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
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)
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
Evolution of 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
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

<table>
<thead>
<tr>
<th>Re-experiencing  &gt;1</th>
<th>Avoidance  &gt;3</th>
<th>Hyperarousal  &gt;2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrusive thoughts or memories</td>
<td>Efforts to avoid trauma-related thoughts or feelings</td>
<td>Difficulty with sleep</td>
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<tr>
<td>Trauma related dreams</td>
<td>Avoidance of people, places or activities that trigger reminders of trauma</td>
<td>Irritability and anger</td>
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<tr>
<td>Flashbacks</td>
<td>Psychogenic amnesia</td>
<td>Attention and concentration problems</td>
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<tr>
<td>Emotional distress in response to triggers</td>
<td>Loss of interest in activities</td>
<td>Hypervigilance</td>
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<tr>
<td>Physical sx's in response to triggers</td>
<td>Feelings of estrangement from others</td>
<td>Exaggerated startle reaction</td>
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<td>Expectation of foreshortened future</td>
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</table>
### DSM-5 Criteria

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

<table>
<thead>
<tr>
<th>Re-experiencing (1)</th>
<th>Avoidance (1)</th>
<th>Neg. Alterations in Cogn. &amp; Mood (2)</th>
<th>Arousal (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrusive memories</td>
<td>Avoiding thought/feelings</td>
<td>- Psychogenic amnesia</td>
<td>Irritability and anger</td>
</tr>
<tr>
<td>Nightmares</td>
<td>Avoiding people, places, etc.</td>
<td>- Exaggerated negative beliefs (self, others, world)</td>
<td>Reckless or self-destructive behavior</td>
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<tr>
<td>Flashbacks</td>
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<td>- Distorted cognitions about the trauma (e.g., self-blame)</td>
<td>Hypervigilance</td>
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<tr>
<td>Emotional distress to triggers</td>
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<td>- Persistent negative emotions</td>
<td>Exaggerated startle response</td>
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<tr>
<td>Physical reactions to triggers</td>
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<td>- Loss of interest</td>
<td>Concentration problems</td>
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<tr>
<td></td>
<td></td>
<td>- Estrangement from others</td>
<td>Difficulty with sleep</td>
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<td></td>
<td></td>
<td>- Lack of positive emotions</td>
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</table>
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

<table>
<thead>
<tr>
<th></th>
<th>CS</th>
<th>+</th>
<th>US</th>
<th>→</th>
<th>CR</th>
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<tbody>
<tr>
<td>Laboratory</td>
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<tr>
<td>fear conditioning</td>
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<td>Tone</td>
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<td>Shock</td>
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<td>Freezing to tone</td>
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<tr>
<td>Traumatic</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>fear conditioning</td>
<td></td>
<td></td>
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<td></td>
<td>Bundle on side of road</td>
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<td>Improvised Explosive Device</td>
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<td></td>
<td>Fear of objects on side of road</td>
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</tbody>
</table>
Learned Fear Can Be Extinguished

PTSD appears to represent impaired fear extinction.

→ PTSD appears to represent impaired fear extinction.
Neural Bases of Fear Extinction Recall

- Ventromedial prefrontal cortex (vmPFC)

Quirk et al., 2000
Recall of Fear Extinction: Humans

Milad et al. (2007)
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

![Graph showing SCR (sqrt) vs. CS+E, CS+U, CS+E, CS+U](image)

![Images of L-vmPFC, R-vmPFC, Hippocampus, and Dorsal ACC](image)

![Bar graphs showing % Signal Change for PTSD and TENC](image)
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.

Smith (2005)
Effects of SSRIs on Hippocampal Size

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

Vermetten et al., 2003
Does PTSD *Cause* Hippocampal Volume Differences?

Pitman et al. (2006)
Does PTSD *Cause* Hippocampal Volume Differences?

Pitman et al. (2006)
Cortisol and PTSD
# Heterogeneity Within Categories

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trauma</strong></td>
<td>Childhood sexual abuse</td>
<td>Car accident</td>
</tr>
<tr>
<td><strong>Time since trauma</strong></td>
<td>15 years</td>
<td>18 months</td>
</tr>
<tr>
<td><strong>Reexperiencing</strong></td>
<td>Intrusive distressing recollections</td>
<td>Nightmares</td>
</tr>
<tr>
<td><strong>Numbing/avoidance</strong></td>
<td>Avoiding trauma memory</td>
<td>Avoiding trauma reminders</td>
</tr>
<tr>
<td></td>
<td>Psychogenic amnesia</td>
<td>Lack of interest</td>
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<td></td>
<td>Sense of foreshortened future</td>
<td>Feelings of detachment</td>
</tr>
<tr>
<td><strong>Hyperarousal</strong></td>
<td>Difficulty staying asleep</td>
<td>Irritability</td>
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<tr>
<td></td>
<td>Difficulty concentrating</td>
<td>Hypervigilance</td>
</tr>
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Gillihan & Parens, 2011
Variability Within Categories

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

A. Nonoverlapping

Gillihan & Parens, 2011
Variability Within Categories

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

A. Nonoverlapping

B. Overlapping

Gillihan & Parens, 2011
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
<table>
<thead>
<tr>
<th><strong>In favor</strong></th>
<th><strong>Opposed</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>“PTSD is a physical disorder because it damages the brain, making it no different from shrapnel wounds.”</td>
<td>“I don’t think people should get the Purple Heart for almost getting wounded.”</td>
</tr>
<tr>
<td>“These guys have paid at least as high a price as ... anybody with shrapnel wounds.”</td>
<td>PTSD could be diagnosed in soldiers who <em>were confronted with</em> traumatic experiences outside the battlefield</td>
</tr>
<tr>
<td>Effects of PTSD often last much longer than those of physical wounds</td>
<td>PTSD is susceptible to faking</td>
</tr>
<tr>
<td>Decrease stigma surrounding PTSD and seeking treatment for it</td>
<td>Rewards soldiers who are vulnerable to PTSD</td>
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<td></td>
<td>If PTSD, why not other trauma-related disorders with neural correlates (e.g., depression)?</td>
</tr>
<tr>
<td></td>
<td>PTSD criteria change over time.</td>
</tr>
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</table>
### No Purple Heart for PTSD

<table>
<thead>
<tr>
<th><strong>Purple Heart Criteria</strong></th>
<th><strong>DOD Verdict</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>First injury suffered to any part of the body from an outside force or agent</td>
<td>“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.”</td>
</tr>
<tr>
<td>Must happen in a combat theater</td>
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<tr>
<td>Must be a direct result of enemy action</td>
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<tr>
<td>Excluded: frostbite, heat stroke, food poisoning, accidents, self-inflicted wounds, jump injuries</td>
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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.