

Trauma: Continuing to Find Ways to Heal

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Overview

- **Historical perspective on PTSD**
- **PTSD in DSM-5**
- **Epidemiology of PTSD**
- **Neurobiology of PTSD**
- **Current treatments for PTSD**
- **Looking to the future**

Historical Perspective on PTSD

Hysteria and Sexual Abuse

- **Sigmund Freud – patients told him of sexual abuse and incest**
- **1896 Freud published “The Aetiology of Hysteria” – 18 case studies**
- **Privately repudiated by Freud within one year due to criticism and ostracism from his medical and psychiatric colleagues**

“Shell Shock” during World War I

- 8 million men died in 4 years
- Brutal trench warfare
- Combat soldiers acted like “hysterical woman”
- Soldiers lost their memory and ability to feel
- “Mental breakdowns” accounted for 40% of British battle casualties
- Medical interest in psychological trauma faded a few years after the war ended

Lessons from World War II

- “It was recognized for the first time that any man could break down under fire and that psychiatric casualties could be predicted in direct proportion to the severity of combat exposure”
- Shortly after the war: “the lasting effects of war trauma were once again forgotten”

Herman, J.; Trauma and Recovery; BasicBooks; 1992.

Vietnam War

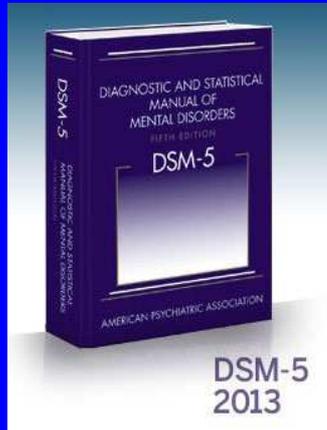
- **Traumatized veterans, often decorated war heroes, wouldn't let us forget**
- **1970 – Psychiatrists met with a veteran formed group “Vietnam Veterans Against the War”**
- **Vietnam Veterans self-organized “rap groups”**

1980

**American Psychiatric Association
created a new diagnostic entity which
was listed in the Diagnostic and
Statistical Manual of Mental Disorders,
Third Edition (DSM-III):**

**Posttraumatic Stress Disorder
(PTSD)**

PTSD in DSM-5



DSM-5; Fifth Edition; American Psychiatric Publishing;
Washington, DC; 2013.

**In DSM-5, PTSD was moved
into a new category**

**DSM-IV-TR:
PTSD was listed as an Anxiety Disorder**

**DSM-5:
PTSD is listed in a new category –
Trauma and Stressor Related Disorders**

Traumatic Event

Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:

- 1) Directly experiencing the traumatic event(s).**
- 2) Witnessing, in person, the event(s) as it occurred to others.**
- 3) Learning that the traumatic event(s) occurred to a close family member or close friend.**
- 4) Experiencing repeated or extreme exposure to aversive details of the traumatic event(s).**

Re-experiencing

Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:

- 1) Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).**
- 2) Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).**
- 3) Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring.**
- 4) Intense or prolonged psychological distress at exposure to internal or external cues.**
- 5) Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).**

Avoidance/Numbing

Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:

- 1) Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).**
- 2) Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).**

Negative cognitions/mood

Negative alterations in cognition and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by 2 (or more) of the following:

- 1) Inability to remember important aspects of the traumatic event(s).**
- 2) Persistent and exaggerated negative beliefs or expectations about oneself, others or the world.**
- 3) Persistent distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.**
- 4) Persistent negative emotional state.**
- 5) Markedly diminished interest/participation in significant activities.**
- 6) Feelings of detachment or estrangement from others.**
- 7) Persistent inability to experience positive emotions.**

Hyperarousal

Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by 2 (or more) of the following:

- 1) Irritable behavior and angry outbursts**
- 2) Reckless or self-destructive behavior**
- 3) Hypervigilance**
- 4) Exaggerated startle response**
- 5) Problems with concentration**
- 6) Sleep disturbance**

“Complex” PTSD Subtype??

- Common among individuals exposed at an early age to severe and chronic trauma**
- More disabling**
- Chronic symptoms are common**
- More Comorbidity**
- More severe dissociation**

PTSD as part of a Spectrum?

