

Combat-related PTSD and the Brain

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PTSD & Ethics: Guiding Questions

- What is PTSD?
- Should we prevent combat-related PTSD?
 - Screening for PTSD risk
 - Administration of drugs post-trauma
- As a nation, what do we owe our veterans with PTSD?

Outline

1. Evolution of PTSD concept
2. PTSD as a brain disorder
3. PTSD-related ethical and policy issues

“PTS” in Ancient Literature

- Battle of Marathon: “Epizelus, ... an Athenian, was in the thick of the fray, and behaving himself as a brave man should, when suddenly he was stricken with blindness, without blow of sword or dart; and this blindness continued thenceforth during the whole of his after life. ... He said that a gigantic warrior, with a huge beard, which shaded all his shield, stood over against him, but the ghostly semblance passed him by, and slew the man at his side.”
(Herodotus, 490 BCE)



“PTS” in Ancient Literature (cont.)

■ Spartan commander Leonidas at Battle of Thermopylae recognized that some of his troops “had no heart for the fight” and dismissed them (Herodotus, 480 BCE)



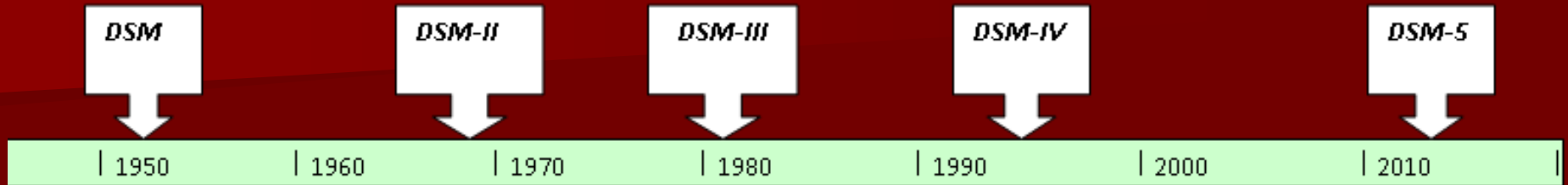
Evolving Concept of “PTS”

- US Civil War: Da Costa’s Syndrome (“soldier’s heart”)
 - Chest pain, palpitations, breathlessness, fatigue, sweating
 - No physical abnormalities
 - Now believed to be manifestation of anxiety disorder
- WW I: Shell Shock
 - Staring eyes; violent tremors; blue, cold extremities; unexplained deafness, blindness, paralysis
 - Hypothesized to be disruption of brain circuitry

Evolving Concept of “PTS” (cont.)

- WW II: Combat Fatigue
 - Understanding that intensity/duration of combat exposure increased risk
- Vietnam: Stress Response Syndrome
 - If symptoms lasted >6 mos after return from Vietnam, it was “pre-existing condition” making it a “transient situational disorder”
 - not service connected

Diagnostic & Statistical Manual of Mental Disorders



- 1952: Stress Response Syndrome caused by “gross stress reaction”
- 1968: Trauma-related disorders under “Situational Disorders”
- 1980: Posttraumatic stress disorder (anxiety disorder)
 - “Experienced an event that is outside the range of usual human experience and that would be markedly distressing to almost anyone.”
 - Re-experiencing, avoidance/numbing, increased arousal
- 1987: PTSD (anxiety disorder)
- 1994: PTSD (anxiety disorder; physiologic reactivity moved to re-experiencing)
- 2013: PTSD (trauma and stressor-related disorders)
 - Re-experiencing; avoidance; negative alterations in cognitions and mood; alterations in arousal and reactivity

DSM-IV Criteria

- Person experienced, witnessed, or was confronted with traumatic event
- **Person experienced fear, helplessness or horror**
- Person experiences the following symptoms for at least 1 month
- Significant distress or impairment

Re-experiencing ≥ 1

- Intrusive thoughts or memories
- Trauma related dreams
- Flashbacks
- Emotional distress in response to triggers
- Physical sx's in response to triggers

Avoidance ≥ 3

- Efforts to avoid trauma-related thoughts or feelings
- Avoidance of people, places or activities that trigger reminders of trauma
- Psychogenic amnesia
- Loss of interest in activities
- Feelings of estrangement from others
- Expectation of foreshortened future

Hyperarousal ≥ 2

- Difficulty with sleep
- Irritability and anger
- Attention and concentration problems
- Hypervigilance
- Exaggerated startle reaction

DSM-5 Criteria

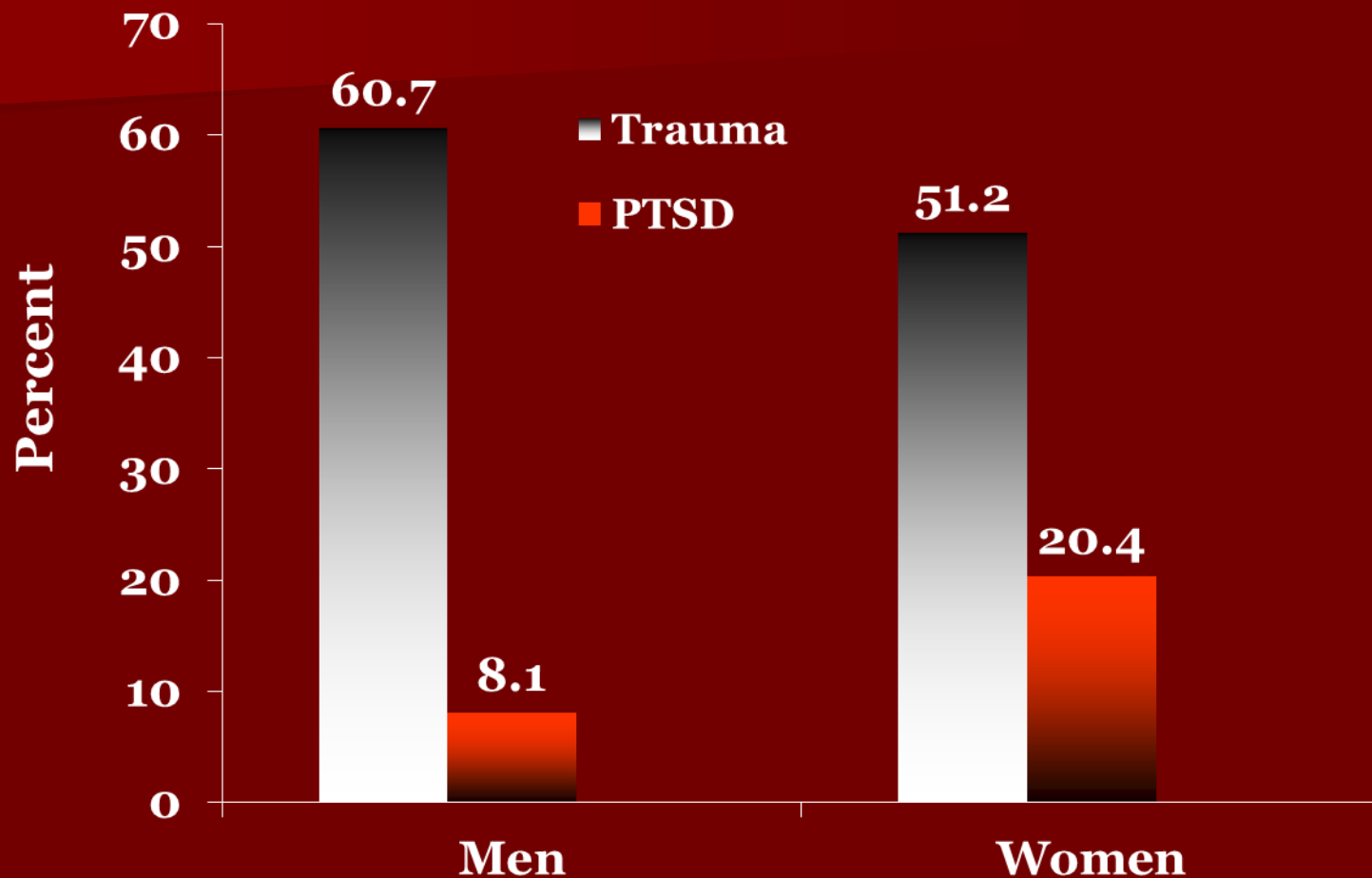
- Greater specificity about traumatic events
- Removal of “fear, helplessness, or horror” at time of trauma

