated exposure to sports-related activities such as heading a soccer ball may cause a more subtle concussion (e.g., headaches, dizziness, feeling "dazed," etc.) with an associated dose–response effect (Webbe & Ochs, 2003; Witol & Webbe, 2003).

Although it is clear that most patients suffer at least some acute cognitive difficulties associated with concussion or mild traumatic brain injury (MTBI) more generally, the nature and course of postacute cognitive recovery remains an area of intense controversy. In non-sports-related MTBI, most cases recover completely within the first 3 months (Dikmen et al., 1986, 1995; Gentilini et al., 1985; Gronwall & Wrightson, 1974; Levin et al., 1987), however, a significant minority continue to manifest cognitive deficits beyond that point, with prevalence estimates varying across study from 7–8% (Binder et al., 1997) to 33% (Rimel et al., 1981). In addition, a number of individuals continue to report dis-

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Cognitive Recovery: SRC

- Meta-analysis: 21 studies, 790 concussions, 2014 controls
- Acute effects (w/n 24 hrs) greatest for delayed memory (d=1.00), memory acquisition (d=1.03), and global cognitive functioning (d=1.42)
- Overall ES (d=0.49) comparable to non-sports (d=0.54)
- No residual neuropsych impairment > 7 days postinjury

Cognitive Effects of SRC

Table I. Characteristics of the 39 studies included in the meta-analysis

Study	Sample size; study design	Immediate post-injury: assessment	neurocognitive assessment	time from injury (days)[a]	effect size	95% CI	14 Days post-injury: assessment	effect size	95% CI	Mean study quality score
Barr and McCrea[49]	118; control	NC	SAC	0.003	−2.52	−2.82, −2.22				8.75
Bruce and Echemendia[50]	38; control	NC	B&B	0.08	−0.69	−1.30, −0.08	NC	−0.52	−1.13, 0.10	9.00
Collie et al.[18]	109; control					−0.56, 0.33				
Collins et al.[51]	136; baseline–post-concussion					−1.03, −0.57 −1.56, −1.13				
Collins et al.[52]	78; baseline–post-concussion					−1.16, −0.57 −1.19, −0.6				
Cremona-Meteyard and Geffen[37]	21; control					−1.08, 0.62				
Echemendia et al.[53]	49; control					−1.98, −0.95 −1.50, −0.43				
Erlanger et al.[17]	26; baseline–post-concussion					−1.42, −0.40				
Field et al.[54]	92; control					−1.47, −0.69 −1.86, −1.11				
Guskiewicz et al.[38]	20; control					−4.61, −3.37 −2.06, −0.45				
Guskiewicz et al.[14]	22; control					−1.26, 0.37 −1.65, −0.09				
Guskiewicz et al.[27]	72; control					−0.88, 0.02 −1.91, −1.09				
Guskiewicz et al.[39]	196; baseline–post-concussion					−12.45, −12.1				
Hinton-Bayre et al.[55]	20; control					−1.19, 0.52				
Hinton-Bayre et al.[40]	50; control					−2.08, −1.07				
Iverson et al.[56]	41; baseline–post-concussion	NC	Computer	1.3	−0.72	−1.13, −0.30				6.50
Iverson et al.[35]	19; baseline–post-concussion	NC	Computer	1.6	−0.16	−0.79, 0.47				6.50
Iverson et al.[57]	30; baseline–post-concussion	NC Sympt	Computer	1.5	−0.88 −1.45	−1.36, −0.40 −1.91, −0.99	NC Sympt	−0.23 0		

ACUTE (24 HR) COGNITIVE EFFECT SIZES:

-0.81 (LARGE)

SYMPTOMS: -3.31
BALANCE: -2.56

SUBACUTE (14 DAYS) COGNITIVE EFFECT SIZES:

