Neuropsychology of Mild TBI: What Do We Know?

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Diagnosis

American Congress of Rehabilitation Medicine Criteria Definition of Mild TBI

- Traumatically induced physiologic disruption of brain function as indicated by at least one of the following:
  - Any period of loss of consciousness
  - Any loss of memory for events immediately before or after the accident
  - Any alteration in mental state at the time of the accident
  - Focal neurologic deficits that may or may not be transient
- Severity of the injury does not exceed:
  - Loss of consciousness of 30 min
  - GCS score of 13-15 after 30 min
  - Posttraumatic amnesia of 24 hr

Mild Traumatic Brain Injury

- Mild TBI accounts for about 80-90% of reported new cases of head injuries each year
- Controversy exists regarding the long-term effects of mild TBI on cognitive functioning

Criteria for Severity of TBI

Mild	Moderate	Severe
LOC $\leq$ 30 min with normal CT &/or MRI	LOC $\leq$ 6 hours with normal or abnormal CT &/or MRI	LOC > 6 hours with normal or abnormal CT &/or MRI
GCS 13-15	GCS 9-12	GCS < 9
PTA $\leq$ 24hr	PTA $\leq$ 7days	PTA > 7days

Complicated Mild TBI

- When clinical neuroimaging findings are present following a MTBI, the classification changes to "complicated MTBI," which has a 6-month outcome more similar to moderate TBI[1,2]

[1]Williams DH, Levin HS, Eisenberg HM. Mild head injury classification. *Neurosurgery* 1990;27(3):422-8.

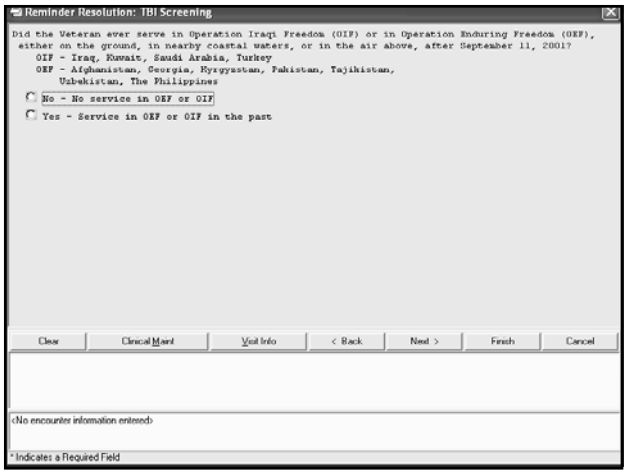
[2]Kashluba S, Hanks RA, Casey JE, Millis SR. Neuropsychologic and functional outcome after complicated mild traumatic brain injury. Arch Phys Med Rehabil 2008; 89(5): 904-11.

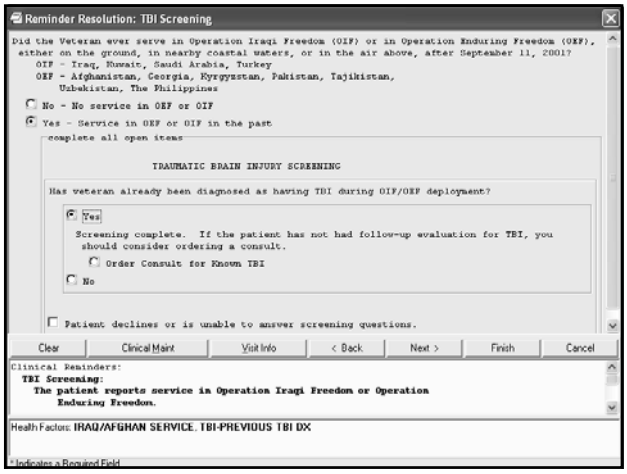
TBI Screening Reminder

April 2007

"TBI Screening Reminder" Functions

- Identify possible OIF/OEF Participants
- Confirm deployment to OIF/OEF Theatres of Deployment
- Screen for TBI if deployed in OIF/OEF Theatres
- Identify those with an OIF/OEF-related history of TBI





Screening Questions: 4 Sections

- Section 1: *Events*
- Section 2: *Immediate Disturbance of Consciousness* Symptoms after Events
- Section 3: *New or Worsening* Symptoms after the event
- Section 4: *Current* Symptoms