Re-experiencing (1)	Avoidance (1)	Neg. Alterations in Cogn. & Mood (2)	Arousal (2)
<ul style="list-style-type: none"> • Intrusive memories • Nightmares • Flashbacks • Emotional distress to triggers • Physical reactions to triggers 	<ul style="list-style-type: none"> • Avoiding thought/feelings • Avoiding people, places, etc. 	<ul style="list-style-type: none"> • Psychogenic amnesia • Exaggerated negative beliefs (self, others, world) • Distorted cognitions about the trauma (e.g., self-blame) • Persistent negative emotions • Loss of interest • Estrangement from others • Lack of positive emotions 	<ul style="list-style-type: none"> • Irritability and anger • Reckless or self-destructive behavior • Hypervigilance • Exaggerated startle response • Concentration problems • Difficulty with sleep

Comparison to Depression

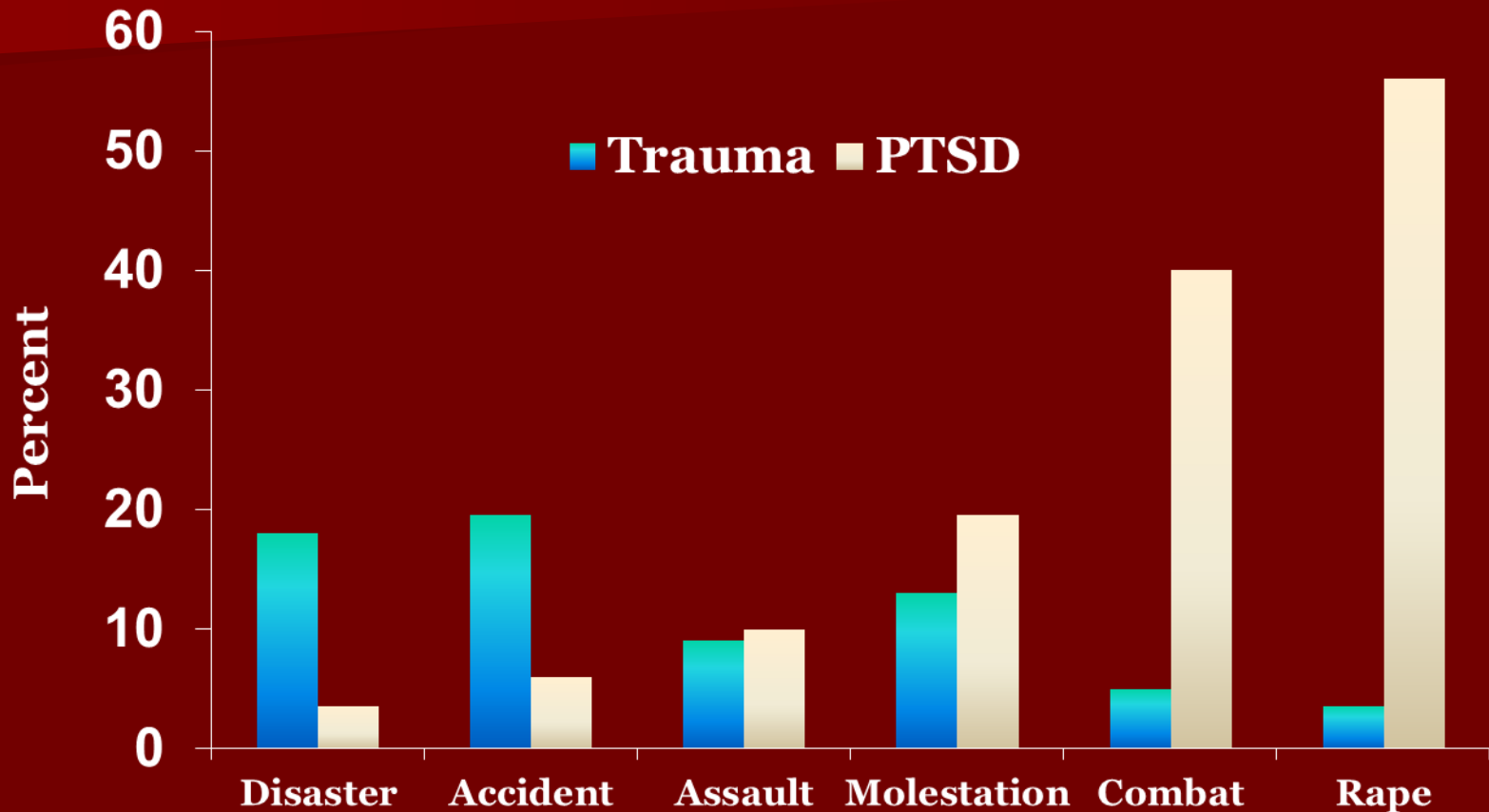
- Same 9 symptoms, same wording
- Still require 5 of 9 symptoms
 - Although *DSM-5* removed the bereavement exclusion for MDD

Prevalence of Trauma & PTSD in US



Kessler et al. (1995)

Rate of PTSD by Trauma Type



Kessler et al. (1995)

Implications of PTSD Definition?

- Differing rates of PTSD across *DSMs*
- Reliability of diagnoses across *DSMs*
- Susceptibility of PTSD to faking
 - Motivation for secondary gain?
 - Cases of “PTSD” among individuals who were not in combat, not in Vietnam, or even not in military (Burkett & Whitley, 1998, *Stolen Valor*)
- Does looking at physiological measures provide any clarity?

