

Differentiating the long-term consequences of TBI and psychological trauma:

When and why does it matter?

Jennifer J. Vasterling, Ph.D.

Mieke Verfaellie, Ph.D.

VA Boston Healthcare System

HSR & D Cyberseminar

May, 2014







Overview

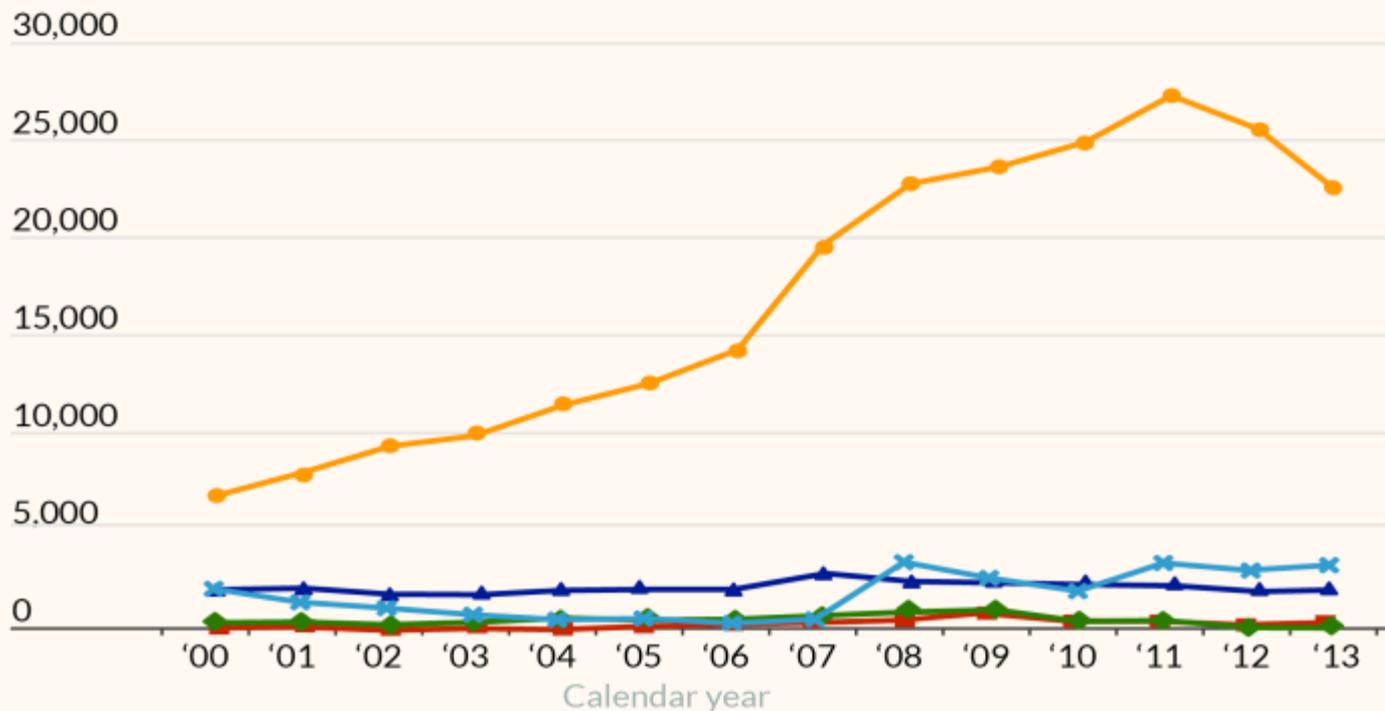
- Epidemiology
- Clinical manifestations
- Mechanisms leading to comorbidity
- Clinical implications

Epidemiology



DoD Numbers for Traumatic Brain Injury Worldwide - Incidence by Severity

No. of cases



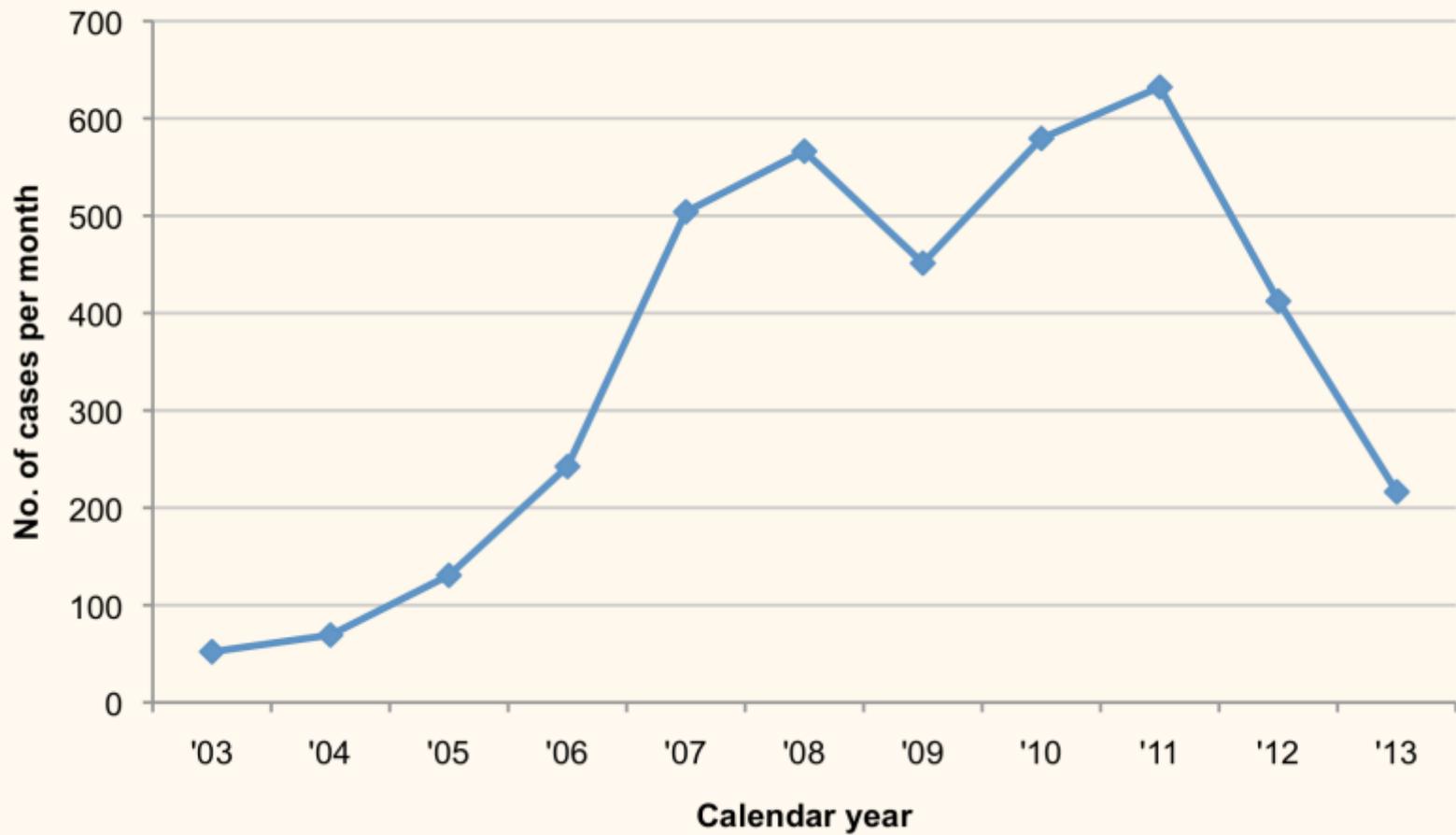
—●— Mild —▲— Moderate —■— Severe —◆— Penetrating —×— Unclassified