Screen Interpretations

- A “no” response to any of the sections terminates screening and is a “negative screen”
- A “yes” response to ALL FOUR sections is a “positive screen”

Screen Interpretations

- The screen will not yield a positive result if there is an historical TBI and there are currently no symptom complaints
- This is therefore *not* a screen for mild TBI but rather a screen for ongoing symptom complaints + history of “possible” TBI

Private Sector Diagnosis

- Accuracy of Mild Traumatic Brain Injury Diagnosis

  (Powell, Ferraro, Dikmen, Temkin & Bell, 2008)

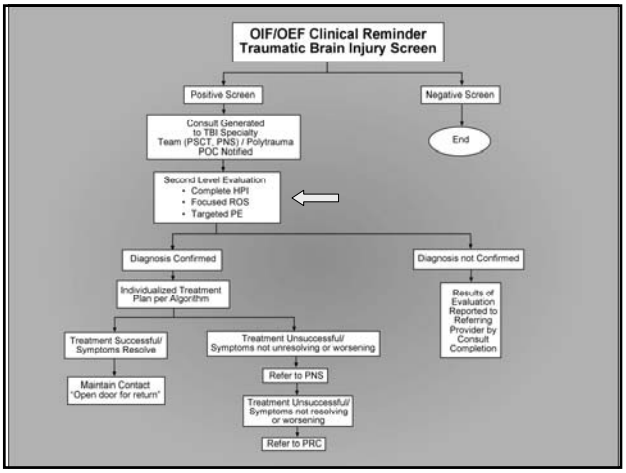
  - Compared identification of mild TBI via
    - (1) retrospective chart reviews of Emergency Department
    - (2) prospective identification of cases using structured interview and medical record data.

Private Sector Diagnosis

- Accuracy of Mild Traumatic Brain Injury Diagnosis

  (Powell, Ferraro, Dikmen, Temkin & Bell, 2008)

  - Of those cases identified in the ED by study personnel as having mild TBI, 56% did not have a documented diagnosis from the ED physician indicative of mild TBI.



Neuropsychologist Role

- Assist in clarifying diagnosis
- Symptoms can support a diagnosis of mild TBI but cannot be used to make the diagnosis
- In most cases (due to lack of injury severity medical records) diagnosis based on: Careful interview of events:
  - Ask them to describe in detail what happened
  - Assess for mechanism of injury (i.e., blunt trauma or acceleration/deceleration forces)
  - Assess for any period of confusion, disorientation, or impaired consciousness associated with mechanism

Postconcussion Symptoms

- Physical
  - Headache, dizziness, fatigue, noise/light intolerance, insomnia
- Cognitive
  - Memory complaints, poor concentration
- Emotional
  - Depression, anxiety, irritability, lability

PCS-Like Complaints of NP Dysfunction

- Common
- Nonspecific
- Potentially related to non-neurological factors (anxiety, depression, fatigue, stress)
- Correlate better with distress than with objective indicators of CNS injury
- Susceptible to attribution bias

Problems with Using Complaints as Evidence of Cognitive Dysfunction

- Mittenberg et al. (1992, 1997): "expectation as etiology"
  - 'imaginary concussion' produces symptom complaint cluster identical to that reported by patients with 'real' head injury
  - patients with minor TBI significantly underestimate degree of pre-injury problems

Cognitive Sequelae

What we know

Acute Symptoms

- There is no doubt that a mTBI causes acute disruption of brain functioning
- Initial Symptoms:
  - At Best: dazed, confused, temporarily disoriented, often with memory gaps for the injury itself and for some period of time thereafter (seconds to hours)
  - At worst: unconscious for up to 30 minutes
- Unresolved are questions of how long the disruption of normal brain functioning lasts and whether symptoms and impairments can continue long-term

Mild TBI: Five Meta-analytic Studies: I

(Binder, Rohling, & Larrabee, 1997; Binder & Rohling, 1996; respectively)

- Found the long-term cognitive impairment effect size for mild TBI was very small (0.1 - 0.2) and not statistically significant
- In contrast the long-term effect of financial incentives on cognitive impairment in a mild TBI population was larger (0.5) and significant

Mild TBI:
Five Meta-analytic Studies: II

(Schretlen & Shapiro, 2003)

- A second recent meta-analytic study found that overall neuropsychological effect size (d) for MTBI in prospective studies was 0.24
- Categorized into 4 time-since-injury intervals the effect sizes were:

< 7 days	7-29 days	30-89 days	> 89 days
0.41	0.29	0.08	0.04

Mild TBI:
Five Meta-analytic Studies: III

(Frencham, Fox & Maybery, 2005)

- Overall effect size was moderate (g=.32) but tended toward zero with increasing time since injury.
- Categorized into 2 time-since-injury intervals the effect sizes were:

Less than 3 months	More than 3 months
0.33	0.11

Mild TBI – Cognitive Findings: Meta-Analysis IV

(Belanger, Curtiss, Demery, Lebowitz, Vanderploeg, 2005)

- Inclusion Criteria
  - Evidence of mild head injury
  - Control group utilized
  - Separate results by severity level
  - Time since injury reported
  - Cognitive measures, experimental or clinical
  - Means and SDs presented

Mild TBI – Cognitive Findings: Meta-Analysis IV

(Belanger et al., 2005)

Study Search

- 1970 to March 2004 PubMed and PsychINFO, other MTBI study reference sections
- 133 studies from which 39, with a total of 41 effect sizes, met inclusion criteria
- 1463 cases of MTBI and 1191 control cases

Mild TBI – Cognitive Findings: Meta-Analysis IV

(Belanger et al., 2005)

- Moderators Examined:
  - Cognitive domain
  - Time since injury (< 90 days versus ≥ 90 days)
  - Selection context of the study participants
    - Litigation
    - Symptomatic/clinic-based
    - Unselected samples

Mild TBI – Cognitive Findings: Meta-Analysis IV

Cognitive Domains Examined:

- Global Cognitive Ability
- Attention
- Executive Functions
- Fluency
- Memory Acquisition
- Delayed Memory
- Language
- Visuospatial Skill
- Motor Functions

Mild TBI – Cognitive Findings: Meta-Analysis IV

(Belanger et al., 2005)

- Overall effect size, d, associated with MTBI was **0.54**
- Statistically significant deficits in all domains except motor functions (only two studies included motor functions)
- Most effect sizes were moderate to large (Cohen, 1988) with fluency **(*d* = 0.77)** and delayed memory **(*d* = 0.69)** having the largest overall effect sizes
- Smallest overall effects were found on motor **(d = 0.16)** and executive measures **(d = 0.21)**

Mild TBI: Meta-Analysis IV

(Belanger et al., 2005)

Time Post-Inj.	Litigation Based	Clinic Based	Unselected Samples
< 90 days	**0.52**	**No studies**	**0.63**
≥ 90 days	**0.78**	**0.74**	**0.04**

Sport Injury Mild TBI – Cognitive Findings: Meta-Analysis V

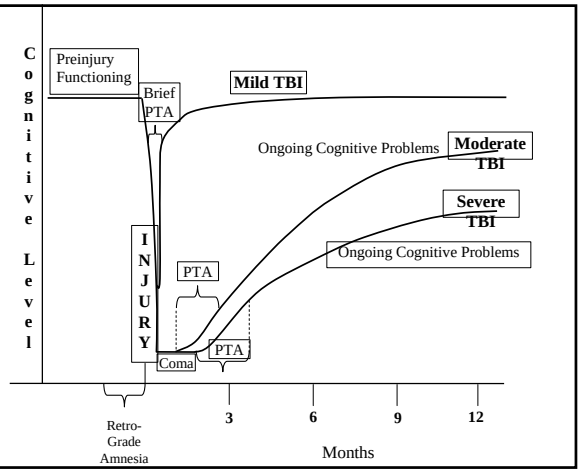
(Belanger & Vanderploeg, 2005)

- Literature reviewed from 1970 to August 2004
- 21 studies from which a total of 41 effect sizes, met inclusion criteria
- 790 cases of MTBI and 2016 control cases

Sport Concussion Cognitive Findings: Meta-Analysis V (cont.)

Overall effect size of concussion was **0.49**

- Comparable to general MVA acceleration/ deceleration effect size in mTBI; **d = 0.54**
- Acute effects (< 24 hrs) largest for:
  - Delayed memory; **d = 1.00**
  - Memory acquisition; **d = 1.03**
  - Global cognitive functioning; **d = 1.42**
- However, **no residual effects** when evaluated > 7 days postconcussion



Conclusion

- When looking at the mild TBI population, there are generally no long-term cognitive sequelae

Yes, But….