Neural Accounts of PTSD

Fear Conditioning: Model of PTSD

CS + US → CR

Laboratory
fear
conditioning

Tone

Shock

Freezing
to tone

Traumatic
fear
conditioning

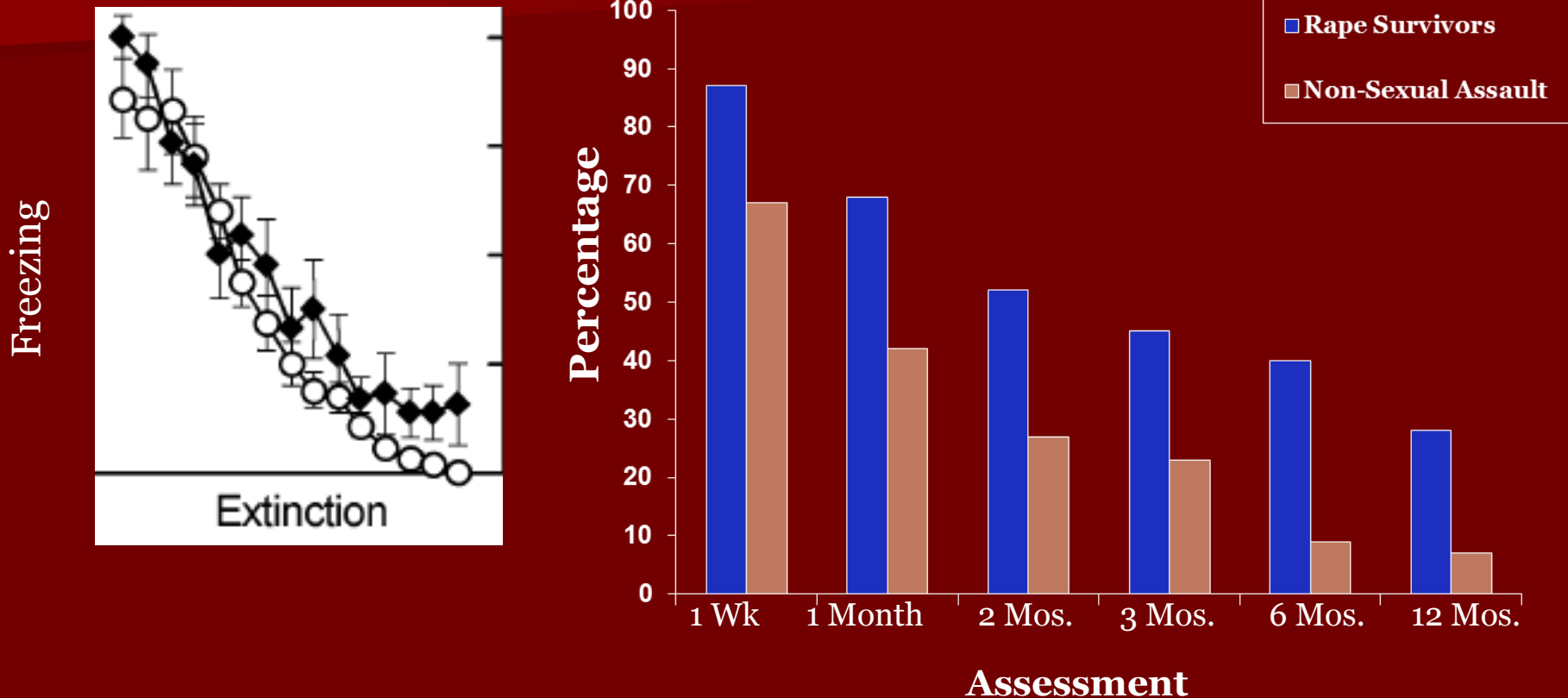
Bundle on
side of road

Improvised
Explosive
Device

Fear of
objects on
side of
road

Learned Fear Can Be Extinguished

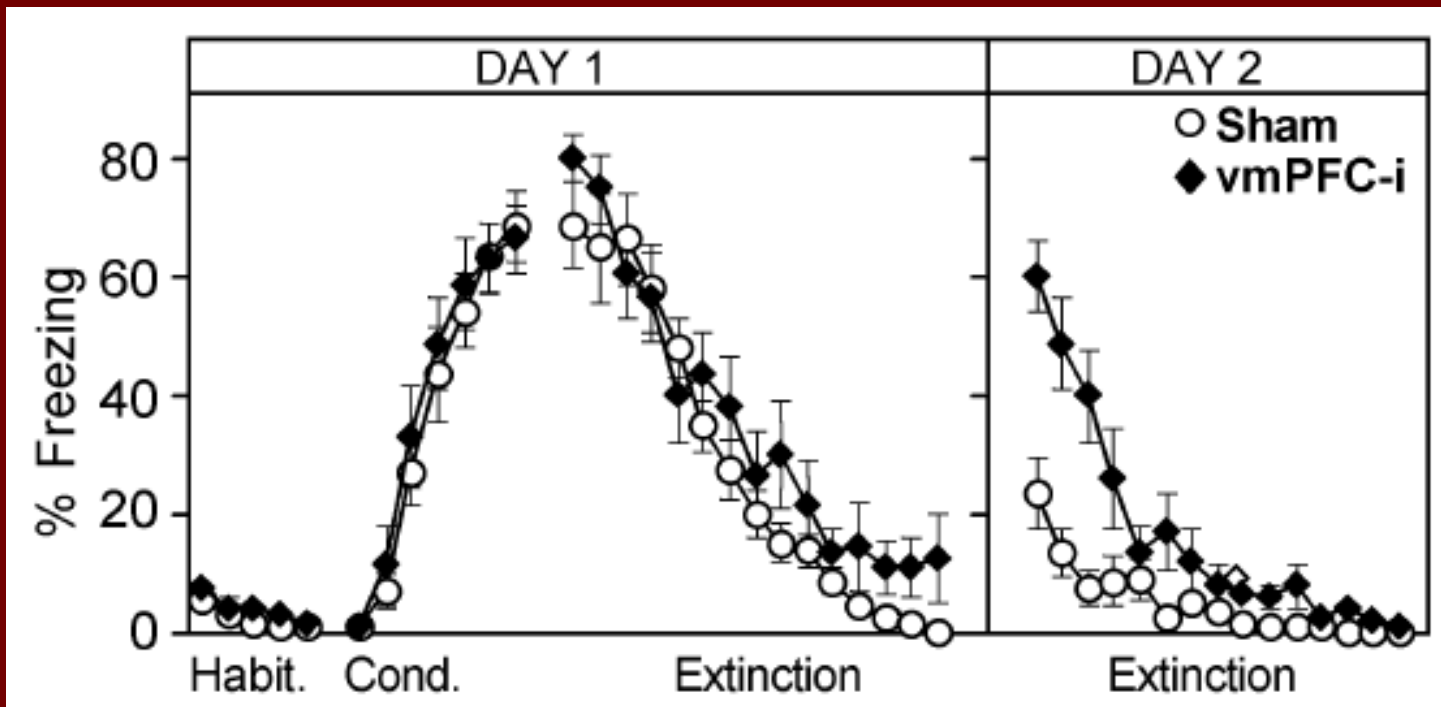
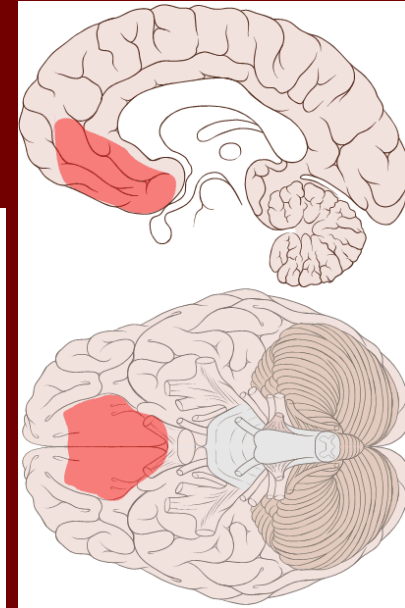
Trauma Survivors With PTSD



