The Neural Costs of War: PTSD and TBI Among U.S. Combat Veterans

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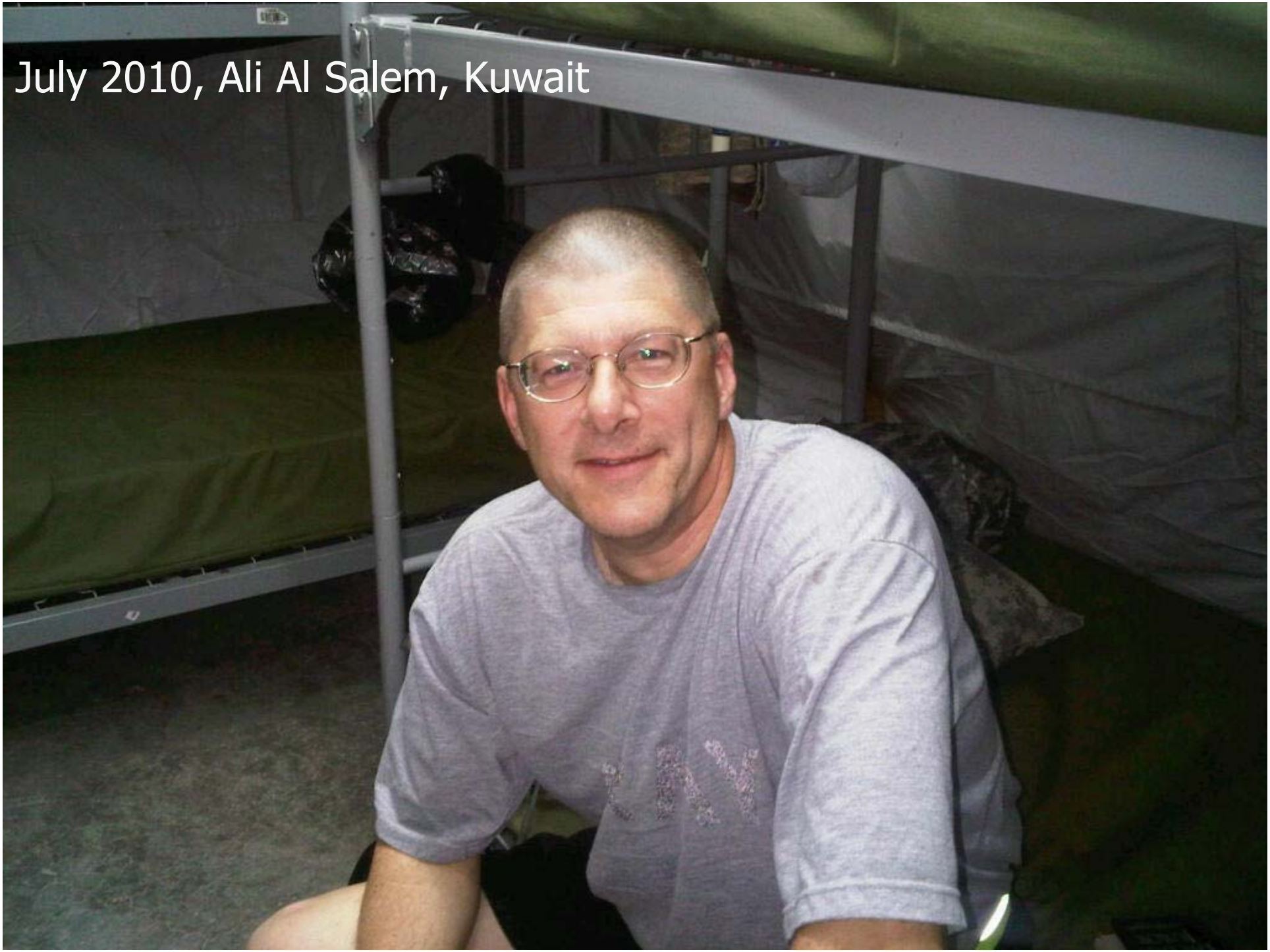
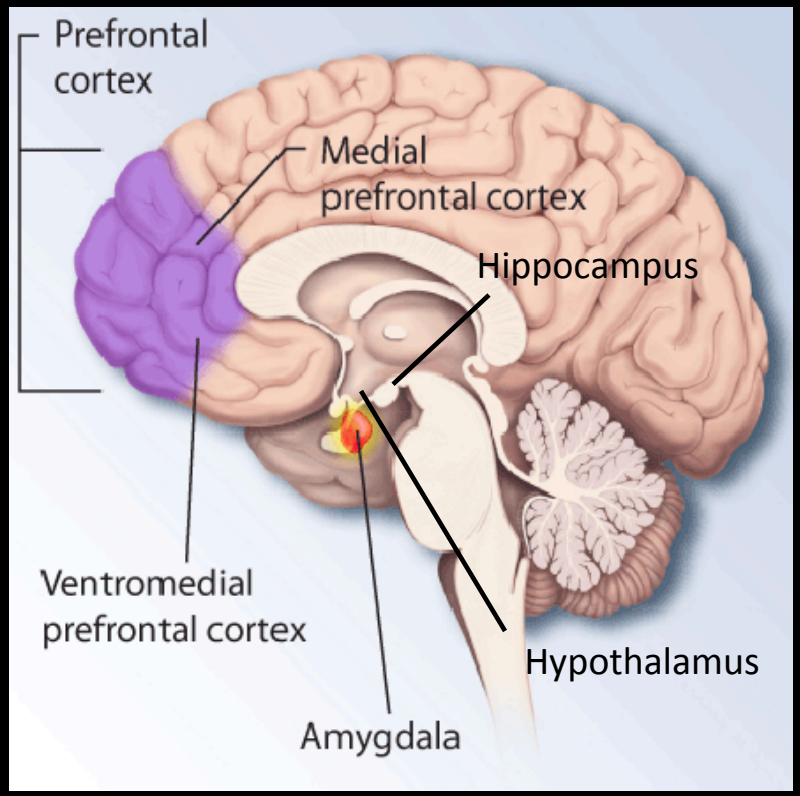