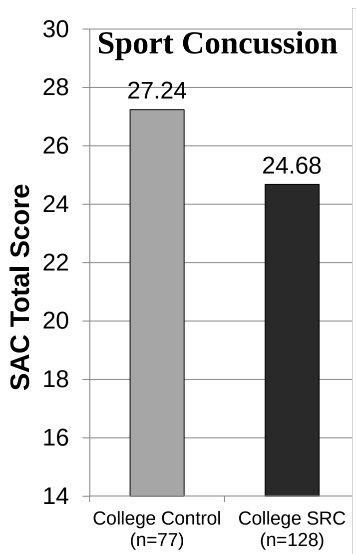
-0.26 (SMALL)

SYMPTOMS: -1.09
BALANCE: -1.16

Broglio et al., 2008

Acute Sports vs. Civilian vs. Military mTBI:

Cognitive Test Performance on Day of Injury



Journal of the International Neuropsychological Society (2012), **18**, 1–11.

doi:10.1017/S1355617712000239

Neuropsychological Outcome from Blast *versus* Non-blast: Mild Traumatic Brain Injury in U.S. Military Service Members

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(Received July 29, 2011; Final Revision January 31, 2012; Accepted February 7, 2012)

Abstract

The purpose of this study was to compare the neuropsychological outcome from blast-related *versus* non-blast related mild traumatic brain injury (MTBI). Participants were 56 U.S. military service members who sustained an MTBI, divided into two groups based on mechanism of injury: (a) non-blast related (Non-blast; $n = 21$), and (b) blast plus secondary blunt trauma (Blast Plus; $n = 35$). All participants had sustained their injury in theatre whilst deployed during Operation Iraqi Freedom or Operation Enduring Freedom. Patients had been seen for neuropsychological evaluation at Walter Reed Army Medical Center on average 4.4 months ($SD = 4.1$) post-injury. Measures included 14 clinical scales from the Personality Assessment Inventory (PAI) and 12 common neurocognitive measures. For the PAI, there were no significant differences between groups on all scales ($p > .05$). However, medium effect sizes were found for the Depression ($d = .49$) and Stress ($d = .47$) scales (i.e., Blast Plus > Non-blast). On the neurocognitive measures, after controlling for the influence of psychological distress (i.e., Depression, Stress), there were no differences between the Non-blast and Blast Plus groups on all measures. These findings provide little evidence to suggest that blast exposure plus secondary blunt trauma results in worse cognitive or psychological recovery than blunt trauma alone. (*JINS*, 2012, *18*, 1–11)

Military mTBI

- 56 MSM w/ mTBI in OEF/OIF
  - 21 non-blast, 35 blast+blunt
- Neurocognitive battery and PAI 4.4 (4.1) months post-injury
- PAI: no group differences on any scales; medium ES for Dep (.49), Stress (.47) (Blast+ > NB)
- No group differences on any cognitive measures after controlling for Dep, Stress
- Little evidence to suggest that blast+blunt results in worse cognitive or psych recovery than blunt

Cognitive Recovery: Civilian mTBI

Journal of the International Neuropsychological Society (2005), **11**, 215–227.

DOI: 10.1017/S1355617705050277

Factors moderating neuropsychological outcomes following mild traumatic brain injury: A meta-analysis

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Abstract

There continues to be debate about the long-term neuropsychological impact of mild traumatic brain injury (MTBI). A meta-analysis of the relevant literature was conducted to determine the impact of MTBI across nine cognitive domains. The analysis was based on 39 studies involving 1463 cases of MTBI and 1191 control cases. The overall effect of MTBI on neuropsychological functioning was moderate ($d = .54$). However, findings were moderated by cognitive domain, time since injury, patient characteristics, and sampling methods. Acute effects (less than 3 months postinjury) of MTBI were greatest for delayed memory and fluency ($d = 1.03$ and $.89$, respectively). In unselected or prospective samples, the overall analysis revealed no residual neuropsychological impairment by 3 months postinjury ($d = .04$). In contrast, clinic-based samples and samples including participants in litigation were associated with greater cognitive sequelae of MTBI ($d = .74$ and $.78$, respectively at 3 months or greater). Indeed, litigation was associated with stable or worsening of cognitive functioning over time. The implications and limitations of these findings are discussed. (*JINS*, 2005, *11*, 215–227.)