Source: Defense Medical Surveillance System (DMSS), Theater Medical Data Store (TMDS) provided by the Armed Forces Health Surveillance Center (AFHSC)

Prepared by the Defense and Veterans Brain Injury Center (DVBIC)

Updated 26 Feb. 2014

Number of Deployment-Related TBIs



OEF/OIF TBI, PTSD, Depression Prevalence

RAND study (N = 1965)

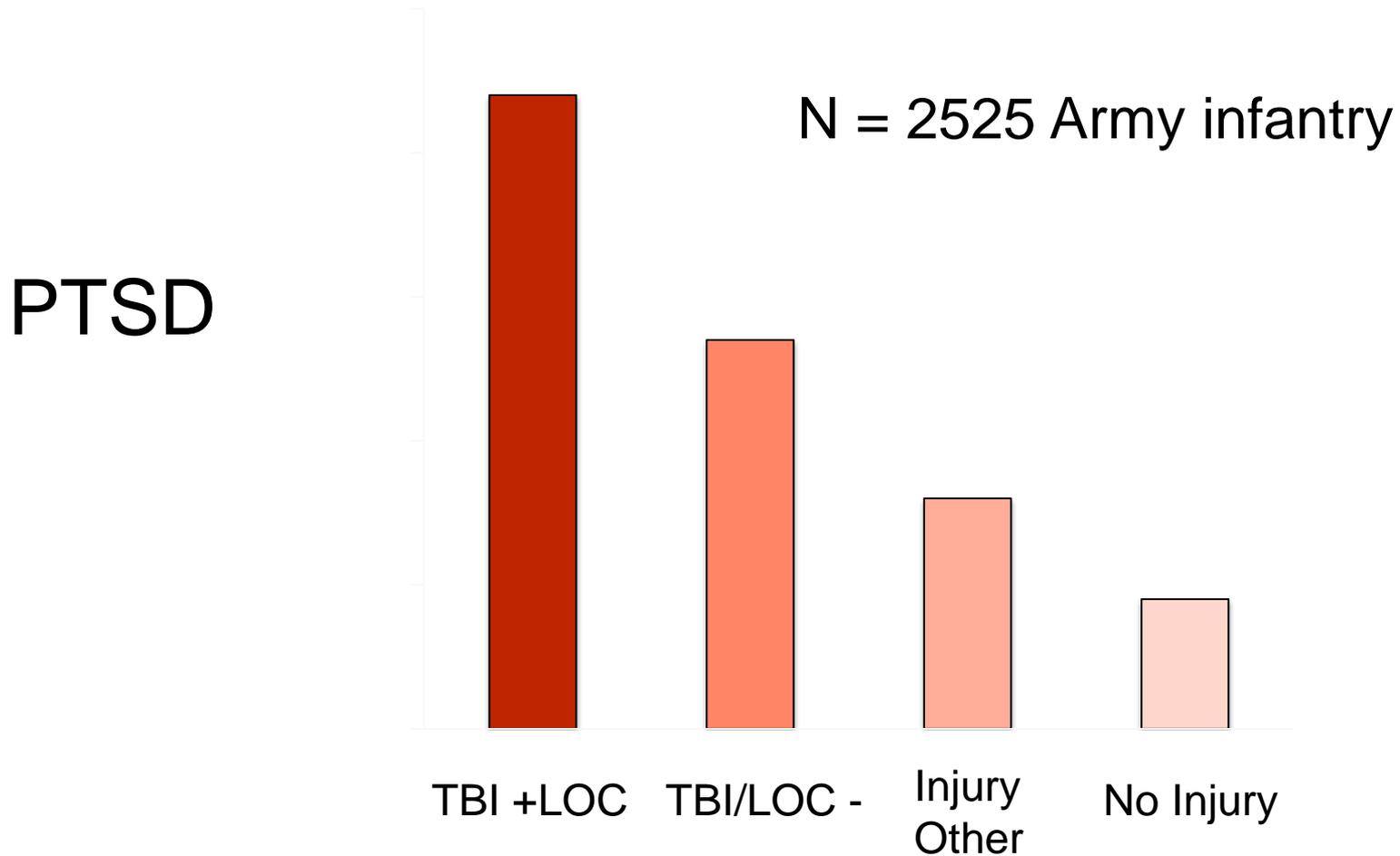
	Overall	If TBI:
TBI	20%	-----
PTSD	14%	34%
Depression	14%	32%