Acute Stress Disorder



PTSD



Dissociative Disorders



Dissociative Identity Disorder

Epidemiology of PTSD

PTSD - Prevalence

- PTSD is the 5th most prevalent psychiatric condition*
- PTSD prevalence in the United States**
 - Lifetime = 8.7%
 - Annual = 3.5%
- Highest rates (ranging from 1/3 to more than 1/2 of those exposed) are found among**
 - Survivors of rape
 - Military combat and captivity
 - Ethnically or politically motivated internment and genocide

*From Part 2 of the National Comorbidity Survey
(from 5,877 respondents ages 15 to 54 from Sept 1990 to Feb 1992)

**DSM-5

PTSD – Risk Factors

Characteristics of the traumatic event

- Severity
- Duration
- Proximity of exposure

PTSD – Risk Factors

Characteristics of the individual

- Family history
- Genetic vulnerability
- Social supports
- Childhood events
- Preexisting psychiatric disorders
- Individual personality traits

Common Traumatic Events

Some common traumatic events in the National Comorbidity Survey included:

- Witnessing injury/death
- Sexual molestation/rape
- Natural disaster/fire
- Physical attack or abuse/threatened with a weapon
- Life-threatening accident
- Combat
- Shock

Lifetime incidence of experiencing a traumatic event severe enough to cause PTSD is over 50%*

Females = 51%

Males = 61%

Approximately 20% of individuals exposed to a traumatic event may develop PTSD

*From Part 2 of the National Comorbidity Survey
(from 5,877 respondents ages 15 to 54 from Sept 1990 to Feb 1992)

PTSD – Clinical Course

Can occur at **any age**, beginning after the first year of life

PTSD symptoms **usually begin within the first 3 months** following the traumatic event

Symptom onset **may be delayed for months or years** after the traumatic event (onset > 6 months post trauma = **“delayed expression”**)

Symptoms of PTSD may persist for months or years following the traumatic event

PTSD – Clinical Course

Approximately 50% of all cases of PTSD are chronic

Acute:

Duration of symptoms is less than 3 months

Chronic:

**Duration of symptoms is 3 months or more;
cases have been reported to have lasted over 50
years.**

In PTSD – Comorbidity is the Rule



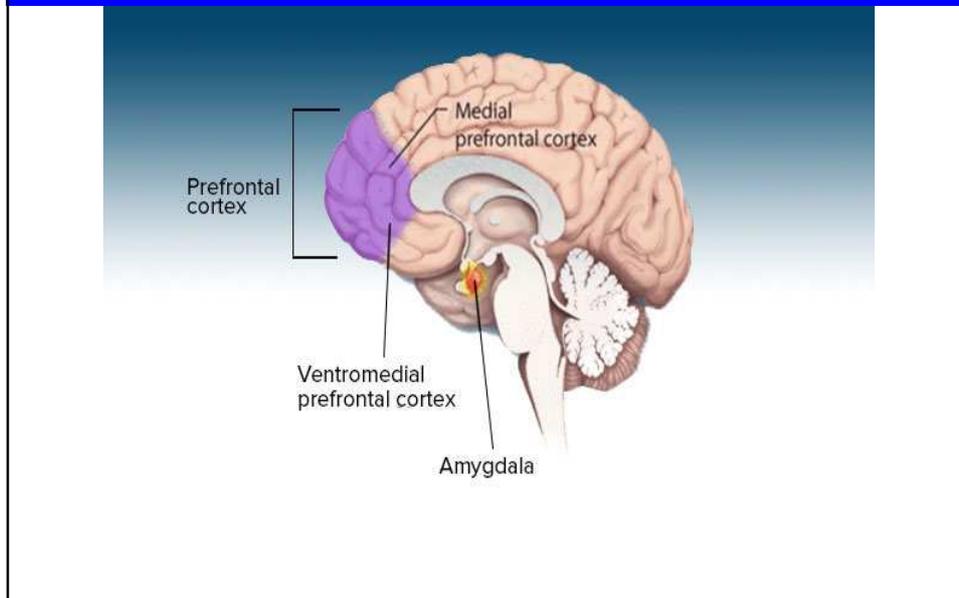
**Comorbid diagnoses can help design
a pharmacologic strategy**

Neurobiology of PTSD

Brain Regions Activated by Fear and Life-Threatening Situations

- **Amygdala**
 - Activates the circuitry of fear in milliseconds
 - Epicenter of emotional understanding
- **Hippocampus**
 - Learning and memory encoding
 - Feedback inhibition of the stress response
- **Locus Coeruleus**
 - Part of the brainstem involved with physiological responses to stress and panic
- **Prefrontal Cortex**
 - “thinking brain”