Is our population (OEF/OIF) somehow different?

"Diagnostic Threat"

(Suhr & Gunstaad, 2002, 2005)

- Evaluations of the same mild TBI population if conducted under the "explanation" of studying mild TBI results is poorer neuropsychological performance than the same evaluation conducted with a neutral "explanation"
- Unfortunately, the context of the evaluation influences the findings

PTSD and Cognitive Deficits

- Persian Gulf War veterans
- PTSD was associated with relative performance deficiencies on tasks of:
  - sustained attention
  - mental manipulation
  - verbal learning
  - executive control, and
  - performances were characterized by errors of commission and intrusion

Vasterling et al., *Neuropsychology*, 1998;12:125-33

Neurocognition Deployment Health Study

Vasterling et al., JAMA, 2006

- 600+ soldiers tested before and after Iraq deployment
- "Neuropsychological compromise" on sustained attention, verbal learning, and visuospatial memory
- Increased negative state affect
- History of mild TBI had no effect on neuropsychological findings

Screening for cognitive dysfunction in OIF/OEF service members with explosion injuries admitted to a burn unit.

(Mercado et al., 2008, published abstract in Archives of Clinical Neuropsychology)

- 123 evaluations on patients with burns secondary to explosive munitions.
- No differences on cognitive measures (RBANS) between those with mild TBI and no mild TBI.
- Mild TBI group more likely to have psychiatric diagnoses.

Performance on the Automated Neuropsychological Assessment Metrics (ANAM) in a Non-Clinical Sample of Soldiers Screened for Mild TBI after Returning from Iraq and Afghanistan: A Descriptive Analysis

(Ivins, Kane & Schwab in press JHTR)

- Convenience sample of 956 soldiers administered the ANAM
- History of deployment-related mild TBI up to two years prior to cognitive testing was not associated with poor ANAM performance post deployment.
- No associations between poor ANAM performance and the number of lifetime TBIs, injury severity or the number post-concussive symptoms

What about Different Mechanisms?

Functional Outcomes of Blast vs. Non-Blast Injuries

(Sayer, Chiros, Sigford, Scott, Clothier, Pickett, Lew, APMR, 2008)

- Chart reviews of 188 OEF/OIF patients admitted to PRCs during 1st 4 years of OEF/OIF
- Outcomes assessed were:
  - Cognitive FIM
  - Motor FIM
  - Length of Stay (LOS)

	Mechanism of Injury		
	Blast	**Other**	**p-value**
Injured System	(n=106)	(n=82)	
Brain Injury	96%	99%	NS
Type of brain injury			.001
Closed	42%	70%	
Penetrating	58%	30%	
Cognition	88%	93%	NS
Pain	83%	80%	NS
Balance	68%	62%	NS
Motor Fx	62%	65%	NS
Sleep	60%	57%	NS

	Mechanism of Injury		
	Blast	**Other**	**p-value**
Injured System	(n=106)	(n=82)	
Seeing	58%	46%	NS
Hearing Loss	48%	33%	<.05
Tinnitus	26%	12%	<.05
Communication	50%	49%	NS
Mental Health Sxs	61%	52%	NS
Depressive Sxs	37%	36%	NS
PTSD Sxs	42%	24%	<.01
Other anxiety	26%	24%	NS
Psychotic Sxs	4%	4%	NS
Behavior	26%	22%	NS

Functional Outcomes of Blast vs. Non-Blast Injuries

(Sayer, Chiros, Sigford, Scott, Clothier, Pickett, Lew, APMR, 2008)

- Mechanism of injury (blast vs other) did not predict functional gain scores (FIM).
  - Baseline fx was strongest predictor of FIM gain and LOS

Neuropsychological Effects of Blast vs. Non-Blast TBI

(Belanger, Kretzmer, Yoash-Gantz, Pickett, Tupler, JINS, 2009)

- 102 consecutively assessed post-TBI individuals primarily returning active-duty or veteran military personnel who were injured in Afghanistan or Iraq (67% active duty).
- Excluded:
  - failed SVT (*n* = 31)
  - comorbid neurological disorders (e.g., stroke) (*n* = 1)
  - brain injury due to gunshot (*n* = 3)