Iverson et al. (2011; *Women's Health Issues*)

N=12,605 Veterans with a dx of deployment-related TBI

	Total (%)	Women (%)	Men (%)	Odds Ratio
Etiology				
Blast	82.7	60.9	83.9	
Bullet	4.3	2.3	4.5	
Fall	25.4	36.1	24.8	
Vehicular Injury	27.3	30.6	27.1	
Other blunt trauma	33.8	37.3	33.6	
Psychiatric diagnosis				
PTSD	67.4	59.6	67.8	0.87
PTSD + Depression	28.9	37.8	28.4	1.66**

Hoge et al. (2008; *N Eng J Med*)

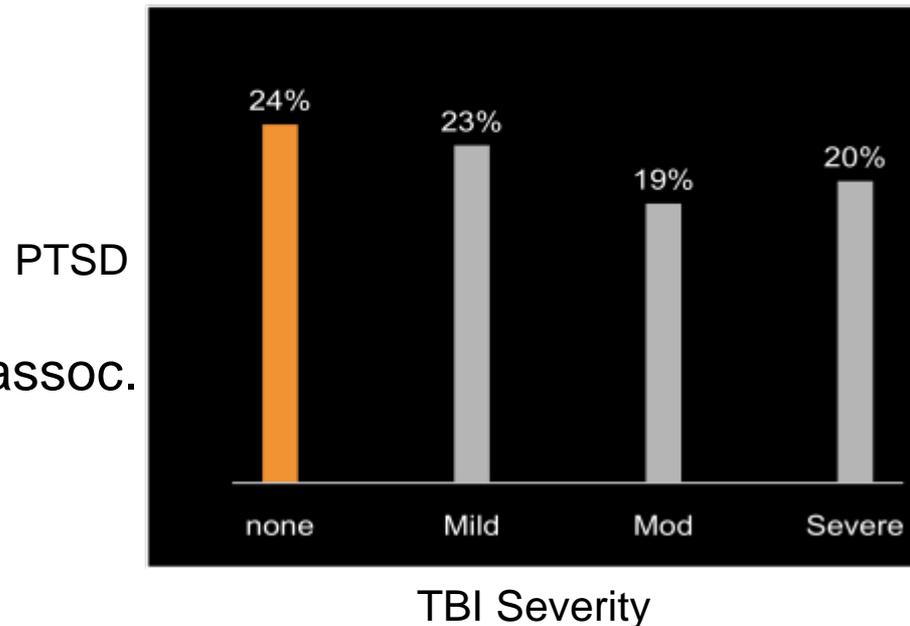


TBI Severity and PTSD

Zatzick et al. (2010; Arch Gen Psychiatry)

N = 3047 civilians

- Moderate and severe TBI decreased risk of PTSD, compared to other injury controls



- PTSD assoc.

tive symptoms.

Clinical Manifestations

TBI v. Postconcussive Symptoms

TBI = pathophysiological injury

PCS = expression of symptoms following mild TBI

Post-mTBI:

Clinical presentation:

0-72 hrs

Symptoms at worst

1-3 months

Symptoms resolve

3 months

Full recovery

Postconcussional Disorder (DSM-IV)

- Objective neuropsychological deficits
- 3 or more of the following symptoms:
fatigue, disordered sleep, headache, vertigo, dizziness, irritability/aggression, anxiety/depression/lability, personality change, apathy/lack of spontaneity
- Persists 3+ months
- Functional impairment