The Human Brain



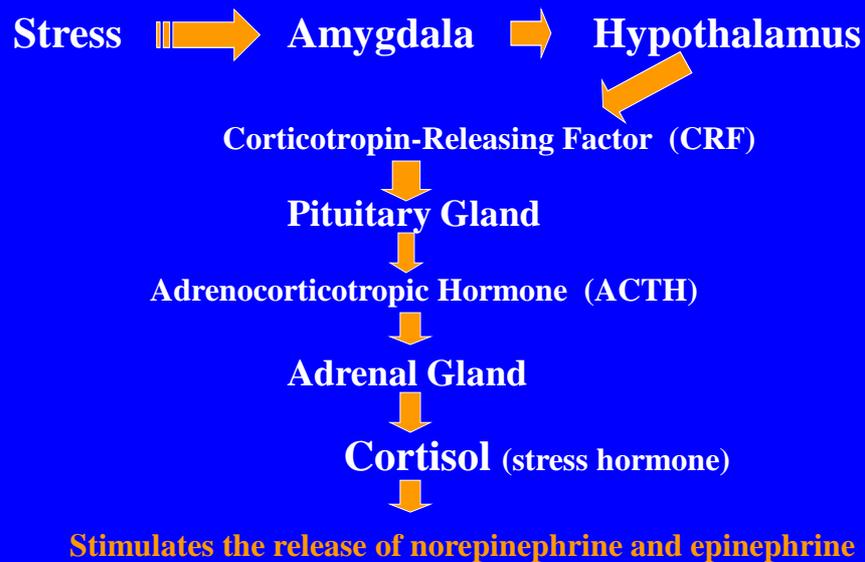
Genetic risk factors for PTSD

- Pre-trauma small hippocampi
- Phenotype of the serotonin transport pump gene's (SLC6A4) promoter sequence
 - s,s transporter gene = less transport pumps
 - s,l or l,s transporter gene = intermediate
 - l,l transporter gene = more transport pumps
- Epigenetic modifications
 - Methylation of promoter sequences of genes

Systems Activated by Stress

- **Adrenergic**
- **Noradrenergic**
- **Dopaminergic**
- **Serotonergic**
- **Opiate**
- **Benzodiazepine**
- **Hypothalamic-Pituitary-Adrenal (HPA)**
- **Hypothalamic-Pituitary-Thyroid (HPT)**

Hypothalamic-Pituitary-Adrenal Axis



Observations in PTSD

- **Plasma cortisol levels in the immediate aftermath of a MVA or rape who later develop PTSD are lower than in trauma survivors who do not develop PTSD**
- **Significantly lower urinary cortisol levels in Holocaust survivors with PTSD than in Holocaust survivors without PTSD and in a control group**

Neuroimaging Findings in PTSD

- **Four MRI studies have examined hippocampal (involved in learning & memory) volume in individuals with PTSD**
- **Right hippocampal volume was decreased 8% in Vietnam veterans with combat-related PTSD compared to controls**
- **Left hippocampal volume was decreased 5% in 21 sexually abused women compared with 21 non-abused women controls**

Effects of Severe Trauma During Childhood

- **Effects the Neurobiological Development of the Brain (Especially the HPA Axis)?**
- **Creates Brain Neurophysiology that requires a unique pharmacological strategy?**

Current Treatments for PTSD

Current Treatments for PTSD

- **Pharmacotherapy**
- **Stress-Inoculation Training (SIT)**
- **Prolonged Exposure (PE)**
 - Computer variation = “virtual reality”
- **Trauma Focused Cognitive Behavioral Therapy**
- **Cognitive Processing Therapy**
- **Dialectic Behavioral Therapy**
- **Eye Movement Desensitization and Reprocessing (EMDR)**
- **Art Therapy**

Current Treatments for PTSD

Pharmacotherapy

- **Antidepressants (many)**
 - Only 2 medications are FDA approved for PTSD = Zoloft (sertraline) and Paxil (paroxetine)
- **Anxiolytics (many)**
- **Atypical Antipsychotics (many)**
- **Alpha-2-agonists (clonidine, guanfacine)**
- **Alpha-1B-antagonists (prazosin)**
- **Beta-adrenergic antagonists (Inderal, others)**
- **Mood stabilizers (lithium, Depakote, Tegretol)**

SSRIs

- **Sertraline was the first medication FDA approved for PTSD (December 7, 1999)**
 - Dosage range is 50-200mg per day
- **Paroxetine is the only other FDA approved medication**
 - Dosage range is 20-60mg per day
- **Efficacious in three core symptom clusters of PTSD: reexperiencing, avoidance/numbing, and hyperarousal**
- **Maintain treatment for *at least* one year**
- **Fluoxetine and fluvoxamine seem efficacious as well (several published studies)**
- **case reports for venlafaxine & nefazodone**

Current Treatments for PTSD

Stress-Inoculation Training (SIT)

- **conceptualization phase**
- **skills acquisition and rehearsal**
- **application and follow through**

Current Treatments for PTSD

Prolonged Exposure (PE)

Computer variation = “virtual reality”



Current Treatments for PTSD

Trauma Focused Cognitive Behavioral Therapy

CBT modified for use with children and adolescents (ages 3 to 18).

Provide psycho-education to both the child and the caregivers and help them to identify and cope with emotions, thoughts and behaviors.

Individual sessions for both the child and the parents, as well as parent-child joint sessions.