Demographic Information

(Belanger, Kretzmer, Yoash-Gantz, Pickett, Tupler, JINS, 2009)

- Mean age = 28.7 (sd 7.7)
- Mean education = 12.9 years (sd 2.0)
- WTAR-predicted FSIQ = 97.2 (sd 13.7)
- 96% male
- 91% right-handed
- 63% inpatient

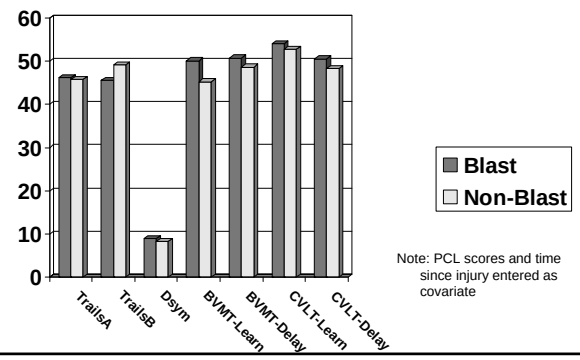
Demographic Information

(Belanger, Kretzmer, Yoash-Gantz, Pickett, Tupler, JINS, 2009)

	Blast (n=61)	Non-Blast (n=41)	*p-value*
Age	29 (7.9)	28.2 (7.5)	*p*>.59
Education in years	13.1 (2.1)	12.16 (1.7)	*p*>.21
WTAR FSIQ	98.5 (14.2)	95.2 (13.0)	*p*>.24
Days Since Injury			
<90 days	28	24	*p*>.13
90 days to one year	8	3	
>1 year	25	14	

Blast vs. Non-Blast in Mild TBI

(Belanger, Kretzmer, Yoash-Gantz, Pickett, Tupler, JINS, 2009)



Note: PCL scores and time since injury entered as covariate

Blast vs. Non-Blast in Mild TBI

(Belanger, Kretzmer, Yoash-Gantz, Pickett, Tupler, JINS, 2009)

- More PTSD sxs reported by blast group and more PTSD sxs reported over time.

Summary

- No evidence that mild TBI due to blast or experienced in OEF/OIF is any different in terms of cognitive sequelae
- There is evidence that PTSD may impact cognitive functioning
- There is evidence that deployment itself may have an adverse impact on cognition, albeit quite small.

Let's look at an individual study that found long-term cognitive difficulties….

Vietnam Experience Study

Subjects

- Vietnam Experience Study Data/Center for Disease Control Vietnam Experience Study 1988a, 1988b *JAMA*
- 4,462 randomly selected male US Army vets

(community dwelling, not clinic-referred or self-referred)

- Entered military between 1/65 - 12/71
- Minimum of 4 months active duty
- Served only one tour of duty

Subjects cont'd

- Racial makeup of the 4,462 participants:
  - 81.9% Caucasian
  - 11.8% African-American
  - 4.5% Hispanic
  - 1.9% Other
- Mean age = 38.36 years (SD = 2.53)
- Mean level of education = 13.29 years (SD = 2.3)
- Mean IQ = 105 (SD = 20.32) (based on GTT)

Subjects cont'd

- Participants underwent a 3 day evaluation including:
  - extensive medical, psychological, and neuropsychological examination
  - included were questions regarding MVA, head injury, loss of consciousness, and subsequent hospitalization
- Evaluations took place approximately 16 years post-military discharge

Measures

- Diagnostic Interview Schedule (DIS-III-A)
- Extensive surveys of physical functioning and symptoms
- Battery of neuropsychological tests

Groups and Sample Sizes

Groups	Number
No MVA, No Head Injury	3057
MVA, No Head Injury	521
Head Injury with LOC	254

MVAs or TBIs occurred an average of 8 years prior to the current evaluation

Neuropsychological Measures

- Multivariate analysis of variance (MANOVA) was conducted with 14 neuropsychological measures, which cover the domains of:
  - » Complex Attention
  - » Psychomotor Speed & Coordination
  - » Verbal Abilities
  - » Executive Abilities
  - » Non-Verbal Abilities (visuospatial)
  - » Verbal Memory
  - » Visual Memory

Statistical Analyses: Neuropsychological Measures

(Matching groups on premorbid IQ)