July 2010, Ali Al Salem, Kuwait

Outline of Talk

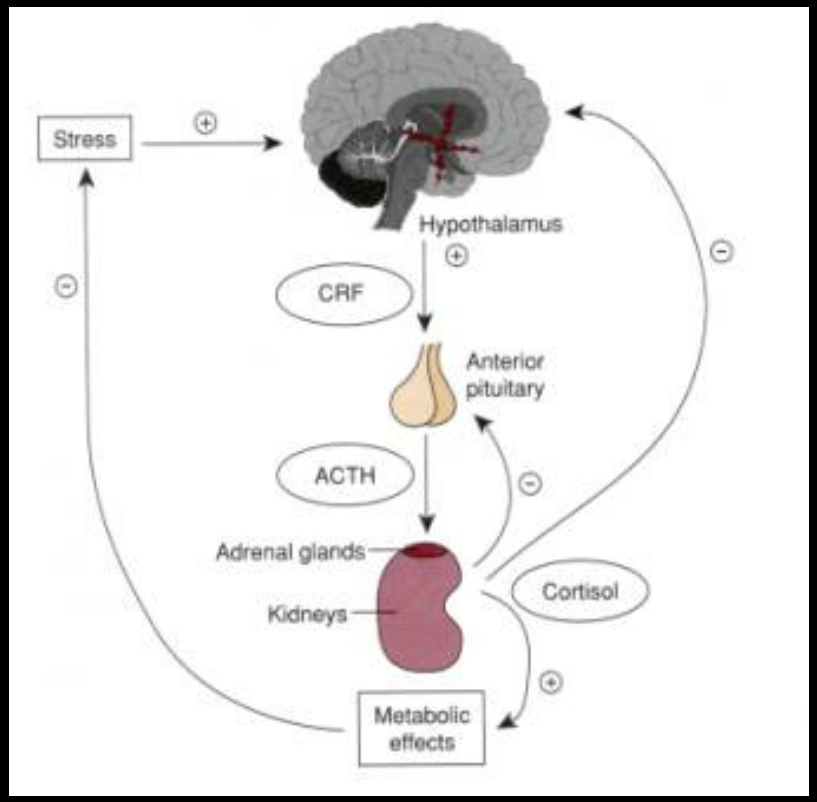
- Stress response under everyday conditions
- Stress response under extreme conditions
- Post-Traumatic Stress Disorder (PTSD)
- Traumatic Brain Injury (TBI)
- Co-occurrence of PTSD and TBI
- PTSD and TBI in OEF/OIF Service Members
- Public health implications and future research

Brain Regions Involved in Fear/Stress



- Amygdala is attuned to danger cues
- Medial PFC interprets danger signals
- Context provided by Hippocampus
- Fear reactions initiate HPA Axis activity

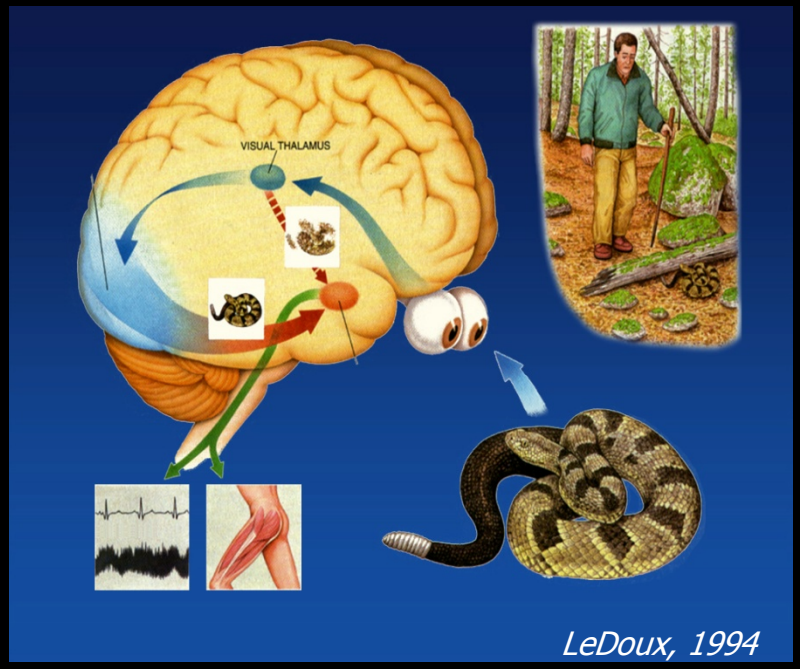
Hypothalamic-Pituitary-Adrenal Axis



- Evolution – fight, flee, or freeze
- Dramatic metabolic changes:
  - increased pupil size
  - increased heart rate
  - rapid muscle contraction
- Hard-wired, short-term stress response

Normal stress response effects:

- Emotions – fear, anger, anxiety, shock, numbing
- Cognition – impacts attention, concentration, decision making
- Behavior – aggression, social withdrawal, conflicts, avoidance
- Physical – agitation, GI distress, fatigue, insomnia, headaches



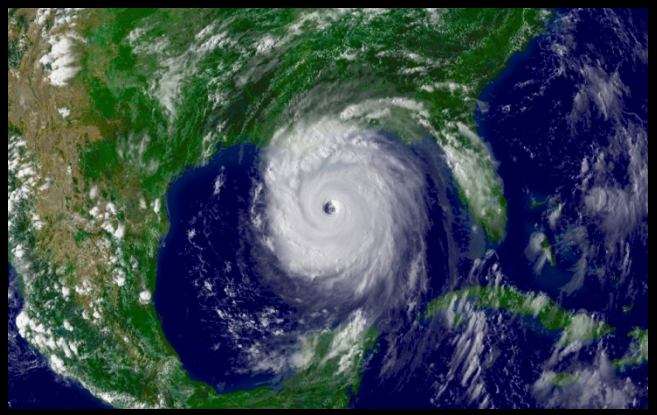
LeDoux, 1994

Stress Response to Extreme Events

- Natural disasters (hurricanes, wildfires, earthquakes)
- Man made disasters (chemical spills, collapsed structures)
- Acts of terrorism (Oklahoma City, 9/11)