Keywords: Brain concussion, Head injury, Minor, Neuropsychological, Sequelae, Litigation

A quantitative review of the effects of traumatic brain injury on cognitive functioning

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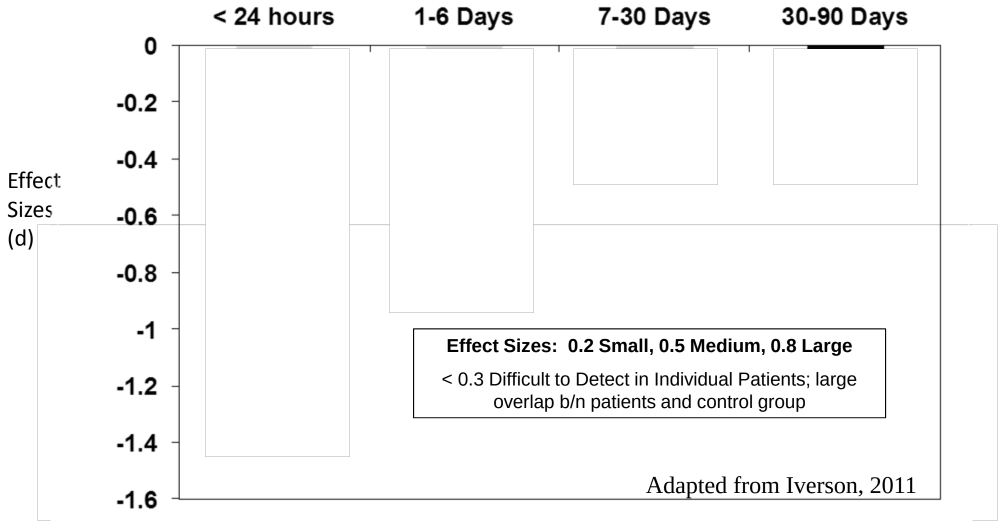
Summary

Changes in cognitive functioning often result from traumatic brain injury (TBI) and predict other important aspects of psychosocial recovery. Despite this pivotal role, no quantitative review of cognitive functioning across the spectrum of TBI severity has been reported. We therefore conducted a meta-analysis of 39 mostly cross-sectional studies of the cognitive effects of mild head injury (MHI) and moderate–severe TBI from the acute phase through long-term follow-up. The studies reported 48 comparisons of patients ($n = 1716$) and control subjects ($n = 1164$). Averaged across all follow-up periods, the effect of moderate–severe TBI (weighted mean Cohen's $d = -0.74$) was more than three times the effect of MHI (weighted mean $d = -0.24$) on overall cognitive functioning. Further, the natural logarithm of the follow-up interval correlated very strongly with estimates of d among patients with MHI, but less so among those with moderate–severe TBI. In short, findings from published research suggest that overall cognitive functioning recovers most rapidly during the first few weeks following MHI, and essentially returns to baseline within 1–3 months. Cognitive functioning also improves during the first two years after moderate–severe TBI, but remains markedly impaired even among patients tested > 2 years post-injury.

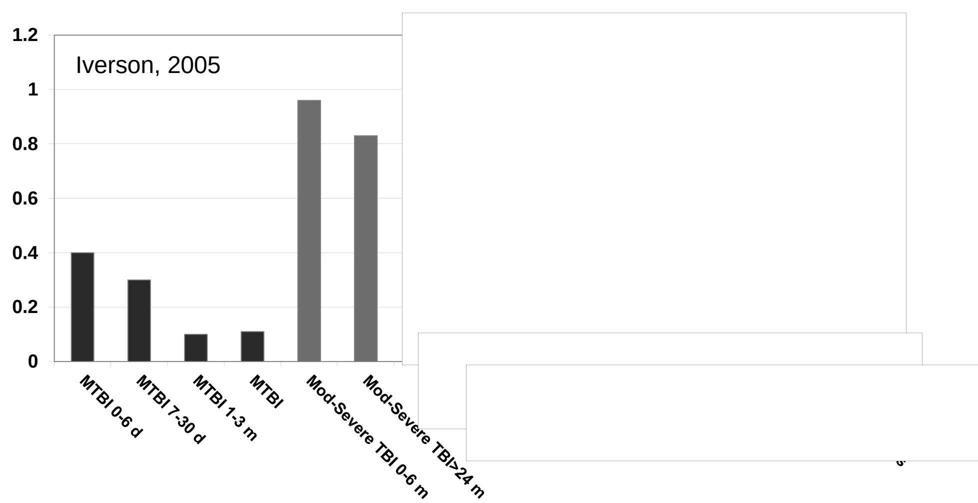
Neurocognitive Effects of mTBI

Meta-Analytic Studies and Reviews:

Frencham, 2004; Belanger et al., 2005; Schretlin & Shapiro, 2005; Broglio et al 2008; Iverson, 2011; Rohling et al 2011



Non-specificity of Neurocognitive Performance



Effect Sizes: 0.2 Small, 0.5 Medium, 0.8 Large

< 0.3 Difficult to Detect in Individual Patients; large overlap b/n patients and control group

mTBI Clinical Recovery & Outcome

World Health Organization (2004):

- 120 "best evidence" studies on mTBI prognosis
- Symptoms temporary after MTBI, with full recovery in days to weeks in overwhelming majority of kids and adults
- Sound evidence for favorable prognosis
- Little evidence of residual cognitive, behavioral or academic deficits
- Persistent symptoms (i.e., PCS) may be attributable to non-injury factors (demographic, psychosocial, medical, situational factors)

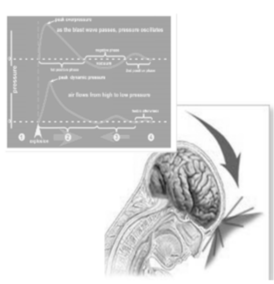
More overlap than discrepancy in evidence on acute effects and recovery after SRC, Civilian and Military mTBI

(Carrol et al., 2004)

Progress in mTBI Research:
Acute Effects & Recovery

INJURY MECHANISMS

TRUE NATURAL HISTORY OF RECOVERY



Threshold/Dynamics:
How much is enough
to cause brain injury?


Acute Effects and Recovery Time Following Concussion in Collegiate Football Players
The NCAA Concussion Study

Michael McCrea, PhD
Kevin M. Guskiewicz, PhD, ATC
Stephen W. Marshall, PhD
William Barr, PhD
Christopher Randolph, PhD
Robert C. Cantu, MD
James A. Onate, PhD, ATC
Jingzhen Yang, MPH
James P. Kelly, MD

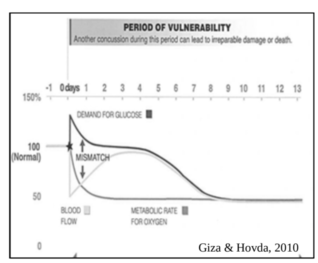
Context Lack of empirical data on recovery time following sport-related concussion hampers clinical decision making about return to play after injury.

Objective To prospectively measure immediate effects and natural recovery course relating to symptoms, cognitive functioning, and postural stability following sport-related concussion.

Design, Setting, and Participants Prospective cohort study of 1631 football players from 15 US colleges. All players underwent preseason baseline testing on concussion assessment measures in 1999, 2000, and 2001. Ninety-four players with concussion (based on American Academy of Neurology criteria) and 56 noninjured controls underwent assessment of symptoms, cognitive functioning, and postural stability immediately, 3 hours, and 1, 2, 3, 5, 7, and 90 days after injury.

Clinical Recovery:
How long does it take for
signs & symptoms to recover?

+

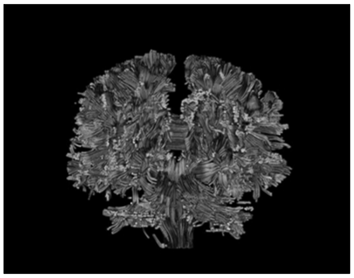


Giza & Hovda, 2010

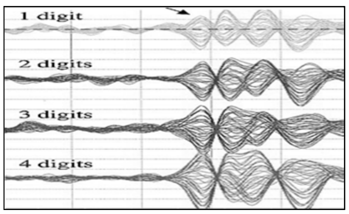
Physiological Recovery:
How long does it take for the
brain to recover?