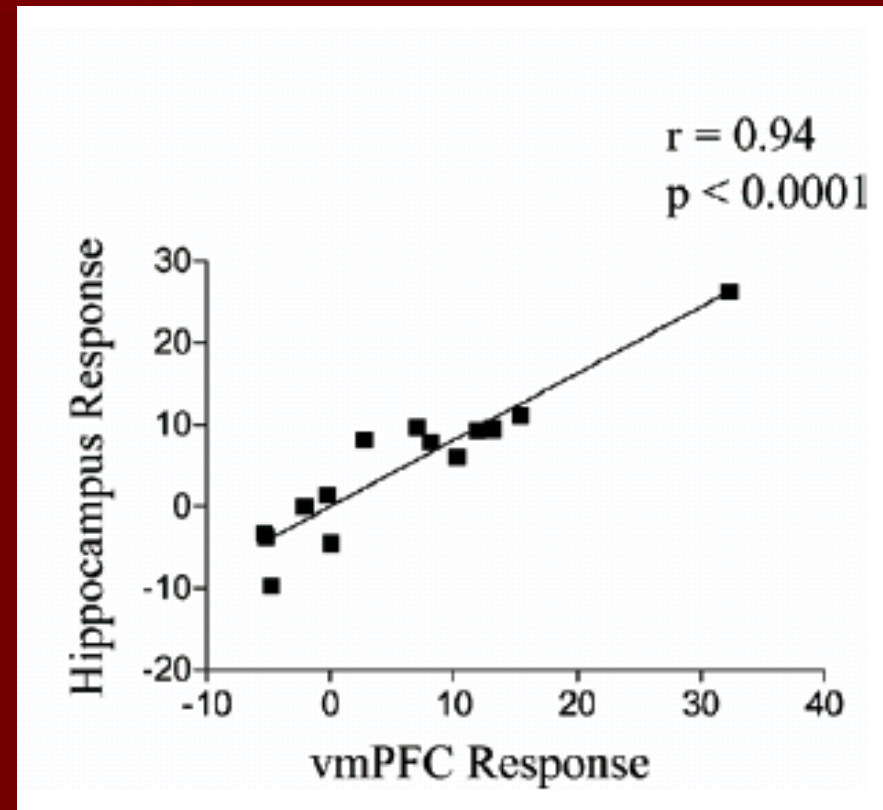
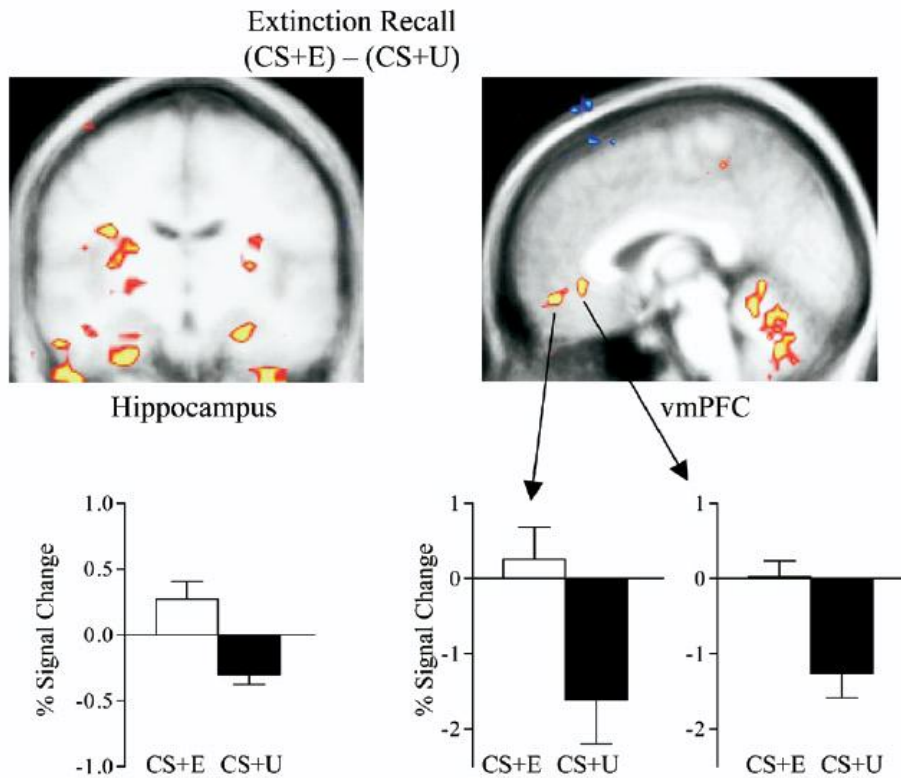
→ PTSD appears to represent impaired fear extinction.

Neural Bases of Fear Extinction Recall

- Ventromedial prefrontal cortex (vmPFC)



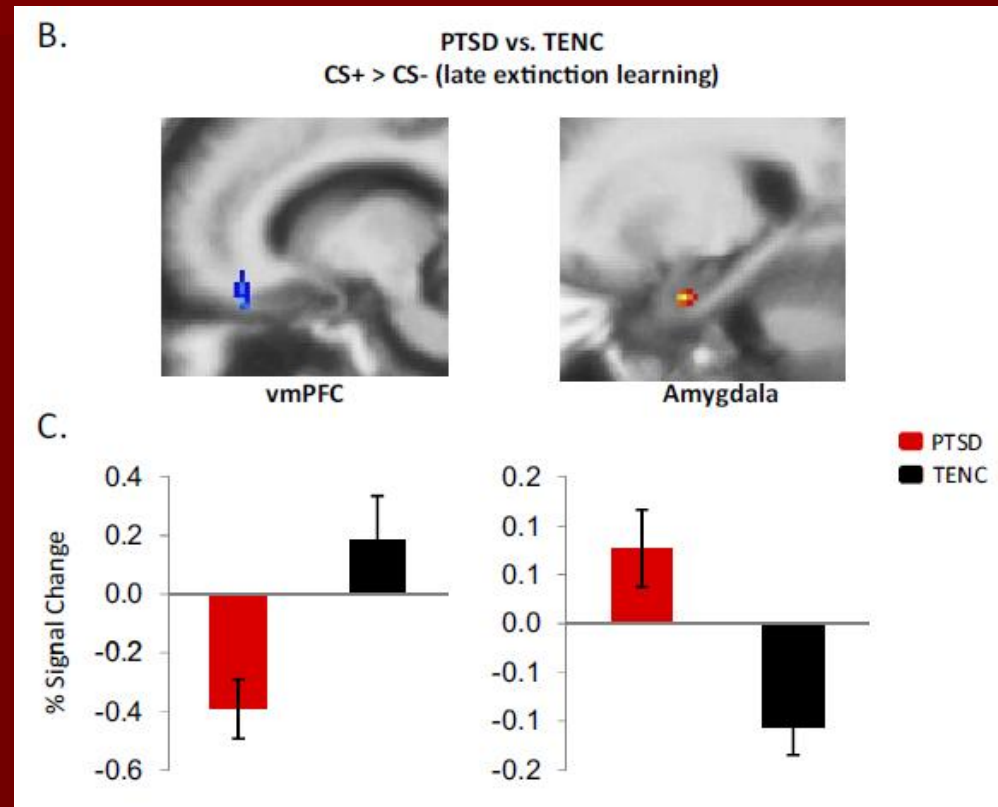
Recall of Fear Extinction: Humans



Milad et al. (2007)

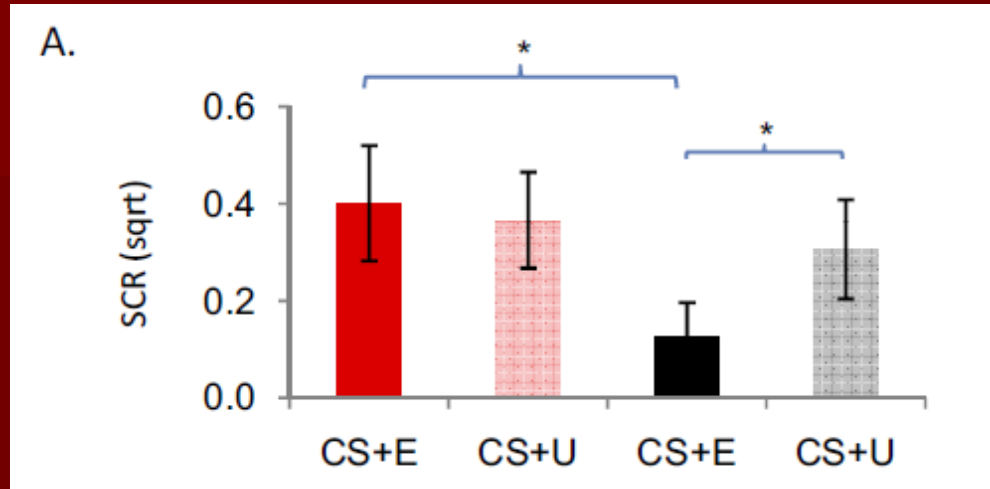
Extinction Recall in PTSD

- Enhanced amygdala and dampened vmPFC activation during extinction vs. trauma-exposed non-PTSD controls