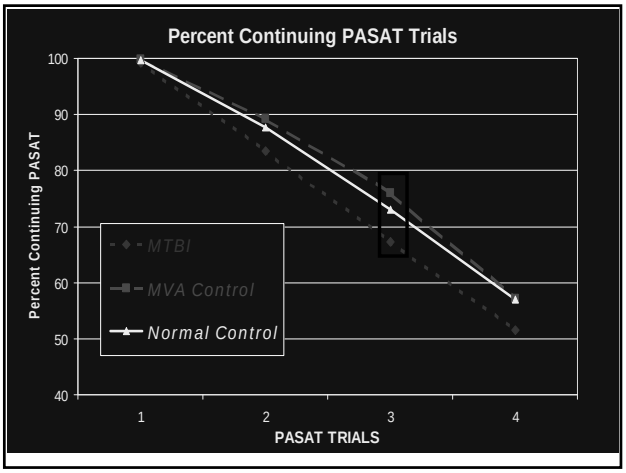
- MANOVA was not significant
  $F(30,7620) = 1.28$, $p = 0.14$,
  eta squared = 0.005
- On average, the MTBI group performed 0.03 of a standard deviation more poorly than either control group

Current Cognitive Functioning: Examples of the 14 Measures

	Normal Control (n = 3057)	MVA Control (n = 521)	Mild TBI (n = 254)
Animal Fluency	20.5 (5.1)	21.0 (5.4)	20.7 (5.3)
Rey-O Copy	32.7 (3.4)	32.8 (3.0)	32.7 (3.0)
CVLT Sum of Trials 1 to 5	46.0 (8.7)	45.9 (8.5)	46.3 (9.7)

BUT:
Subtle Attention Problems

- Using the power of a within subject design (repeated measure within the same subject) can we detect subtle problems with attention?
- Attention is the neuropsychological domain that may be accounting for the reported memory complaints



PASAT Findings

- On this difficult measure of sustained concentration, working memory, and cognitive flexibility
  - Subjects with mTBI “dropped out” of the test at a higher rate than “Normal Controls” or “MVA (non-TBI) Injury Controls”

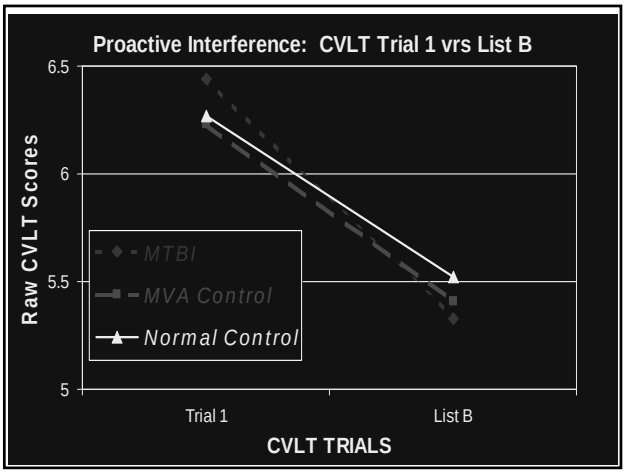
California Verbal Learning Test

- List A – Five learning trials of 16 words
- List B – One learning trial *different* 16 words
- Test for memory of List A

California Verbal Learning Test

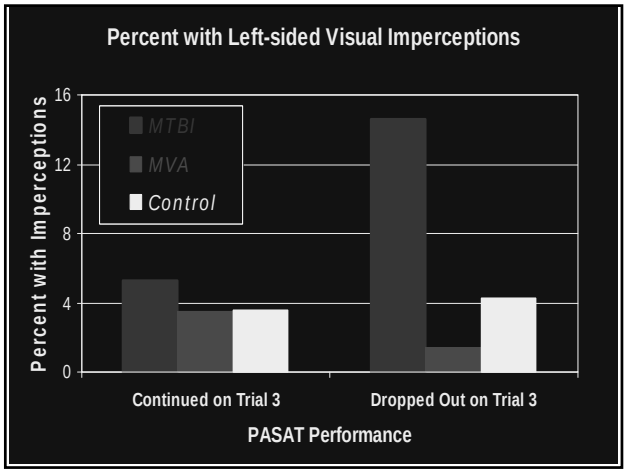
Proactive Interference – previously learned material interferes with learning of new material