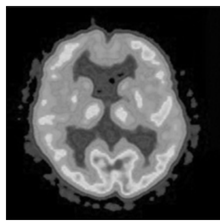
New Evidence Base to Guide Diagnosis, Assessment and Management

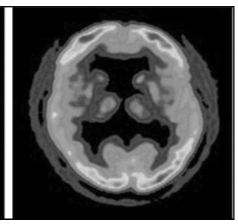
Pursuit of the Perfect "Biomarker"

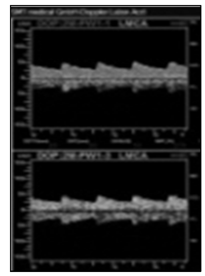


MRI (3-T) / Functional MRI









Magneto Encephalography (MEG) Scanner

When is the *brain* fully recovered from mTBI?

Trans Cranial Doppler Ultrasound

fMRI: Brain Activation Changes after mTBI

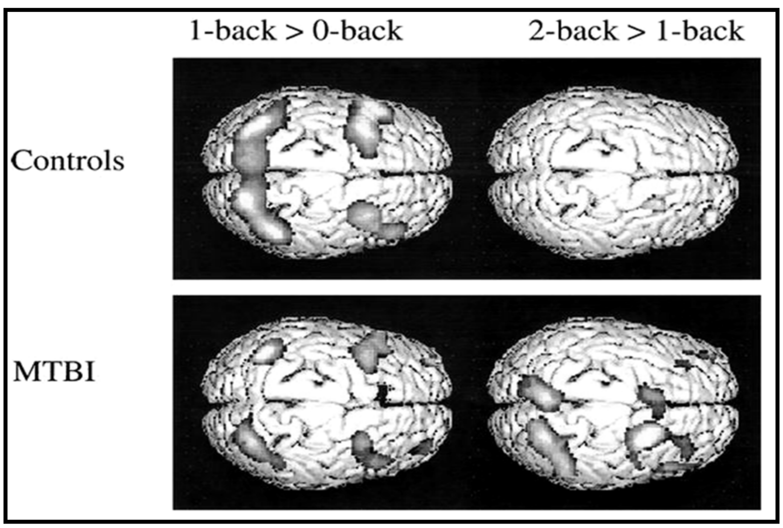
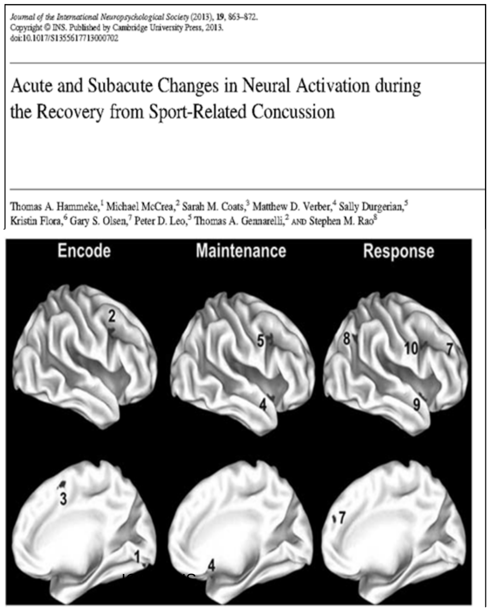


Figure 2. The location of major cortical activation foci are displayed on a surface-rendered projection. The gyral location of activations (bilateral dorsolateral prefrontal and superior parietal) were similar in both groups from the 0-back to 1-back condition. Major differences, as described in the text, were observed in the 1-back to 2-back comparison. Note the more extensive activation of primarily right superior parietal and dorsolateral prefrontal cortex in patients with mild traumatic brain injury (MTBI).

McAllister et al., *Neurology*, 1999, 53, 1300-8.