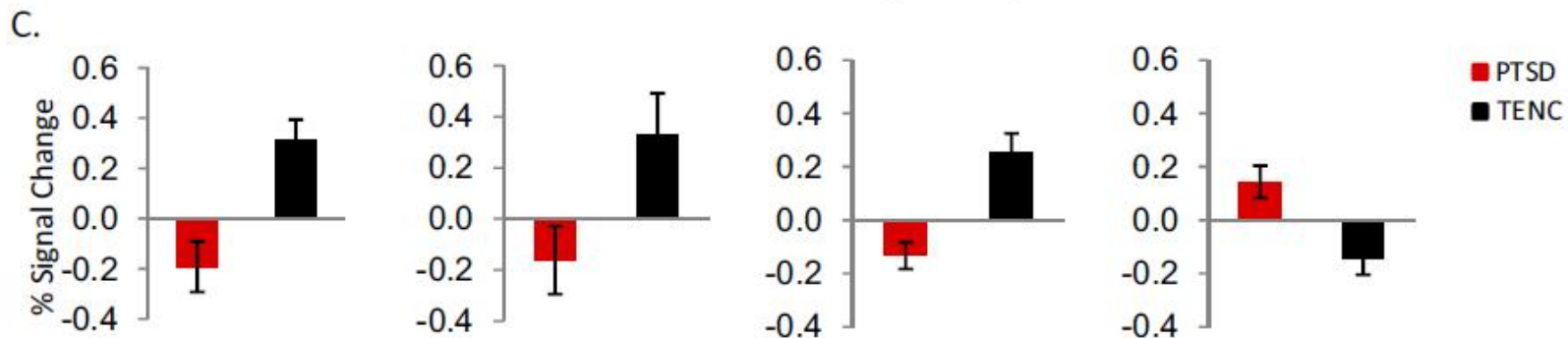
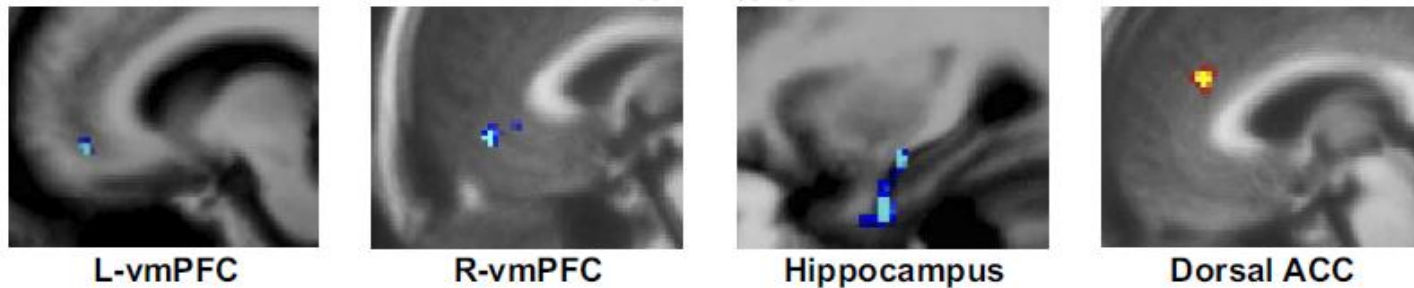


Extinction Recall in PTSD

- Impaired recall of extinction learning
 - Differential activation of vmPFC, hippocampus, and dorsal anterior cingulate

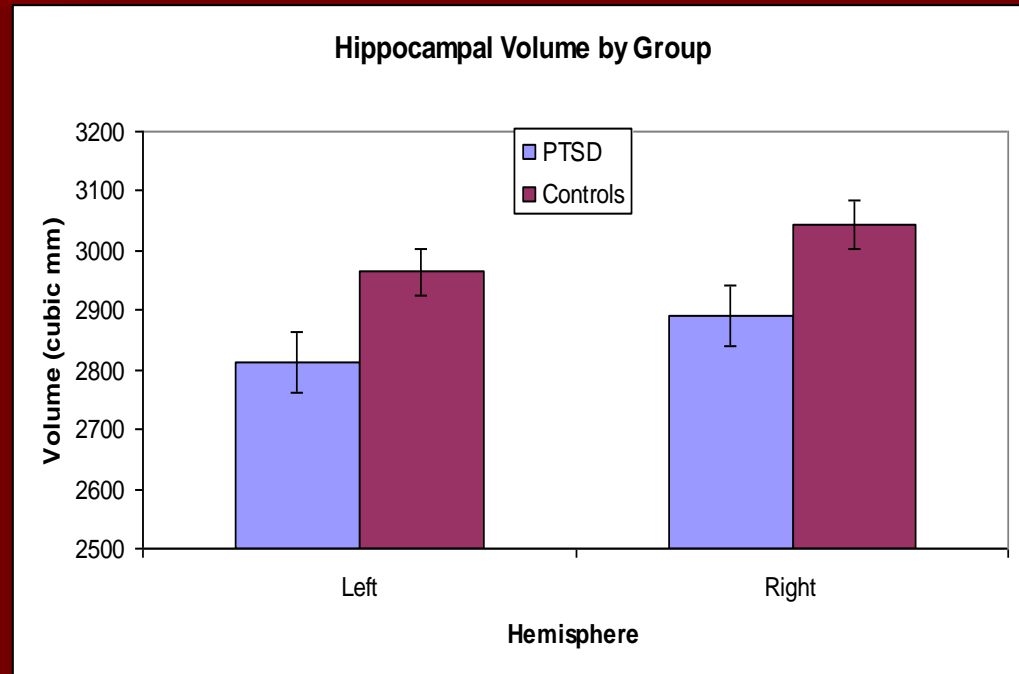


B. PTSD vs. TENC
CS+E > CS+U



Hippocampal Size in PTSD

- Meta-analysis
 - 215 PTSD patients, 325 controls
- Role of hippocampus in overgeneralization of fear learning in PTSD
- PTSD appears to damage the brain.