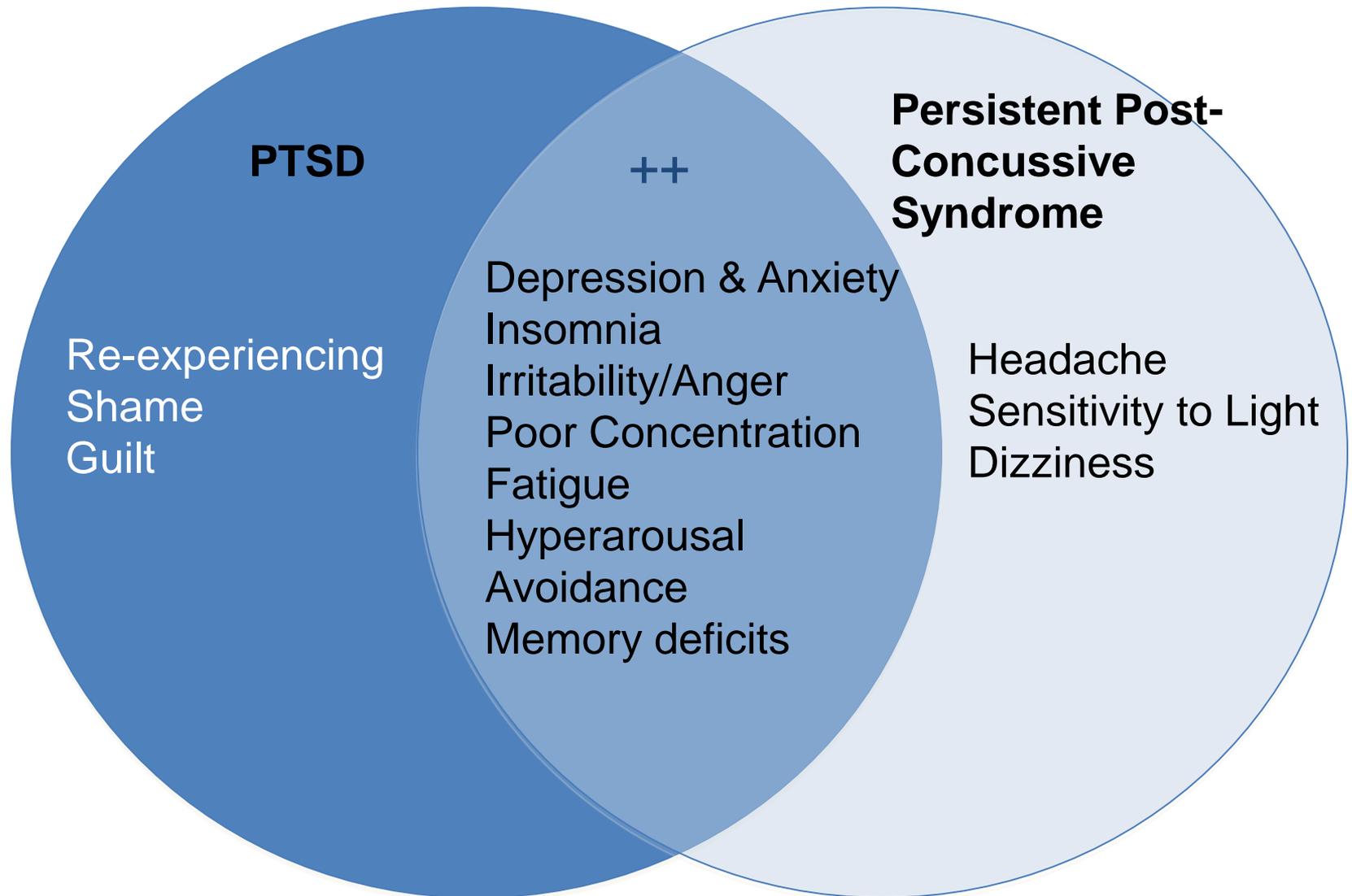
Mild Neurocognitive Disorder due to TBI (DSM-V)

- Decline in cognitive performance
 - Concern by individual/clinician
 - Modest impairment in cognitive performance
- Deficits do not interfere with independence in everyday activities
- Evidence of TBI
- Presents immediately after TBI and persists past acute post-injury period

Postconcussion Symptoms

- Symptoms (e.g., headache, concentration problems) are non-specific
- Subjective complaints occur at relatively high levels in various non-TBI populations including healthy controls
- Symptoms overlap with PTSD