Acute Stress Reactions

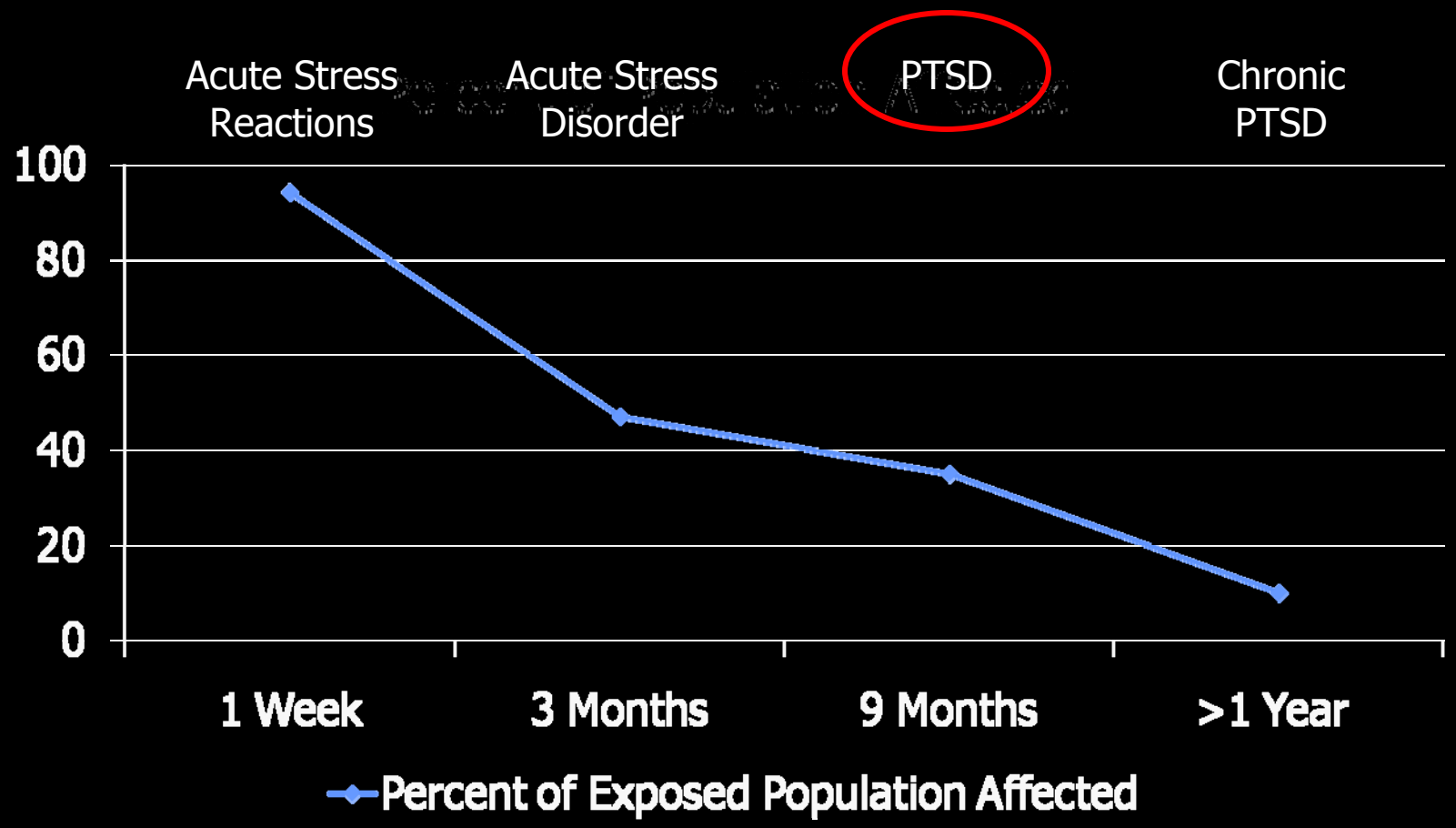
- Fear, anxiety, anger, hopelessness, mistrust, depression, irritability, disbelief, demoralization
- Impaired cognition
- Isolation, withdrawal, interpersonal conflict, poor role functioning
- Can last up to several days following the event



Acute Stress Disorder (DSM-IV-TR)

- Exposure to a potentially life-threatening event
- Persistent re-experiencing of trauma
- Avoidance of trauma-related stimuli
- Numbing of general responsiveness
- Increased physiological/emotional arousal
- Clinically significant distress or impairment in social/occupational/other areas of functioning
- Duration GT than 2 days and LT 4 weeks

Trajectory of Stress Reactions Following a Terrorist Event



Adapted from Shalev, 2004

Post-Traumatic Stress Disorder (PTSD)

"The Invisible Wounds of War"

Tanielian & Jaycox, 2008

Post-Traumatic Stress Disorder (PTSD)

- History of construct
- DSM-IV-TR Diagnosis
- Prevalence in civilian and military samples
- Recent research on PTSD neurocircuitry

History of PTSD

- 1867 “Railroad Spine”
- 1871 “Soldier’s Heart”
- WWI and WWII
  - Shell shock
  - Battle fatigue
  - Traumatic neurosis
- 1970’s “Vietnam Syndrome”
- 1980 – PTSD recognized as an anxiety disorder in the DSM-III

DSM-IV-TR PTSD Diagnosis

- Exposure to a traumatic event in which both of the following were present:
  - Person experienced, or witnessed, or was confronted with an event or events that involved **actual or threatened death or serious injury**, or a threat to the physical integrity of self or others
  - Person's response involved **intense fear, helplessness or horror**

DSM-IV-TR PTSD Diagnosis

- The traumatic event is **re-experienced** persistently in one or more ways:
  - Recurrent and intrusive recollections of the event including images/thoughts/perceptions
  - Recurrent distressing dreams of the event
  - Acting or feeling as if the event were recurring (flashbacks, reliving, illusions)
  - Intense psychological distress on exposure to internal or external cues of event
  - Physiological reactivity on exposure to internal or external cues of event

DSM-IV-TR PTSD Diagnosis

- Persistent **avoidance** of trauma-related stimuli or **numbing** of general responsiveness (3):
  - Avoidance of thoughts, feelings or conversations associated with trauma
  - ★ Avoidance of activities, places, people that arouse recollections of the trauma
  - Inability to recall important aspect of trauma
  - Diminished interest/participation in activities
  - ★ Feeling of detachment/estrangement
  - Restricted range of affect
  - Sense of foreshortened future

DSM-IV-TR PTSD Diagnosis

- Persistent symptoms of **increased arousal** (2):
  - Difficulty falling or staying asleep
  - Irritability or outbursts of anger
  - ★ Difficulty concentrating
  - Hypervigilance
  - Exaggerated startle response
- Duration more than one month
- Disturbance causes clinically significant distress or impairment in social/occupational/other fxn

PTSD in the General Population

- 2-20% of civilians exposed to trauma
- Lifetime 5% males, 10% females
- Women 4x more likely if exposed
- PTSD beyond 3 months often becomes chronic