Effects of SSRIs on Hippocampal Size

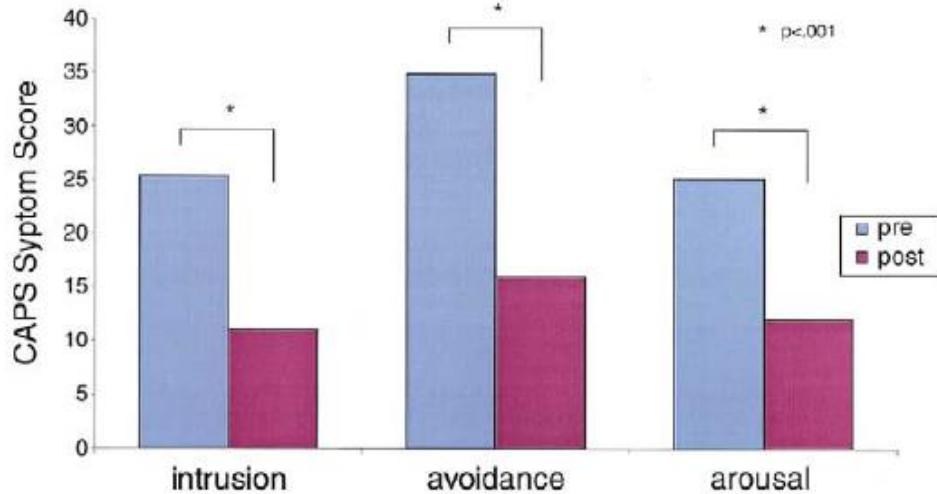
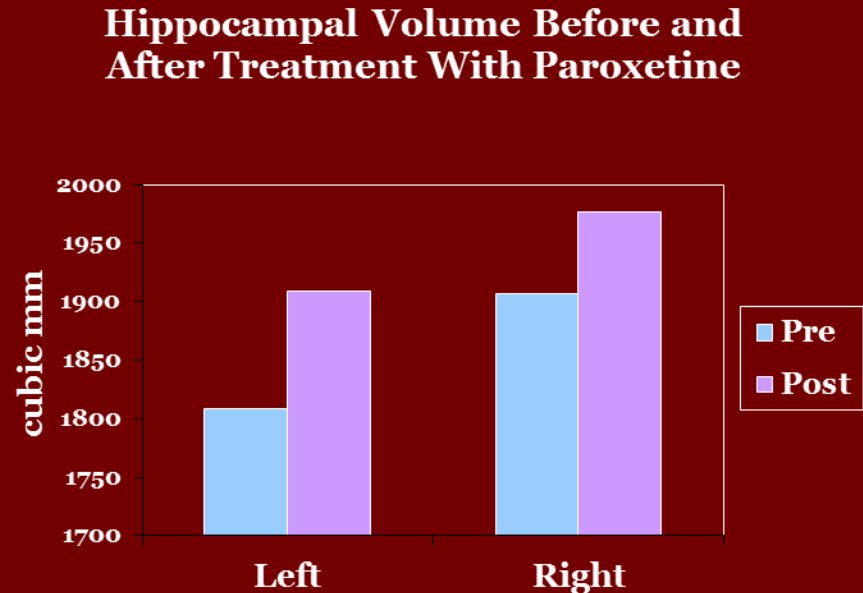
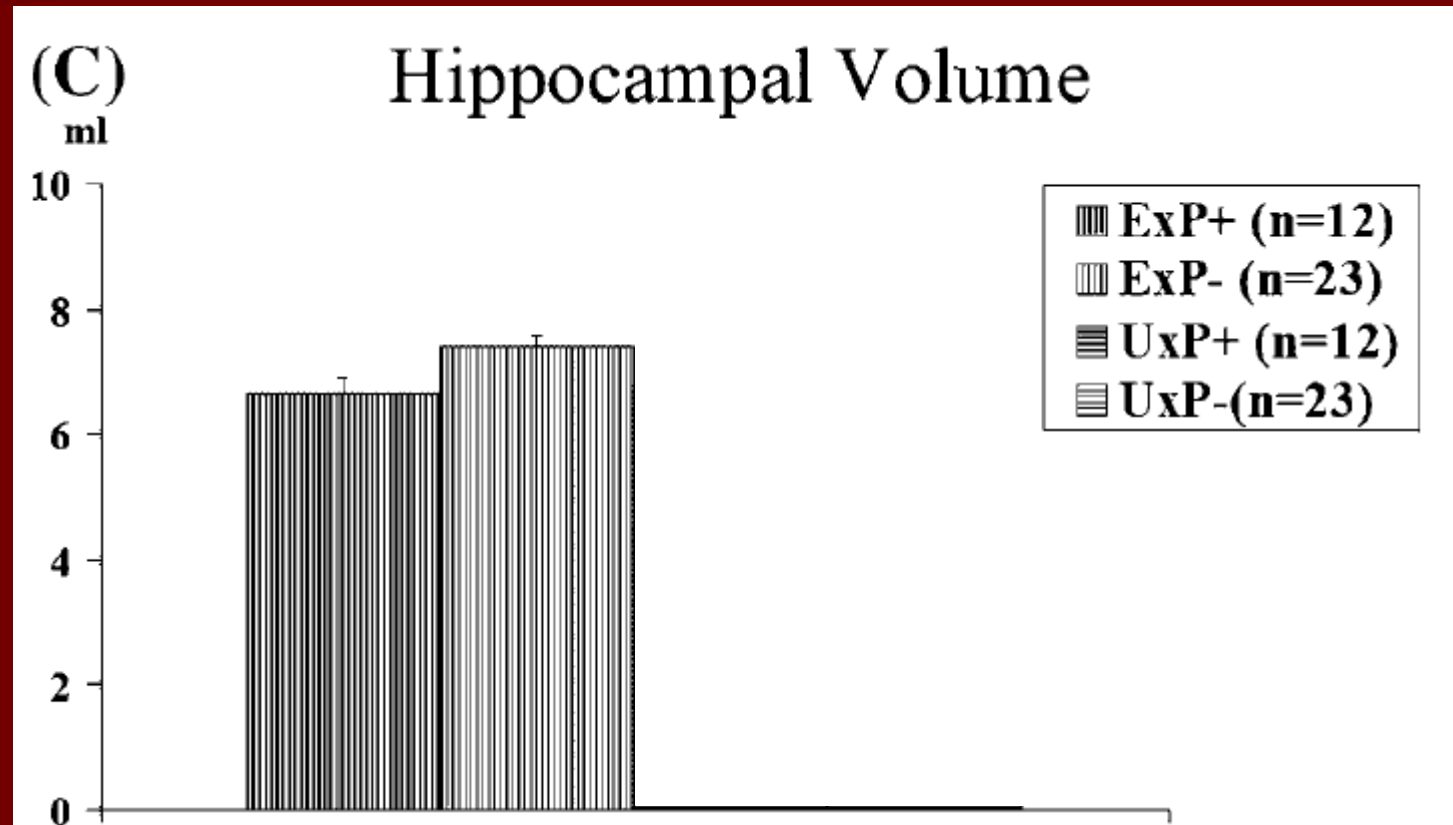


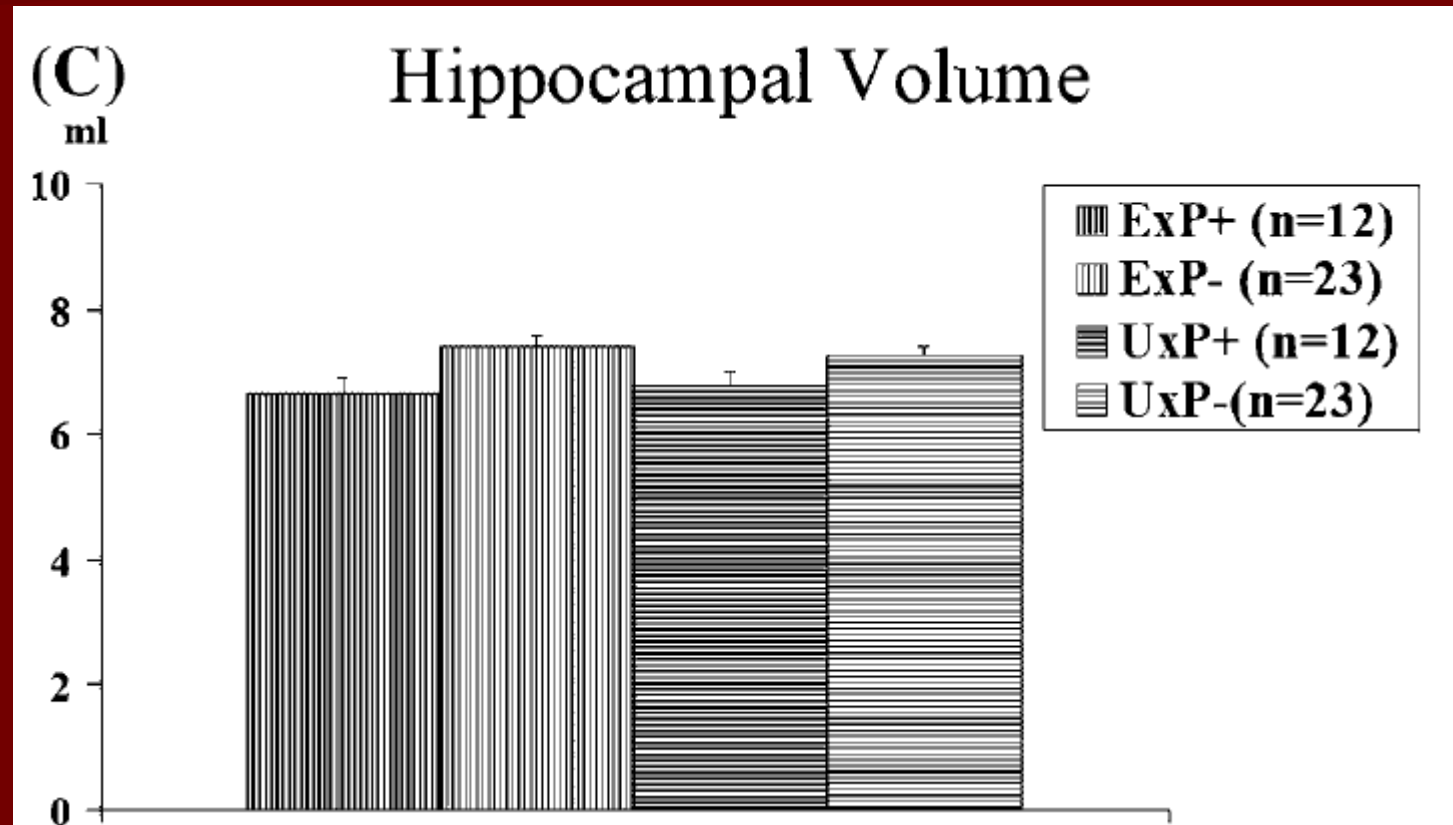
Figure 1. Changes in the Clinician-Administered Posttraumatic Stress Disorder (PTSD) Scale (CAPS) after long-term treatment.