Overlapping Associated Symptoms



Adapted from: Stein & McAllister (2009). *Am J Psychiatry*: 166, 768-776

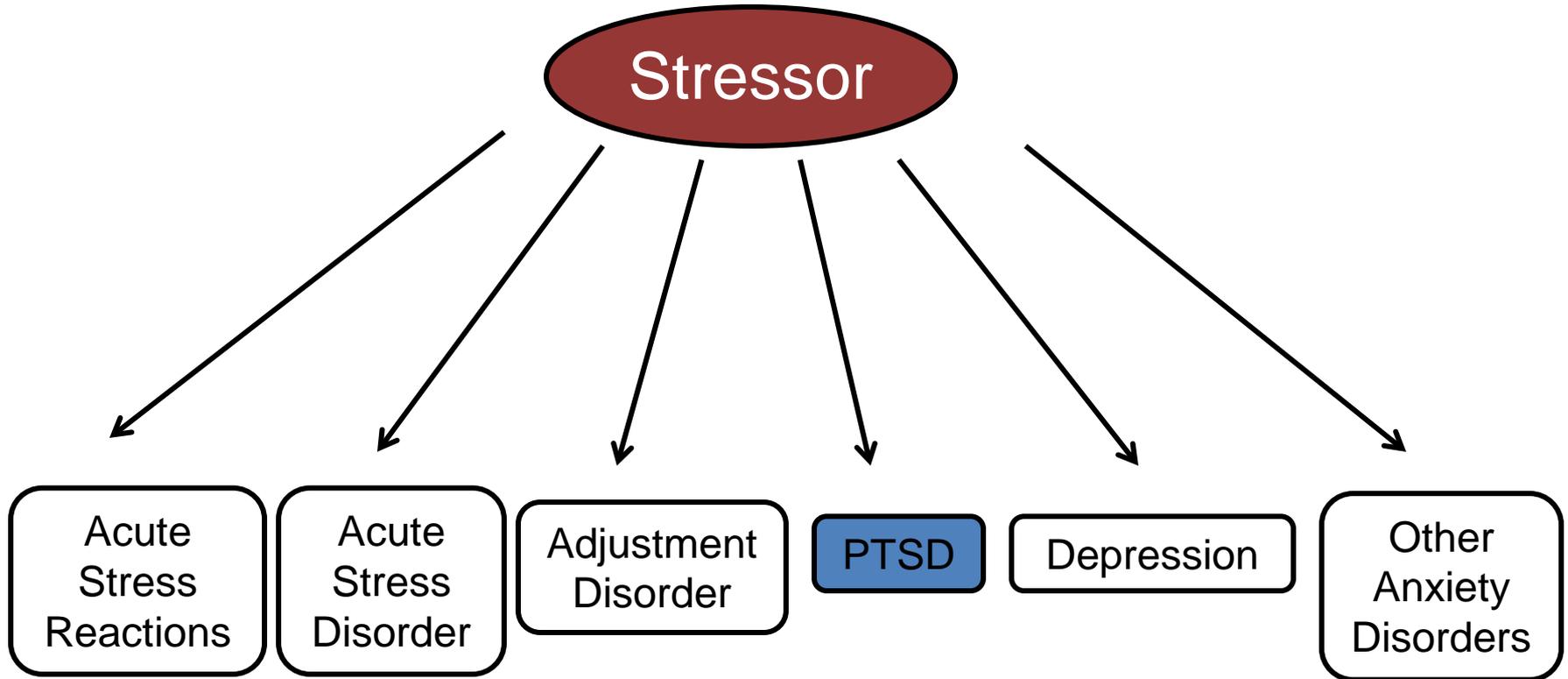
Postconcussion Symptoms

- Symptoms (e.g., headache, concentration problems) are non-specific
- Subjective complaints occur at relatively high levels in various non-TBI populations including healthy controls
- Symptoms overlap with PTSD
- While symptoms associated with acute effects of TBI, psychological factors play role in their maintenance

Scholten et al. (2012; *Brain Injury*)

Variable	TBI (%)	No TBI (%)	TBI vs No TBI	
	(n=30267)	(n=20934)	Odds ratio ^a	95% CI
<u>Moderate-to-very severe symptoms in last 30 days</u>				
Irritability, easily annoyed	85	78	1.64	1.57, 1.72
Sleep disturbance	84	77	1.62	1.55, 1.70
Forgetfulness	83	68	2.21	2.12, 2.30
Anxious or tense	80	71	1.62	1.56, 1.70
Headaches	78	64	2.05	1.97, 2.13
Poor concentration	76	62	1.98	1.90, 2.06
Poor frustration tolerance, easily overwhelmed	75	65	1.62	1.55, 1.68
Fatigue	69	60	1.58	1.52, 1.64
Hearing difficulty	66	54	1.62	1.56, 1.68
Slowed thinking, difficulty organizing, difficulty finishing things	64	50	1.84	1.77, 1.90
Depressed or sad	63	56	1.35	1.30, 1.40
Sensitivity to noise	59	48	1.59	1.53, 1.65
Sensitivity to light	55	44	1.67	1.61, 1.73
Difficulty making decisions	55	43	1.69	1.63, 1.75
Numbness or tingling in parts of body	50	42	1.49	1.44, 1.55
Change in appetite	47	39	1.45	1.40, 1.50
Vision problems, blurring, trouble seeing	44	35	1.57	1.51, 1.63
Feeling dizzy	41	29	1.80	1.73, 1.87
Poor co-ordination	41	28	1.88	1.81, 1.95
Loss of balance	39	27	1.81	1.74, 1.88
Nausea	30	21	1.63	1.56, 1.70
Change in taste or smell	21	15	1.70	1.62, 1.78
Moderate-to-very severe symptom interference in last 30 days ^b	74	65	2.10	2.00, 2.19

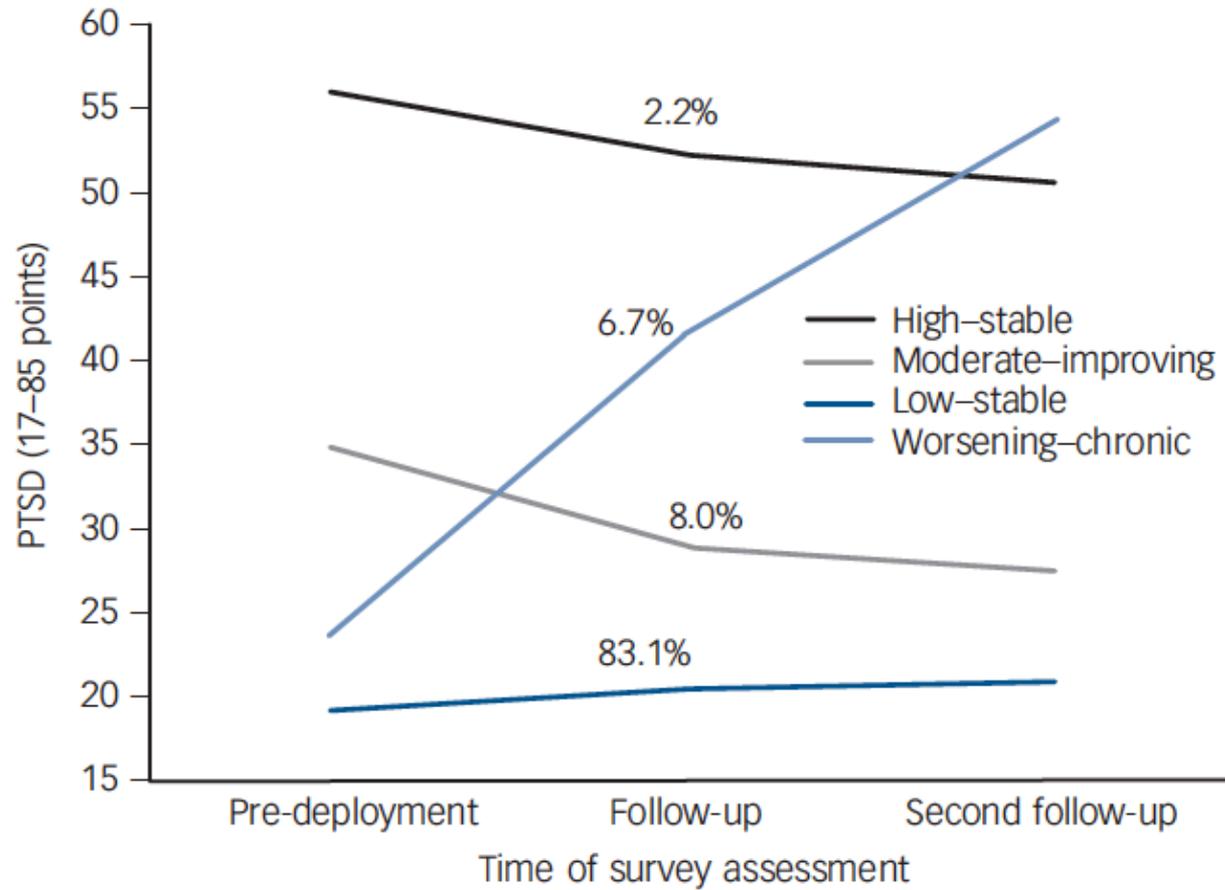
Spectrum of Psychological Trauma Reactions