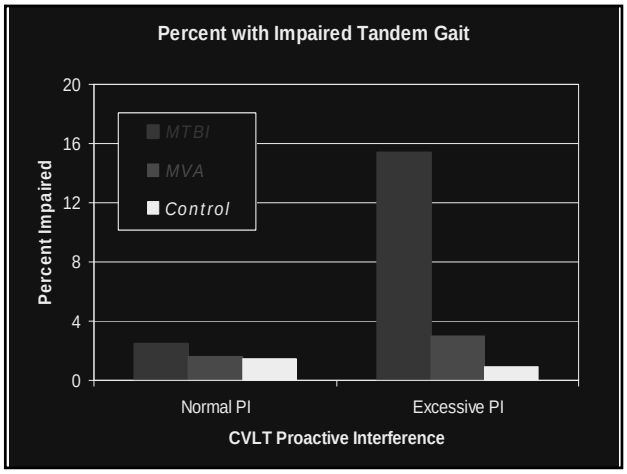
--Memory for List B relative to memory for the 1st trial of List A



CVLT Memory Findings: Proactive Interference

- On a measure of proactive interference, i.e., the ability to "screen out" the effects of previous cognitive tasks on subsequent cognitive tasks
  - Subjects with mTBI had a higher rate of proactive interference than "Normal Controls" or "MVA (non-TBI) Injury Controls"





These Long term Subtle Attention Problems in mTBI had "External" Neurological Correlates

- Excessive problems on the PASAT were associated with subtle visual inattention problems on formal visual examinations
- Excessive proactive interference was associated with higher rates of impaired tandem gait on formal neurological examinations

Neuropsychological Findings: Conclusions

- Most cognitive sequelae associated with MTBI resolves by 3 months post-injury
- Evidence for subtle long-term problems with complex attention (small effect)
- Subtle complex attention problems have external neurologic correlates
- Need prospective study replication!

Cognitive Sequelae

What we don't know…

Unresolved Issues

- Multiple concussions versus single concussions
  - Single concussions resolve w/in 30 days: Do multiple concussions resolve?
  - Multiple concussions are associated with higher levels of trauma exposure: So is it multiple concussions or additional trauma exposure causing increased symptoms?

Multiple Concussions

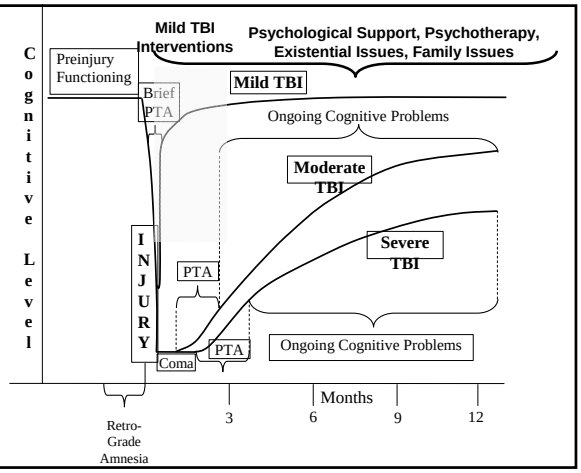
- Adverse long-term effects on cognitive performance (Collins et al.,* 1999; Moser & Schatz, 2002; Moser et al., 2005; Wall et al., 2006),
- No adverse effect (De Beaumont et al., 2007;* Iverson et al., 2006; Pellman et al., 2004).
- Those studies that have found adverse effects found these effects on tests of attention, executive functions, psychomotor speed and total symptoms reported.
  - Notably, these studies did not examine psychological variables and relied exclusively on samples of athletes.

Unresolved Issues (continued)

- Treatment: Diagnosis-based, Symptom-based, Both; Integrated Interdisciplinary Treatment vrs Sequential; etc.

Treatment of Mild TBI

- A standardized postconcussion program developed by Mittenberg (1996)
- Patients receive a 10 page manual, Recovering From Head Injury: A Guide for Patients
  - **Focus on a reattribution of symptoms to: 1) selective attention, 2) normal transient responses to stress, and 3) anxiety-arousing or depressive self-statements**
- Therapist provides stress management and cognitive behavioral therapy for several weeks
- Instructions: resume [illegible]



Unresolved Issues (cont.)

- Differentiating among overlapping conditions: mTBI, PTSD, Depression, Insomnia, Pain, Somatoform disorders, etc.
- Risks versus Benefits of population screening for mTBI