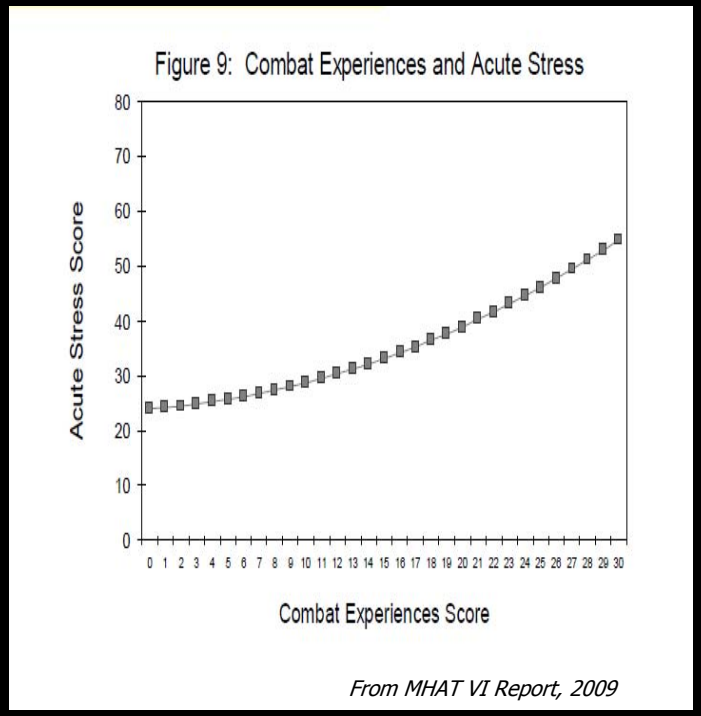
Risk Factors for PTSD - Civilians

- Other anxiety and mood disorders
- ETOH/Substance abuse
- Abuse/PTSD history
- Avoidant coping style
- Behavioral acting out style
- External attribution of blame
- Prior unemployment
- Loss of control during event
- Fear of death
- Chronic pain

Probable PTSD in OIF Military Samples

Study	Pre-Deployment	During Deployment	Post-Deployment	
			3-4 months	4-10 months
Hoge et al., 2004	5.0%		12.2-12.9%	
MHAT I-VI, 2003-2009		9.9-18.6%		
Hoge et al., 2006			9.8%	
Miliken et al., 2007			11.8-12.7%	16.7-24.5%

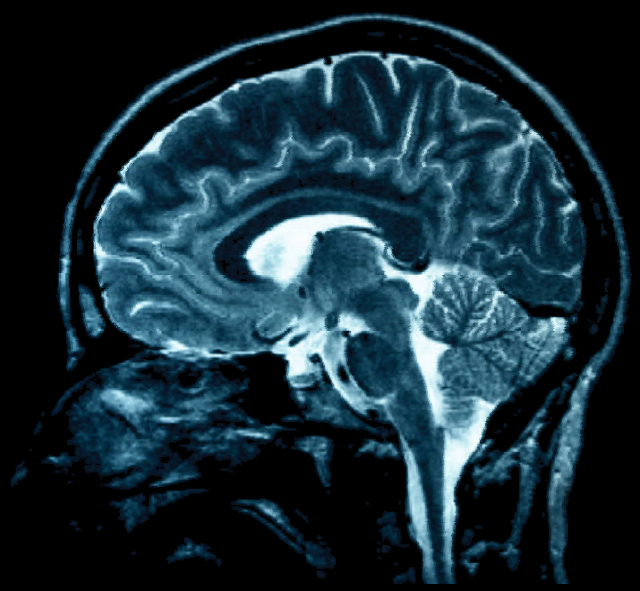
Risk Factors for PTSD – Military SMs



From MHAT VI Report, 2009

- Combat experiences
  - Feeling in great danger of dying
  - Number of firefights
  - Being shot or seriously injured
  - Seeing someone wounded or killed
  - Handling dead bodies
- Prior history
  - Childhood adversity
  - Less formal education
  - Prior violence exposures
- Absence of Protective Factors
  - Being unmarried
  - Lower rank

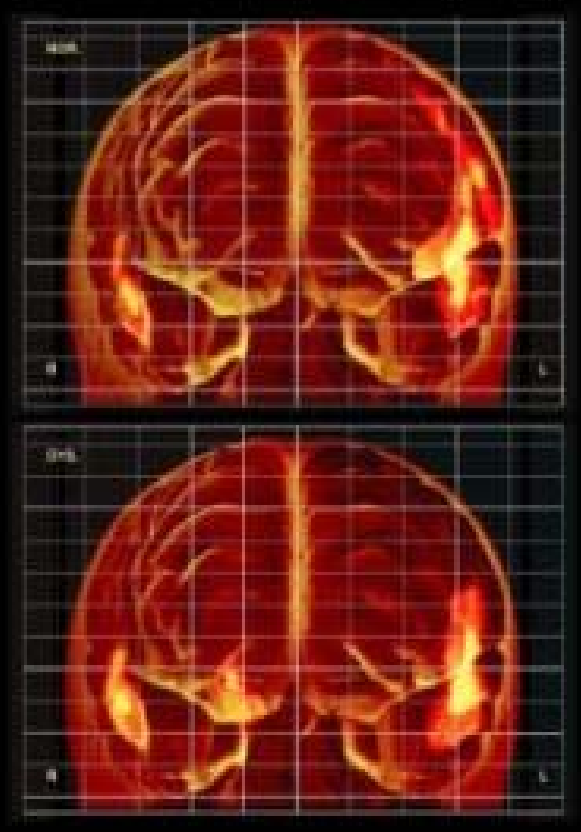
Brain Imaging Studies and PTSD



- Combat vets with PTSD – 8% reduction in hippocampal volume
- Replicated with survivors of childhood abuse with PTSD & correlated with level of abuse
- PET- low hippocampal activation
- Hippocampal reduction is specific to PTSD, not anxiety

Medial Prefrontal Cortex (MPC) in PTSD

- When healthy, MPC inhibits amygdala to modulate fear
- Provoking PTSD symptoms leads to dysfunction in both MPC and Hippocampus (H)
- Impairments in MPC and H are believed to underlie pathological emotional responses in PTSD



PTSD Summary: Clinical Features

- After trauma, acute distress/symptoms are normal
- 10 – 45% of trauma survivors experience PTSD
- Trajectories include recovery and worsening
- Risk factors for PTSD include:
  - Prior trauma and history of mental disorders
  - Exposure to death, personal injury, or witnessing others' injuries
  - Ongoing stressors, low social support
  - Combat experiences