DSM-V PTSD Criteria

- A. death, serious injury, sexual violence
- B. Intrusion symptoms
- C. Avoidance
- D. Negative alterations in cognition/mood
- E. Alterations in arousal
- F. > 1 month, clinical impact

Bonanno et al. (2012; *Br J Psychiatry*)



Mechanisms

Combat



TBI/PCS

Stress/
PTSD



Does TBI Increase Risk of PTSD?

- Bryant et al. (2010; Am J Psych)

n = 1084 civilians with traumatic injuries

At 12 mos., mild TBI patients ~2x more likely to develop new:

	Adj OR	CI
PTSD	1.92	1.08, 3.40
Panic	2.10	1.03, 4.14
Social Phobia	2.07	1.03, 4.16
Agoraphobia	1.94	1.13, 3.39

Functional impairment related to psychiatric status.

**How does TBI
increase risk of
PTSD?**

Disease Burden

Bell et al., *J Neurol, Neurosurg, Psychiatry*, 2008

- N= 366 acute mild TBI, civilian adults
- 2 group RCT (during 1st 3 months post- mild TBI):
 - phone counseling (educ, reassurance, re-activation)
 - emergency care as usual
- Intervention reduced:
 - symptoms (e.g., fatigue, sleep problems) and
 - functional impairment (e.g., work, recreation, cognitive)

Neural Overlap

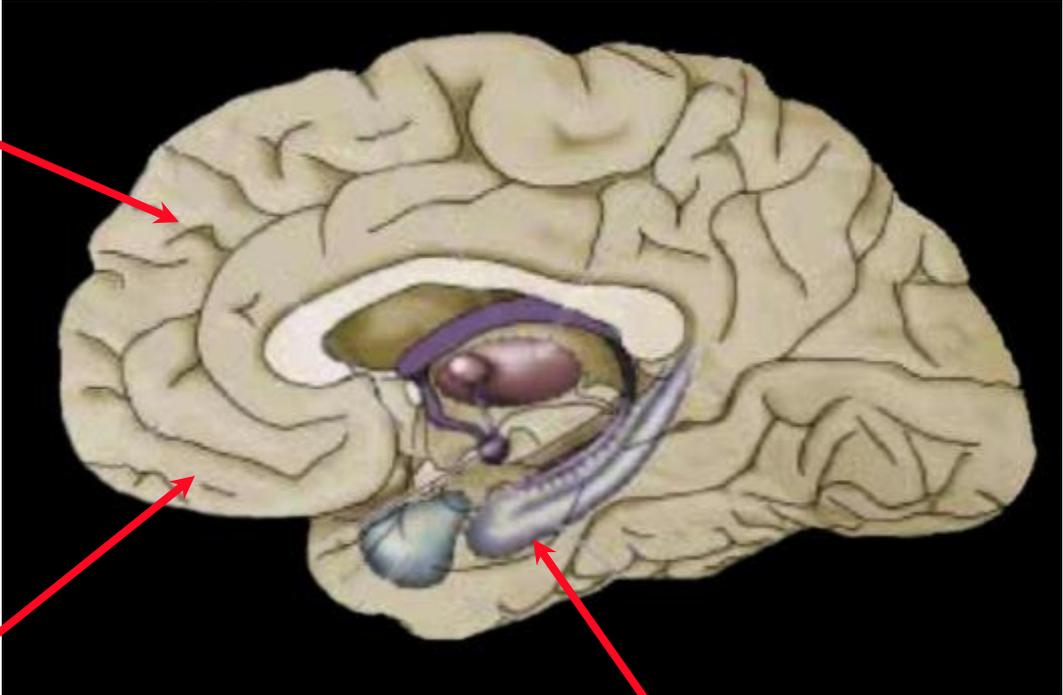
Dorsolateral Frontal Cortex



Orbital Frontal Cortex



Hippocampus



Neurocognitive Mechanisms



- Altered memory formation for the event and associated emotions, leading to poorly controlled recall of the event (i.e., re-experiencing symptoms)
- Changes in cognitive control may lead to emotional dysregulation.

Does Emotional Distress Impede Recovery from TBI?

- Most evidence is from cross sectional work:

When adjusted for PTSD symptoms, the relationship between TBI and most post-concussive symptoms disappears. (Hoge et al, *N Eng J Med*, 2008; Verfaellie et al., *J Int Neuropsych Soc* 2013; Belanger et al., *J Int Neuropsych Soc*, 2010)

- Less longitudinal work, especially for mild TBI

Predictors of Postconcussional Symptoms (PCS) in Mild TBI

- Ponsford et al., *Neuropsychology*, 2012
n = 123 mild TBI; n = 100 no-TBI trauma

<u>Predictors</u>	<u>PCS 1 week</u>	<u>PCS 3 mo.</u>
TBI	+	--
PTA duration	--	--
1 wk cognitive performance	--	--
3 mo cognitive performance	n/a	--
Pre-injury psych hx	+	+
1 week anxiety sx	+	+
3 month anxiety sx	n/a	+
3 month PTSD sx	n/a	+

Predictors of Cognitive Decline Over Deployment

Vasterling et al. *Br J Psychiatry*, 2012



N = 760 Army Soldiers
(n = 68 TBI-D+; n= 692 no TBI-D)