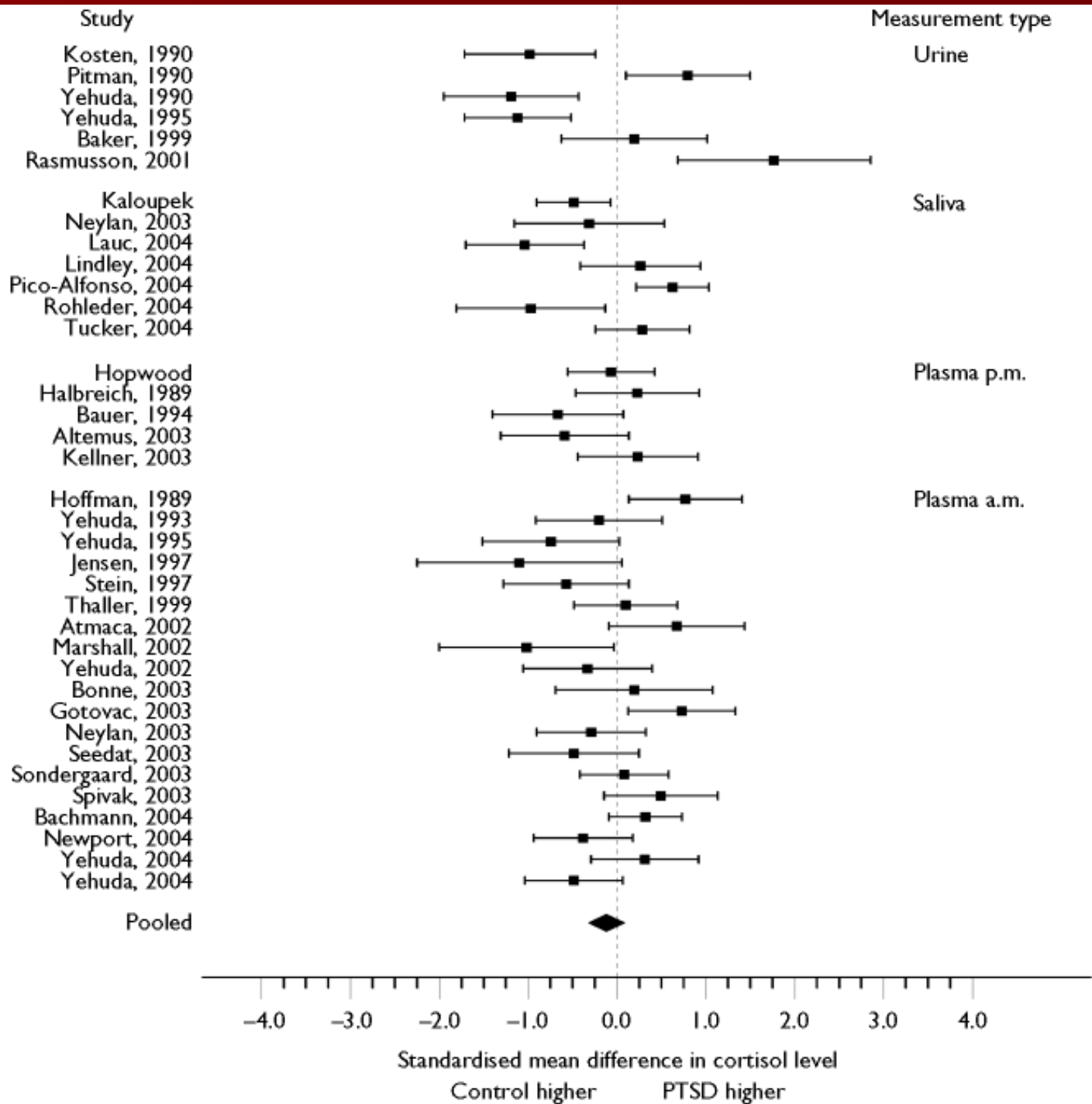
Does PTSD *Cause* Hippocampal Volume Differences?



Does PTSD *Cause* Hippocampal Volume Differences?



Cortisol and PTSD



Heterogeneity Within Categories

Table 1. Different Presentations of Posttraumatic Stress Disorder^a

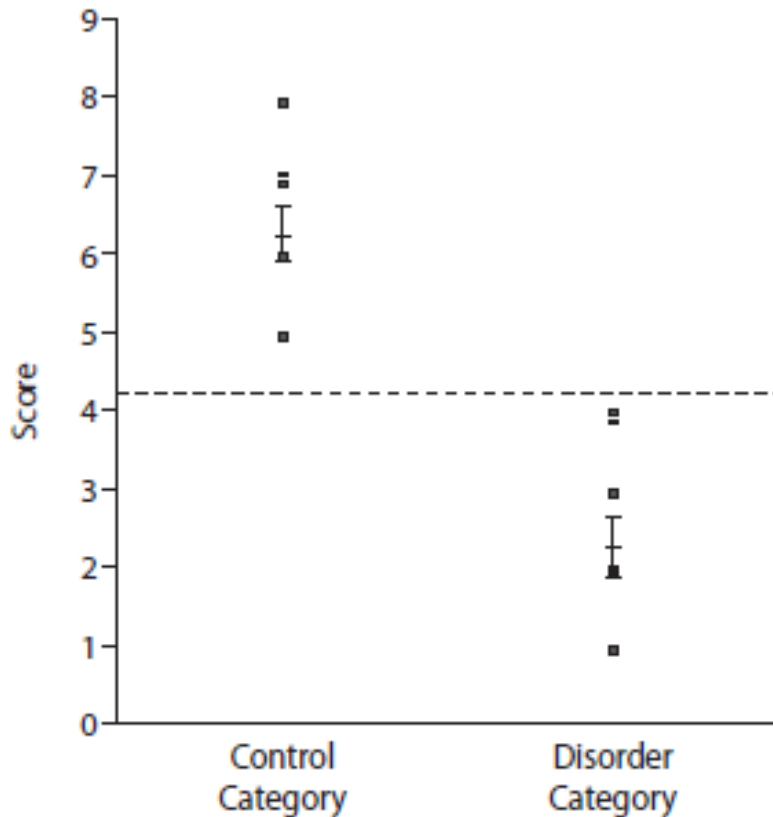
Variable	Patient 1	Patient 2
Trauma	Childhood sexual abuse	Car accident
Time since trauma	15 years	18 months
Reexperiencing	Intrusive distressing recollections	Nightmares
Numbing/avoidance	Avoiding trauma memory Psychogenic amnesia Sense of foreshortened future	Avoiding trauma reminders Lack of interest Feelings of detachment
Hyperarousal	Difficulty staying asleep Difficulty concentrating	Irritability Hypervigilance