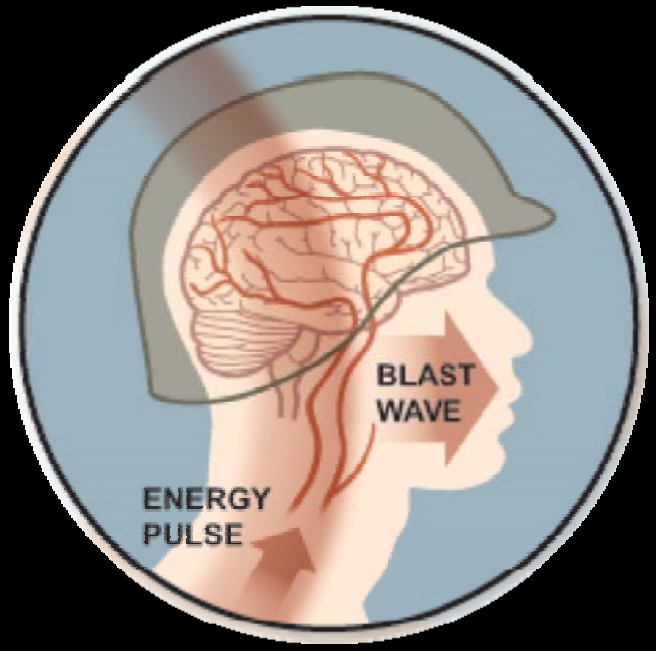
PTSD Summary: Treatment

- Early intervention to normalize neurobiological and cognitive processes implicated in acute arousal
- Patient education emphasizes activation/corruption of the brain's stress and fear circuits; this is truly a psycho<u>biological</u> disorder
- Exposure-based treatments help to process painful memories and feelings, and decrease arousal
- SSRIs are recommended as first line medications
- Chronic PTSD is difficult to treat, and is linked with high health care utilization and impairment

Traumatic Brain Injury (TBI)

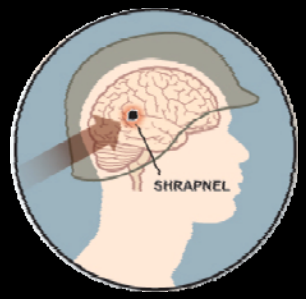
"The Signature Wound of the Current Conflicts"

U.S. Senate Committee on Veterans' Affairs, Oversight Hearing on TBI, 2010

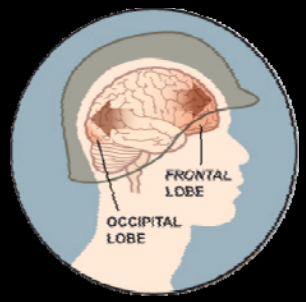


TBIs are Acquired Brain Injuries

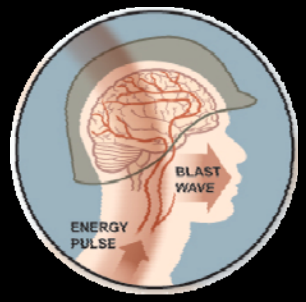
- Blunt force or penetrating trauma damages affected brain regions
  - Contusion, swelling, hemotoma



- Rapid acceleration-deceleration (whiplash) bruises areas of brain
  - Scraping of brain across bony areas of skull can lead to olfactory, oculomotor, acoustic nerve damage



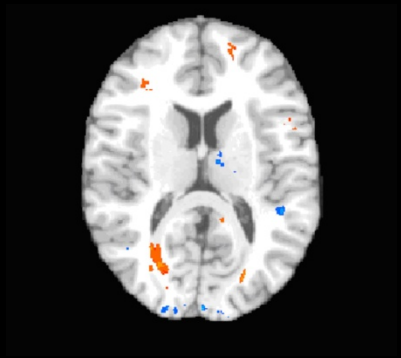
- Blast injuries twist and tear nerve fibers, which results in diffuse axonal injury

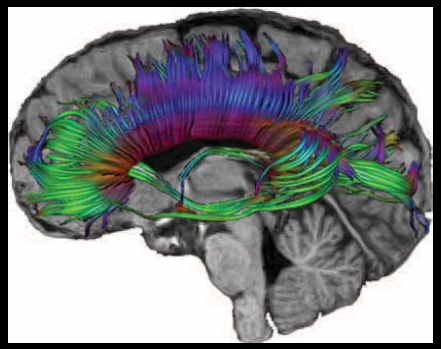


TBI Symptoms

- Physical: sensitivity to light, headaches, sleep disturbance
- Cognitive: disturbances in attention, memory, language, speed of information processing
- Behavioral: mood changes, depression, anxiety, impulsiveness, emotional outbursts, inappropriate laughter

Levels of TBI





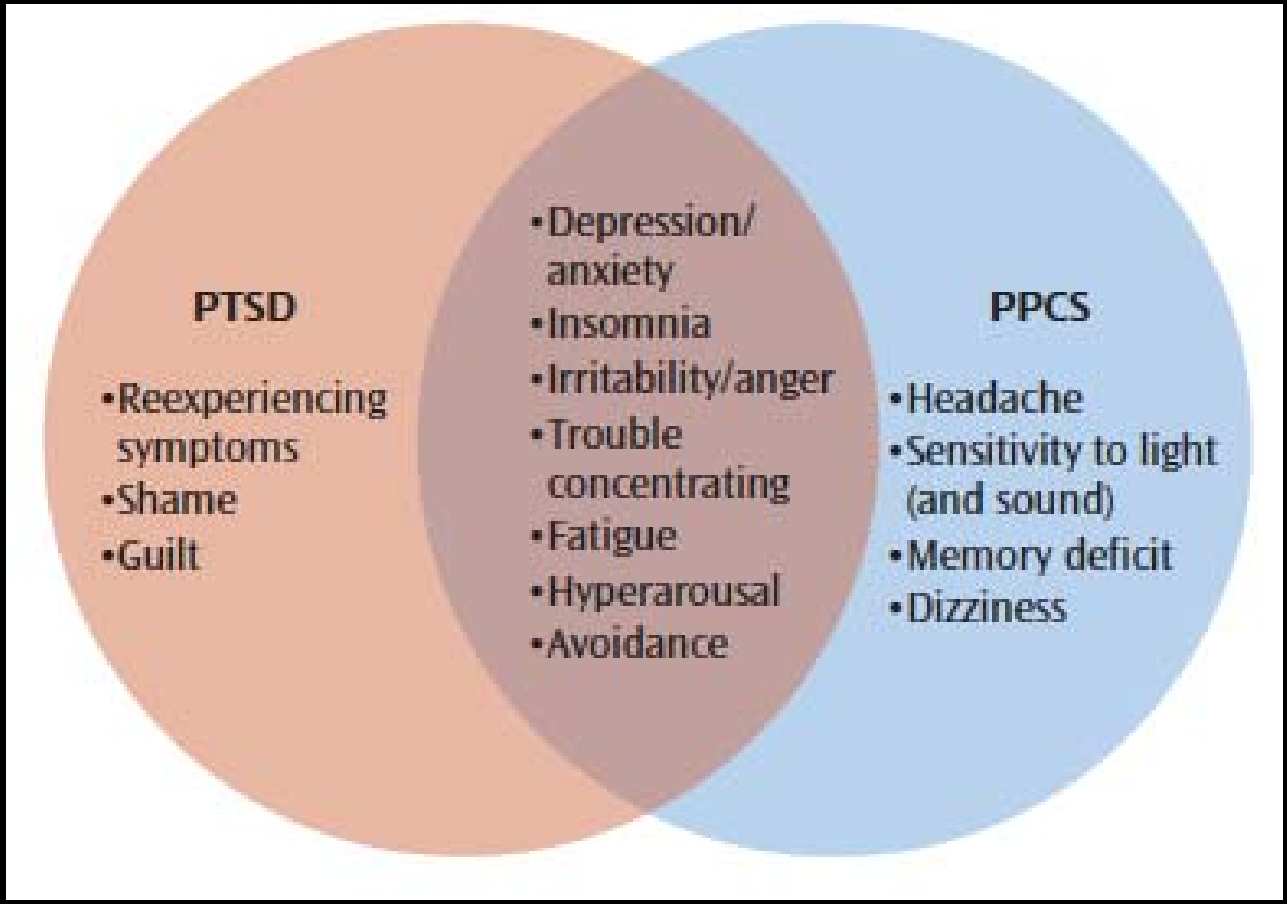
	Mild*	Moderate	Severe
Loss of Consciousness	<1 hour	1-24 hours	>24 hours
Duration of Amnesia	<24 hours	1-7 days	>7 days
Glasgow Coma Scale (3-15)	13-15	9-12	3-8