Table DS3 Results of hierarchical regression analyses examining associations of inter-session traumatic brain injury (TBI), post-deployment CES-D summary scores (Model 2) with functional and neuropsychological performance outcomes^a

Outcome variable	Model 1					
	TBI (unadjusted for PTSD or depression symptom severity)		TBI adjusted for PCL-C summary scores		PCL-C summary scores adjusted for TBI	
	B (95% CI)	P	B (95% CI)	P	B (95% CI)	P
Functional outcomes						
MOS-CF	-0.02 (-0.08 to 0.05)	0.61	0.05 (-0.01 to 0.10)	0.11	-0.51 (-0.56 to -0.45)	<0.001
VR-12 – physical symptoms	-0.12 (-0.19 to -0.06)	<0.001	-0.10 (-0.17 to -0.03)	0.003	-0.17 (-0.24 to -0.10)	<0.001
Attention, working memory, executive						
Trailmaking, B-A	0.03 (-0.04 to 0.07)	0.46	0.02 (-0.05 to 0.09)	0.51	0.02 (-0.05 to 0.09)	0.65
CPT commission errors (log-transformed)	-0.03 (-0.10 to 0.04)	0.40	-0.03 (-0.10 to 0.03)	0.34	0.03 (-0.04 to 0.10)	0.35
CPT omission errors (log-transformed)	0.03 (-0.04 to 0.10)	0.38	0.02 (-0.05 to 0.09)	0.58	0.08 (0.01 to 0.15)	0.02
Learning and memory						
Verbal paired associates, learning trials, total correct	-0.01 (-0.07 to 0.04)	0.62	-0.01 (-0.06 to 0.05)	0.87	-0.07 (-0.13 to -0.02)	0.01
Verbal paired associates, % retention	-0.002 (-0.071 to 0.067)	0.95	-0.001 (-0.072 to 0.070)	0.97	-0.01 (-0.08 to 0.06)	0.83
Visual reproductions, immediate recall	-0.05 (-0.12 to 0.01)	0.09	-0.04 (-0.10 to 0.02)	0.18	-0.09 (-0.15 to -0.03)	0.005
Visual reproductions, % retention	-0.08 (-0.15 to -0.01)	0.03	-0.07 (-0.14 to 0.00)	0.05	-0.07 (-0.14 to 0.00)	0.05
Simple reaction time						
ANAM simple reaction time, throughput	0.03 (-0.04 to 0.09)	0.39	0.04 (-0.02 to 0.11)	0.19	-0.11 (-0.18 to -0.04)	0.001
Cognitive efficiency						
ANAM code substitution, learning throughput	0.02 (-0.03 to 0.07)	0.47	0.03 (-0.02 to 0.08)	0.24	-0.09 (-0.14 to -0.04)	0.001
ANAM code substitution, delay throughput	-0.003 (-0.054 to 0.048)	0.92	0.01 (-0.04 to 0.06)	0.68	-0.11 (-0.16 to -0.06)	<0.001
ANAM match to sample, throughput	0.03 (-0.03 to 0.08)	0.38	0.03 (-0.03 to 0.09)	0.27	-0.05 (-0.11 to 0.01)	0.07
ANAM math processing, throughput	-0.03 (-0.08 to 0.03)	0.35	-0.02 (-0.08 to 0.04)	0.45	-0.04 (-0.09 to 0.02)	0.19
ANAM running memory, throughput	0.003 (-0.054 to 0.060)	0.90	0.01 (-0.07 to 0.05)	0.77	-0.04 (-0.10 to 0.02)	0.19

White Matter Changes in Relation to Deployment TBI

- Hayes et al. (under review)
 - n = 94 OEF/OIF veterans
(healthy control, blast control, TBI+/LOC-, TBI+/LOC+)
 - TBI, but not PTSD, associated with white matter abnormalities
 - TBI only associated with cognitive deficits via white matter abnormalities
 - PTSD associated with cognitive deficits but not via white matter abnormalities

**How does emotional
distress impede
recovery from TBI?**

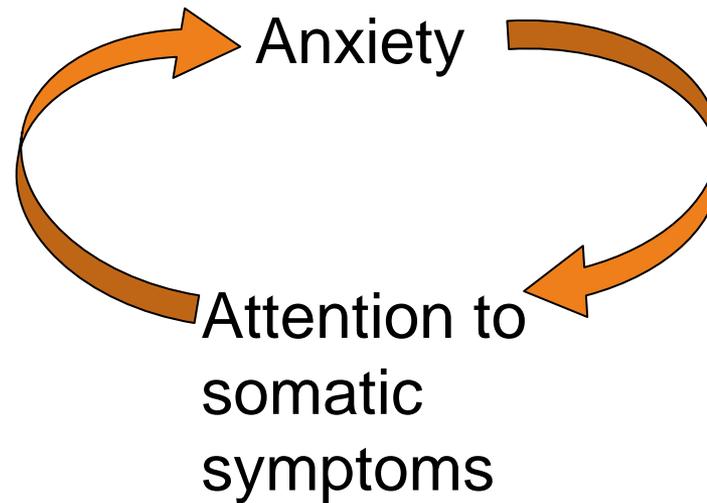
Resilience

- Psychiatric status can affect resilience

Resilience - “adaptive coping, optimism and positive emotion, cognitive re-appraisal, positive reframing and acceptance, social competence and support, purpose in life” (Iverson)

Somatic Pre-Occupation

- Increased somatic pre-occupation
(especially for anxiety disorders)



Clinical Implications

When Does Etiology of Symptoms Matter?

- PTSD symptoms:
 - some symptoms are specific to PTSD (e.g., re-experiencing)
 - can be treated with evidence-based interventions (e.g., prolonged exposure, cognitive processing therapy)

When Does Etiology of Symptoms Matter?