Gillihan & Parens, 2011

Variability Within Categories

Figure 1. Nonoverlapping (A) Versus Overlapping (B) Hypothetical Score Distributions^a

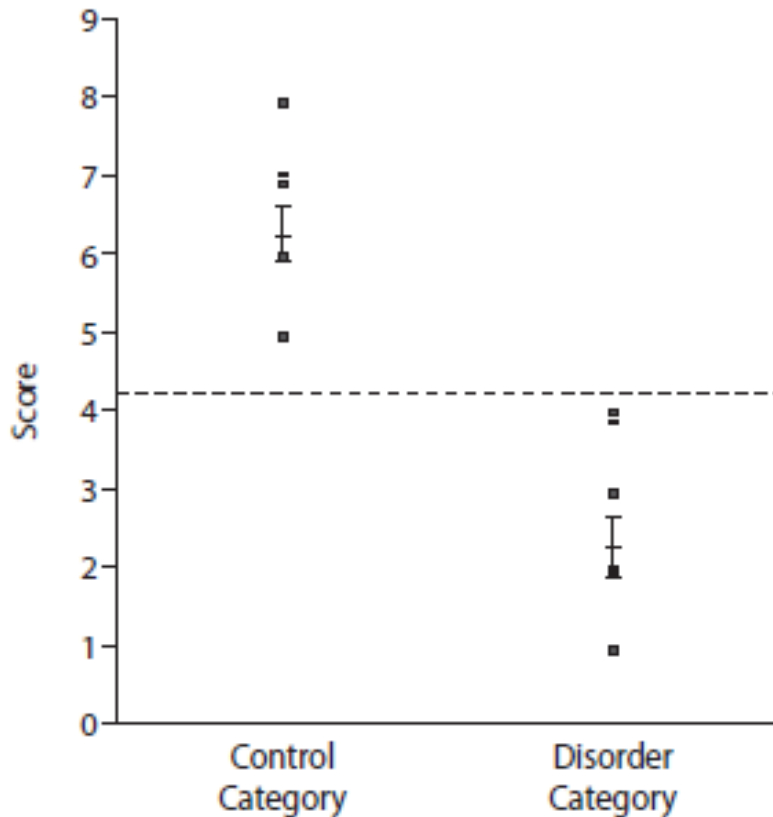
A. Nonoverlapping^b



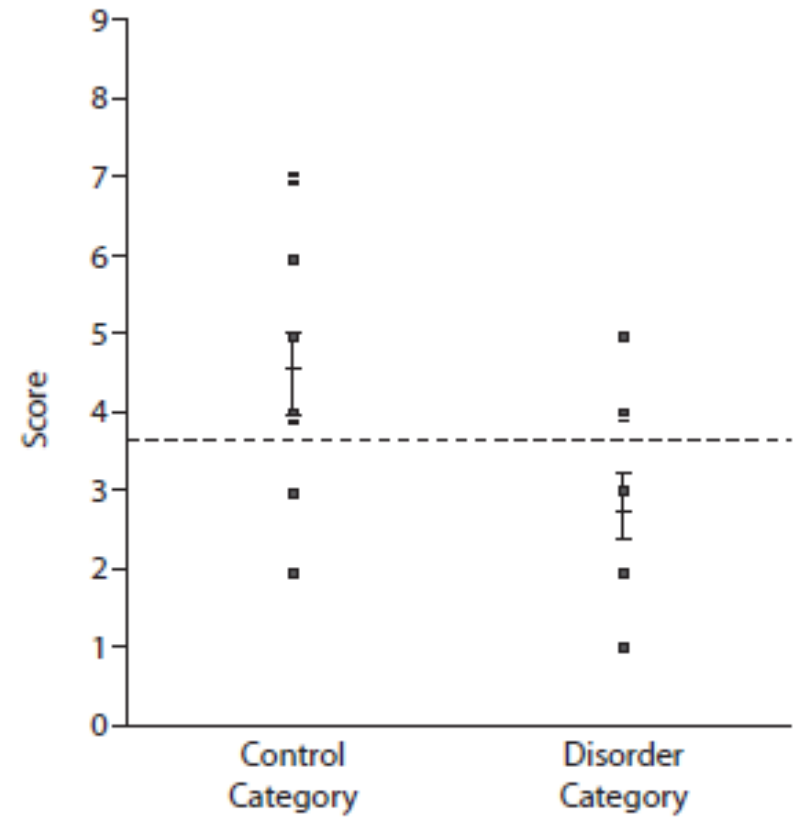
Variability Within Categories

Figure 1. Nonoverlapping (A) Versus Overlapping (B) Hypothetical Score Distributions^a

A. Nonoverlapping^b



B. Overlapping^c



PTSD & Brain: Summary

- PTSD is associated with reliable differences in brain structure, function
 - Unclear whether cause or consequence of PTSD
- Effective PTSD treatment changes the brain
- No psychobiologic diagnostic tests for PTSD

PTSD and Military- related Policy Issues

Who Should Get Treatment?

- Implications of treating and redeploying soldiers with PTSD?
 - Already know they're at risk for PTSD
- Prophylactic treatment?
 - Not yet developed, but trials conducted (propranolol; Pitman et al., 2002)
 - Are PTSD-like reactions at all *desirable* in some cases (e.g., perpetrators of My Lai massacre)?
 - Might the treatments interfere with adaptive changes (e.g., appropriate fear)?
 - Most soldiers would receive medication unnecessarily

Name Change Proposal

■ Posttraumatic Stress *Injury*

– Pro:

- “‘Injury’ suggests that people can heal with treatment. A disorder ... implies that something is permanently wrong.” (Gen. (ret.) Peter Chiarelli, US Army)
- “To be injured in the service to your country is entirely honorable in the military culture.” (Jonathan Shay, psychiatrist)

– Con:

- “The concept of injury usually implies a discrete time period. At some point, the bleeding will stop” (Matthew Friedman, National Center for PTSD)
- “The word ‘disorder’ reflects the fact that some people are more vulnerable than others.” (John Oldham, president, APA)

■ Still “PTSD” in *DSM-5*



Purple Heart for PTSD?

In favor

- “PTSD is a physical disorder because it damages the brain, making it no different from shrapnel wounds.”
- “These guys have paid at least as high a price as ... anybody with shrapnel wounds.”
- Effects of PTSD often last much longer than those of physical wounds
- Decrease stigma surrounding PTSD and seeking treatment for it

Opposed

- “I don’t think people should get the Purple Heart for almost getting wounded.”
- PTSD could be diagnosed in soldiers who *were confronted with* traumatic experiences outside the battlefield
- PTSD is susceptible to faking
- Rewards soldiers who are vulnerable to PTSD
- If PTSD, why not other trauma-related disorders with neural correlates (e.g., depression)?
- PTSD criteria change over time.

No Purple Heart for PTSD

Purple Heart Criteria

- First injury suffered to any part of the body from an outside force or agent
- Must happen in a combat theater
- Must be a direct result of enemy action
- Excluded: frostbite, heat stroke, food poisoning, accidents, self-inflicted wounds, jump injuries

DOD Verdict

- “PTSD is an anxiety disorder caused by witnessing or experiencing a traumatic event; it is not a wound intentionally caused by the enemy from an ‘outside force or agent,’ but is a secondary effect caused by ... a traumatic event.”

Summary

- Posttraumatic reactions to combat are as old as wars.
- PTSD is a highly debilitating condition.
- Specific brain areas are reliably associated with PTSD.
- Controversy has surrounded PTSD and related constructs.