*Altered Mental States = "dazed," "confused," "seeing stars"

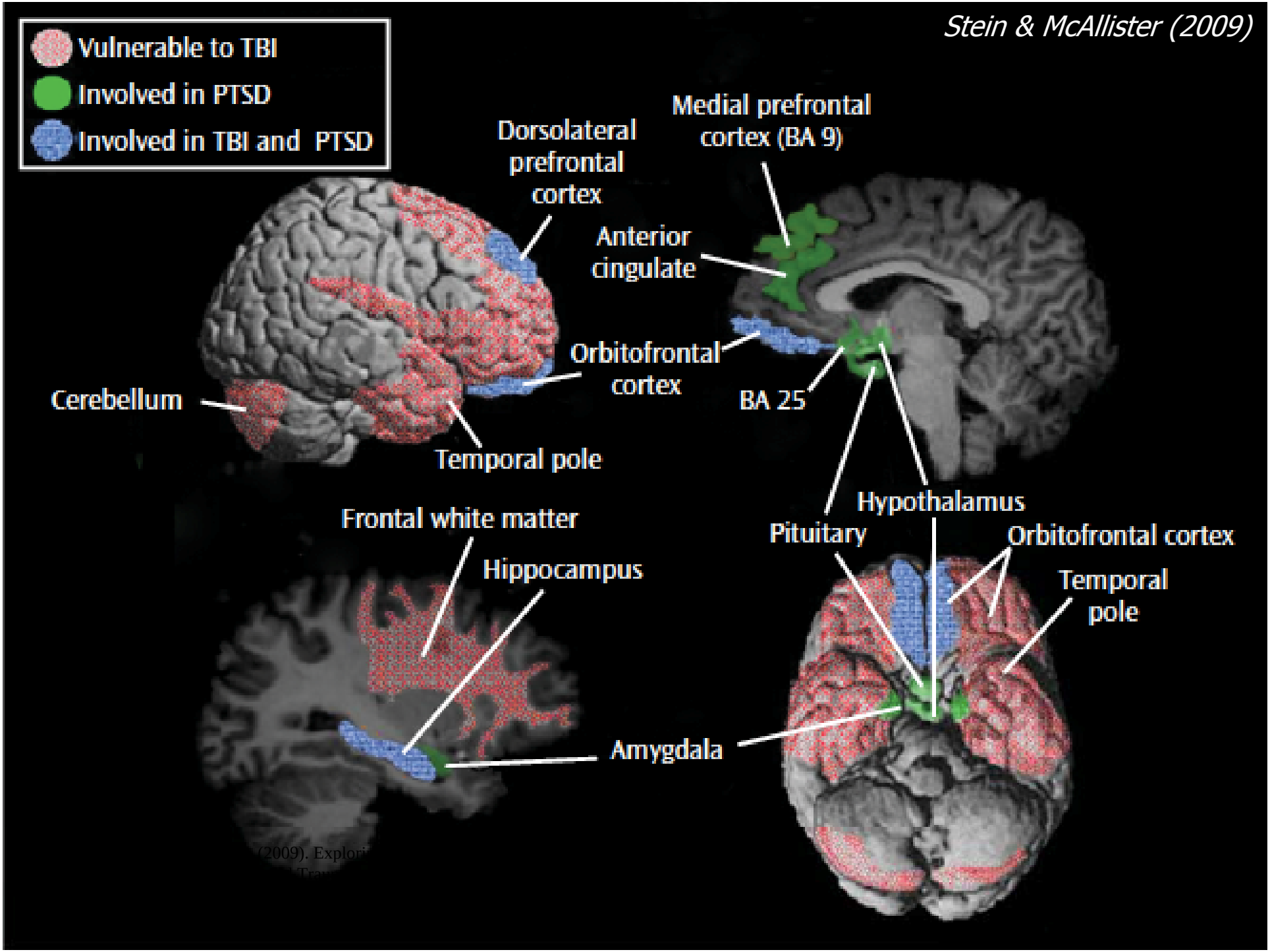
Prognosis Depends on Severity of TBI

- Mild TBI: Recovery expected within 4-12 weeks of injury; however, some symptoms may linger
- Moderate TBI: Recovery may take up to 12-months post-injury; PTSD is often a complicating problem
- Severe TBI: Complete recovery may not occur

Overlap Between TBI & PTSD



Stein & McAllister (2009)


Stein & McAllister (2009)
Vulnerable to TBI
Involved in PTSD
Involved in TBI and PTSD
Dorsolateral prefrontal cortex
Medial prefrontal cortex (BA 9)
Anterior cingulate
Orbitofrontal cortex
BA 25
Cerebellum
Temporal pole
Hypothalamus
Pituitary
Orbitofrontal cortex
Temporal pole
Frontal white matter
Hippocampus
Amygdala

TBI among AD Combat Veterans

- 2,525 Active Duty soldiers assessed 3-4 months post-deployment (OIF)
  - 5% reported injury with LOC (~several minutes)
  - 10% reported injury with altered mental status, but no LOC
  - Only 4 Soldiers reported LOC >30 minutes
- Soldiers meeting criteria for PTSD:
  - 44% of those reporting LOC
  - 27% of those with altered mental state
  - 16% of those with other injuries
  - 9% of those with no injuries