- When there has been a TBI event, *especially soon after the event*
- Education around symptom course and recovery appears to be most effective intervention for mild TBI.



When is Etiology of Symptoms Less Important?

- Treatment of cognitive deficits and non-specific symptoms via cognitive rehab and psychoeducation

- Examples:

CogSMART (Twamley et al., JRRD, 2014)

Cognitive Strategy Training (Huckans et al., JRRD, 2010)



Summary

- PTSD occurs frequently in veterans with history of TBI
- Considerable symptom overlap between post-concussive symptoms and PTSD
- Bi-directional relationships are likely
- Determining the etiology of symptoms is helpful in some circumstances but not others

QUESTIONS?

Jennifer Vasterling:

jennifer.vasterling@va.gov

Mieke Verfaellie:

mieke.verfaellie@va.gov

- Belanger, H. G., Kretzmer, T., Vanderploeg, R. D., & French, L. M. (2010). Symptom complaints following combat-related traumatic brain injury: relationship to traumatic brain injury and posttraumatic stress disorder. *Journal of the International Neuropsychological Society*, *16*, 194-199.
- Bell, K. R., Hoffman, J.M., Temkin, N. R., Powell, J.M., Fraser, R. T., Esselman, P.C., Barber, J. K., & Dikmen, S. (2008) The effect of telephone counseling on reducing post-traumatic symptoms after mild traumatic brain injury: A randomized trial. *Journal of Neurology, Neurosurgery, and Psychiatry*, *79*, 1275-1281.
- Bonanno, G. A., Mancini, A. D., Horton, J. L., Powell, T. M., LearMann, C. A., Boyko, E. J., Wells, T. S., Hooper, T. I., Gackstetter, G. D., & Smith, T. C. (2012) Trajectories of trauma symptoms and resilience in deployed US military service members: prospective cohort study. *British Journal of Psychiatry*, *200*, 317-323.
- Bryant, R. A., O'Donnell, M. L., Creamer, M., McFarlane, A. C., Clark, C. R., & Silove, D. (2010). The psychiatric sequelae of traumatic injury. *The American Journal of Psychiatry*, *167*, 312-320.
- Huckans, M., Pavawalla, S., Demadura, T., Kolessar, M., Seelye, A., Roost, N., et al. (2010). A pilot study examining effects of group-based Cognitive Strategy Training treatment on self-reported cognitive problems, psychiatric symptoms, functioning, and compensatory strategy use in OIF/OEF combat veterans with persistent mild cognitive disorder and history of traumatic brain injury. *Journal of Rehabilitation Research and Development*, *47*, 43-60.
- Hoge, C. W., McGurk, D., Thomas, J. L., Cox, A. L., Engel, C. C., & Castro, C. A. (2008). Mild traumatic brain injury in U.S. soldiers returning from Iraq. *The New England Journal of Medicine*, *358*, 453-463.
- Iverson, K., Hendricks, A. M., Kimerling, R., Kregel, M., Meterko, M., Stolzmann, K. L., Baker, E., Pogoda, T. K., Vasterling, J.J., & Lew, H. L. (2011) Psychiatric diagnoses and neurobehavioral symptom severity among OEF/OIF VA patients with deployment-related traumatic brain injury: A gender comparison. *Womens Health Issues*, *21*, S210-217.
- Ponsford, J., Cameron, P., Fitzgerald, M., Grant, M., Mikocka-Walus, A., & Schonberger, M. (2012) Predictors of postconcussive symptoms 3 months after mild traumatic brain injury. *Journal of the International Neuropsychological Society*, *26*, 304-313.
- Scholten, J. D., Sayer, N. A., Vanderploeg, R. D., Bidelspach, D. E., & Cifu, D. X. (2012) Analysis of US Veterans Health Administration comprehensive evaluations for traumatic brain injury in Operation Enduring Freedom and Operation Iraqi Freedom Veterans. *Brain Injury*, *26*, 1177-1184.

- Stein, M. B., & McAllister, T. W. (2009). Exploring the convergence of posttraumatic stress disorder and mild traumatic brain injury. *The American Journal of Psychiatry*, *166*, 768-776.
- Tanielian, T., & Jaycox, L. H. (2008). *Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery*. Santa Monica, CA: RAND corp.
- Twamley, E. W., Jak, A. J., Delis, D. C., Bondi, M. W., & Lohr, J. B. (2014). Cognitive Symptom Management and Rehabilitation Therapy (CogSMART) for Veterans with traumatic brain injury: Pilot randomized controlled trial. *Journal of Rehabilitation Research and Development*, *51*, 59-70.
- Vasterling, J. J., Brailey, K., Proctor, S. P., Kane, R., Heeren, T., & Franz, M. (2012). Neuropsychological outcomes of mild traumatic brain injury, post-traumatic stress disorder and depression in Iraq-deployed US Army soldiers. *British Journal of Psychiatry*, *201*, 186-192.
- Vasterling, J. J., Bryant, R. A., Keane, T. M. (2012). *PTSD and Mild Traumatic Brain Injury*. NY: Guilford Press.
- Verfaellie, M., Lafleche, G., Spiro, A., & Bousquet, K. (2013). Neuropsychological Outcomes in OEF/OIF Veterans with Self-Report of Blast Exposure. *Neuropsychology*, *28*, 337-346.
- Zatzick, D. F., Rivara, F. P., Jurkovich, G.J., Hoge, C. W., Wang, J., Fan, M. Y., Russo, J., Trusz, S. G., Nathens, A., Mackenzie, E. J. Multisite investigation of traumatic brain injuries, posttraumatic stress disorder, and self-reported health and cognitive impairments. *Archives of General Psychiatry*, *2010*, *67*, 1291-1300.