FUNCTIONAL MRI: ACUTE SRC



Journal of the International Neuropsychological Society (2013), **19**, 863–872.

doi:10.1017/S1355617713000702

Acute and Subacute Changes in Neural Activation during the Recovery from Sport-Related Concussion

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DESIGN & PROTOCOL:

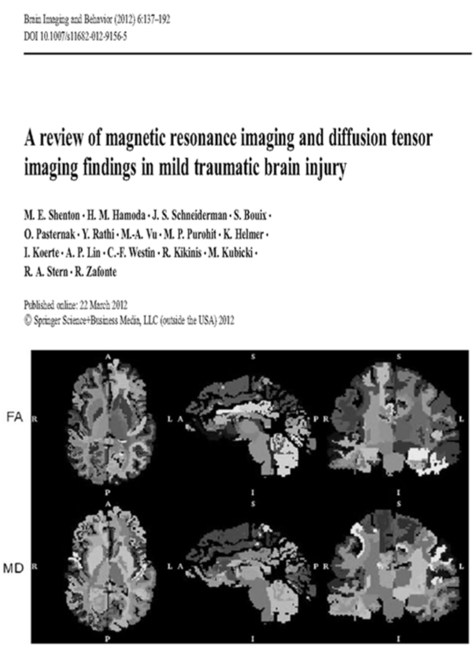
- 12 FB concussed FB players, 12 matched controls studied 13 hr, 45 d PI
- Clinical testing, event-related fMRI (load dependent WM task)

CLINICAL EFFECTS/RECOVERY:

- Acute symptoms and cognitive impairments (RT, WM) at 13 hours
- No impairments at 45 days

fMRI ACTIVATION STUDIES:

- 13 HR: Decreased activation of RH attentional networks in SRC group
- Correlate with cog deficits, symptoms
- 45 D: Reversed pattern (SRC>NC) (compensatory increase=recovery)

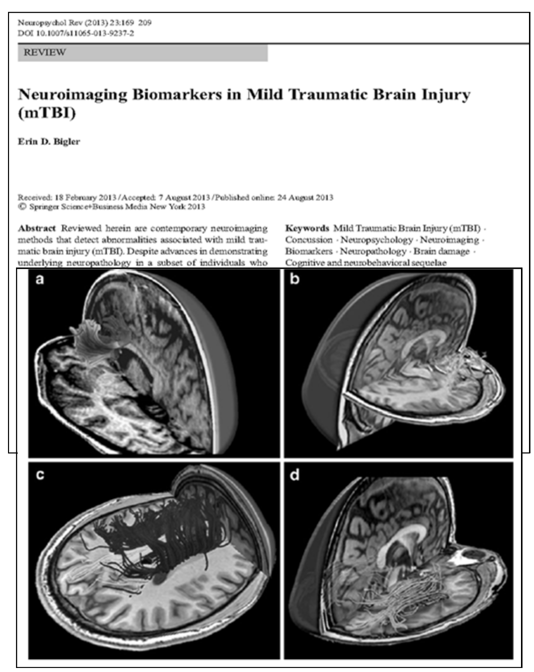


Brain Imaging and Behavior (2012) 6:137–192
DOI 10.1007/s11682-012-9156-5

A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury

M. E. Shenton · H. M. Hamoda · J. S. Schneiderman · S. Bouix · O. Pasternak · Y. Rathi · M.-A. Vu · M. P. Purohit · K. Helmer · I. Koerte · A. P. Lin · C.-F. Westin · R. Kikinis · M. Kubicki · R. A. Stern · R. Zafonte

Published online: 22 March 2012



Neuropsychol Rev (2013) 23:169 209
DOI 10.1007/s11065-013-9237-2

REVIEW

Neuroimaging Biomarkers in Mild Traumatic Brain Injury (mTBI)

Erin D. Bigler

Received: 18 February 2013 / Accepted: 7 August 2013 / Published online: 24 August 2013

Abstract Reviewed herein are contemporary neuroimaging methods that detect abnormalities associated with mild traumatic brain injury (mTBI). Despite advances in demonstrating underlying neuropathology in a subset of individuals who

Keywords Mild Traumatic Brain Injury (mTBI) · Concussion · Neuropsychology · Neuroimaging · Biomarkers · Neuropathology · Brain damage · Cognitive and neurobehavioral sequelae