Hoge et al., 2008

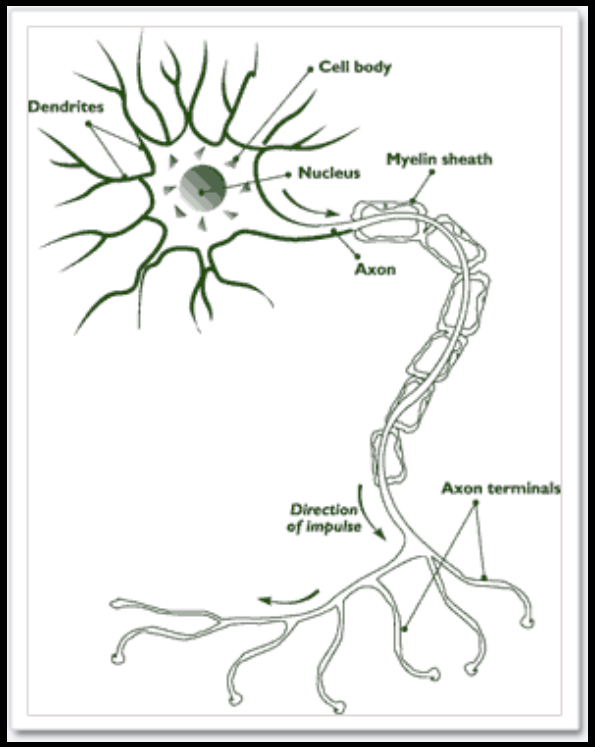
TBI among AD/RC Combat Vets

- 1,965 AD, RC, & Discharged SMs interviewed 0-36 months post-deployment (OIF and OEF)
  - 19% classified "Probable TBI" based on alteration of consciousness following injury during deployment
- TBI and psychiatric comorbidity
  - 12% meet TBI criteria alone
  - 1% meet criteria for TBI and PTSD
  - 1% meet criteria for TBI and Depression
  - 6% meet criteria for TBI, PTSD, and Depression

Tanielian & Jaycox, 2008

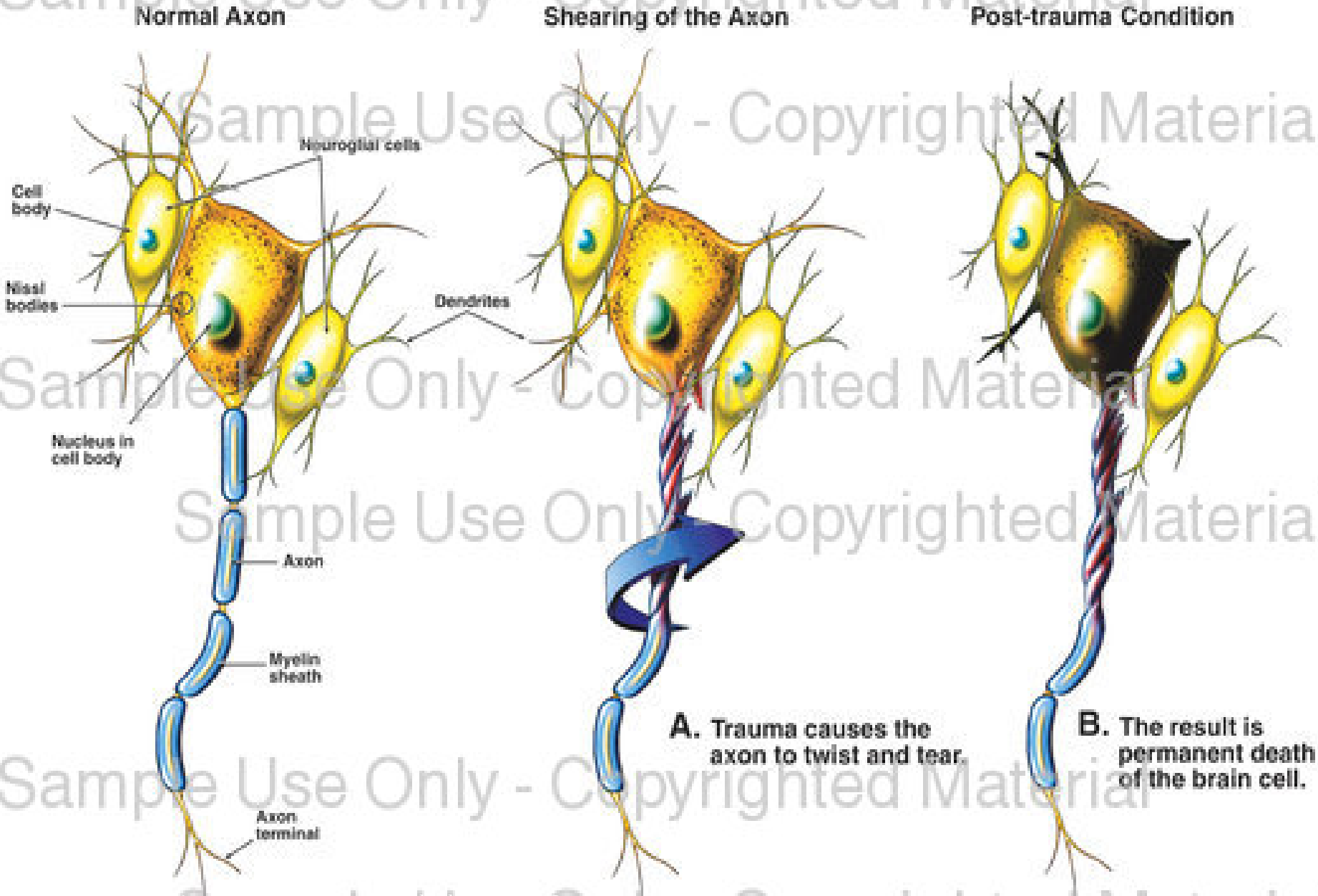
Pathophysiology of Blast Induced TBI

- Blast trauma causes axons to twist and swell
- Axons lose distal projections and synaptic terminals
  - Greatly reduces communication with neighboring cells
  - As the axon becomes disconnected from the cell body, neurotransmitters flood out, killing nearby neurons
- Process begins within minutes of the injury and continues for hours/days



http://www.narconon.ca/BrainOnDrugs.htm

Axon Shear (Post-concussion Syndrome)