Current Treatments for PTSD

Trauma Focused Cognitive Behavioral Therapy

- Psychoeducation and Parenting skills
- Relaxation
- Affective Expression and Regulation
- Cognitive Coping
- Trauma Narrative Development and Processing
- In Vivo Gradual Exposure
- Conjoint Parent-Child sessions
- Enhancing Safety and Future Development

Current Treatments for PTSD

Cognitive Processing Therapy

- Modification of traditional Cognitive Behavioral Therapy
- 12 to 16 sessions
- Individual or group
- Individual writes a narrative of the trauma
- This narrative is then processed with cognitive techniques to help the individual move beyond “stuck points” and stop using avoidance as a defense.
- By processing the memory and emotions of the trauma, the experience can be integrated more fully, facilitating recovery.

Current Treatments for PTSD

Dialectic Behavioral Therapy

- Developed by Marsha M. Linehan, Ph.D. at the University of Washington, Seattle
- Published her core work in two consecutive texts:
Linehan, M.M. (1993). Cognitive behavioral therapy of borderline personality disorder. New York: Guilford Press.
Linehan, M.M. (1993). Skills Training Manual for Treating Borderline Personality Disorder. New York: Guilford Press.
- Remains the most effective treatment intervention for individual's with a Borderline Personality Disorder

Current Treatments for PTSD

Dialectic Behavioral Therapy

- Four elements of DBT:
 - Mindfulness training
 - Cognitive behavioral therapy
 - Psycho-education
 - The “dialectic” of distress tolerance/acceptance and personal change and emotional growth

Current Treatments for PTSD

Eye Movement Desensitization and Reprocessing (EMDR)

Memory encoding and retrieval processes may take place in both the right and left hemispheres simultaneously for a single memory. If so, the corpus collosum would play an important role in inter-hemispheric communication to recall/reprocess memories.

Bilateral saccadic eye movements may increase the interaction between the left and right cerebral hemispheres. Memories and emotions of the trauma are discussed while the clinician directs the saccadic eye movements, theoretically allowing for recall and reprocessing of the trauma.

Propper RE and Christman SD. Interhemispheric Interaction and Saccadic Horizontal Eye Movements. *J of EMDR Practice and Research*. 2008; 2:269-281.

Current Treatments for PTSD

Art Therapy



Images from the NICoE (National Intrepid Center of Excellence) Healing Arts Program/Melissa S. Walker, MA, ATR.

Civilian versus Combat Trauma

- **Civilians seem to respond better to SSRIs than do Veterans with combat exposure**
- **Is childhood onset of trauma (affecting brain development) a factor?**
- **Is type of trauma a factor?**
- **Is PTSD a symptom complex with divergent etiologies/neurodevelopmental risk factors?**

PTSD: Looking to the future

Prevention

- **Eliminate accidents**
- **Eliminate sexual assaults**
- **Eliminate child abuse**
- **Eliminate wars**
- **Eliminate violent crimes**
- **Eliminate natural disasters**
- **Eliminate acts of terror**
- **Eliminate disease**

Novel Medication Development

Our current limited understanding of the physiology of PTSD already provides numerous pharmacological intervention targets that may help reduce symptoms.

Current research and drug development has been significantly eroded by economic and political factors.

Increasing funding for new drug development may facilitate novel medications to help treat PTSD.

D-cycloserine combined with Virtual Reality

- 156 veterans of the Iraq and Afghanistan wars with PTSD
- Five sessions of Virtual Reality exposure augmented with:
 - **D-Cycloserine 50mg**
 - **Alprazolam 0.25mg**
 - **placebo**
- At post treatment, D-cycloserine had the **lowest cortisol reactivity and smallest startle response** during virtual reality scenes.
- Alprazolam impaired recovery

Rothbaum BO, Price M, et al. A Randomized, Double-Blind Evaluation of D-Cycloserine or Alprazolam Combined With Virtual Reality Exposure Therapy for PTSD in Iraq and Afghanistan War Veterans. Am J Psychiatry. 2014; 171:640-648.

Improving on Current Therapies

- Developing new therapies
- Improving on current therapies
- Working closely with individuals with PTSD to optimize interventions
- Tailor treatments to specific type of trauma
- Increase involvement of support network
- Increase access to peer-run support groups

Genetics may facilitate novel treatment modalities

Phenotype of the serotonin transport pump gene's (SLC6A4) promoter sequence

Parental Genotypes	Possible phenotypes of children
s,s	? increased risk of anxiety/depression
s,l	? some risk of anxiety/depression
l,s	? some risk of anxiety/depression
l,l	? protection against anxiety/depression

Genetics may facilitate novel treatment modalities

- Epigenetic modifications
 - Methylation (add -CH₃) of gene promoter sequences
 - may explain heritability of previous generation's trauma induced PTSD increasing current generation's risk

Severe Trauma With Onset OF PTSD

Severe trauma caused methylation of both "long" promoter sequences of serotonin transporter gene - converting epigenetically to "s,s" genes