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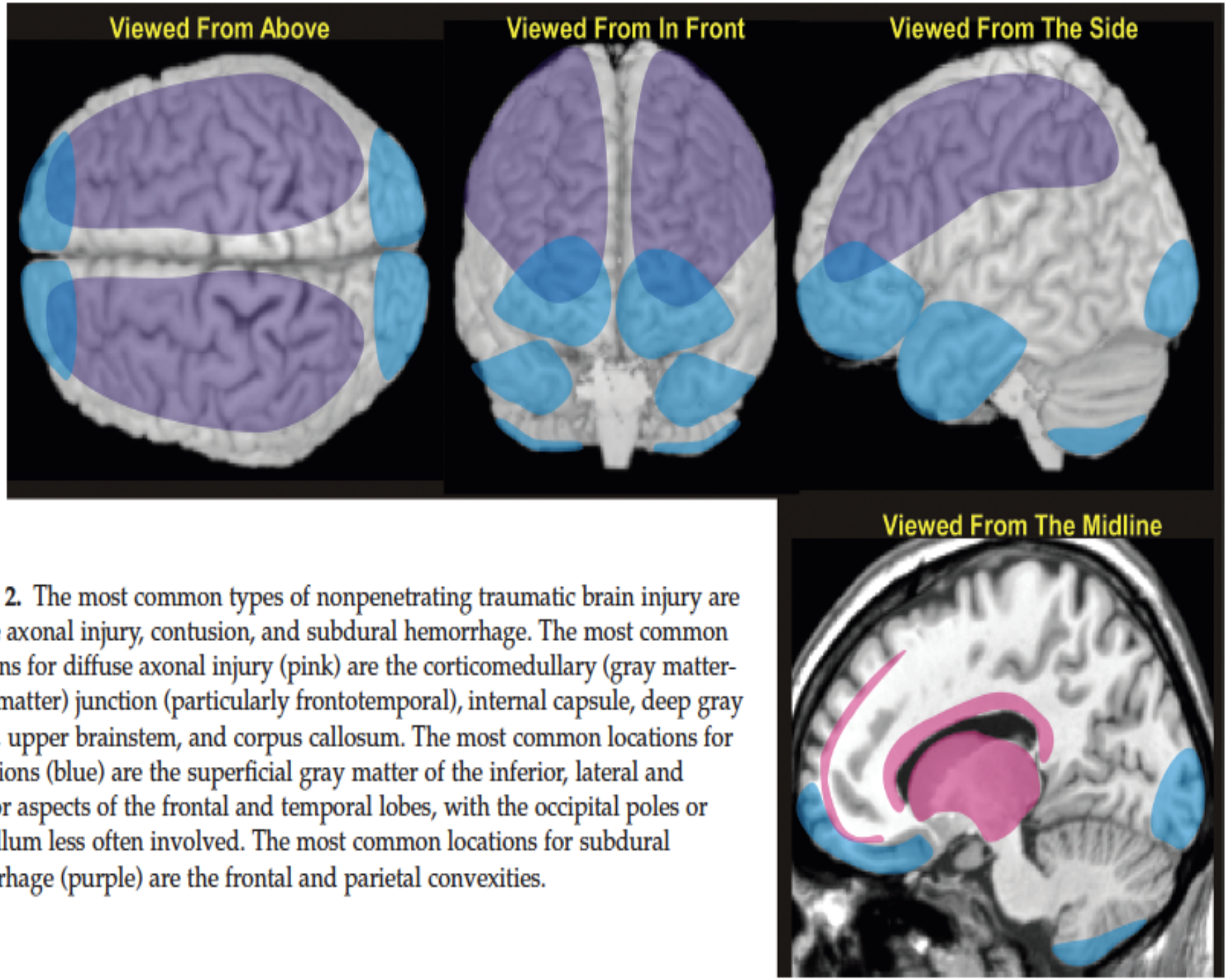


Figure 2. The most common types of nonpenetrating traumatic brain injury are diffuse axonal injury, contusion, and subdural hemorrhage. The most common locations for diffuse axonal injury (pink) are the corticomedullary (gray matter-white matter) junction (particularly frontotemporal), internal capsule, deep gray matter, upper brainstem, and corpus callosum. The most common locations for contusions (blue) are the superficial gray matter of the inferior, lateral and anterior aspects of the frontal and temporal lobes, with the occipital poles or cerebellum less often involved. The most common locations for subdural hemorrhage (purple) are the frontal and parietal convexities.

Treatment for TBI

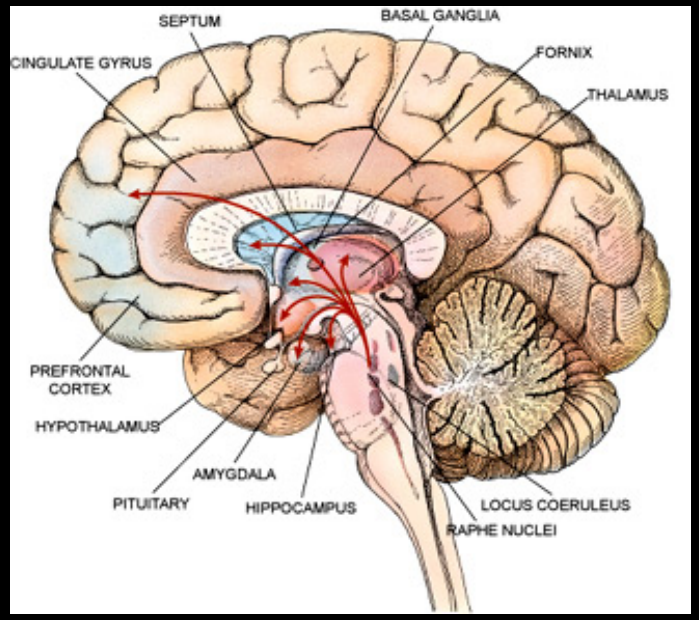
- Immediate
  - Remove foreign bodies from the brain
  - Control bleeding, swelling, intercranial pressure
  - Protect against additional exposures (take a knee)
- Long-Term
  - Pharmacotherapy to manage headaches, sleep problems
  - Rehabilitation to overcome cognitive impairments
  - Combined treatment for irritability, behavioral outbursts, and other PTSD symptoms

Summary: Public Health Implications

- To date, ~2.2 million SMs have served in OIF/OEF
- Based on available evidence, we estimate that
  - ~308,000 have PTSD
  - ~418,000 have TBI
  - >500,000 report conditions that require treatment
- How will the nation meet this need?
  - DOD Behavioral Health initiatives
  - DVA training program in evidence-based PTSD treatments
  - SAMHSA resources to increase access to community care for RC service members

Summary: Future Research

- For PTSD, available treatments are effective, but not perfect. Avenues for future research include:
  - Virtual reality to enhance exposure-based therapy
  - Tele-health to increase access to care
  - Exploit basic science on memory formation, recall, and reconsolidation to address PTSD "problems of forgetting"
- For TBI, more basic science on pathophysiology and mechanisms or repair
  - Fine grained imaging to explore small fiber trauma (DTI)
  - Neurotrophic factors to repair intracellular injuries

Questions?

Thank you!