Care of the Patient with Posttraumatic Stress Disorder

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Epidemiology of PTSD
National Comorbidity Study

- 7.8% (lifetime risk) of adults in the U.S. (10% women, 5% men)
- Type of trauma most often the basis for PTSD -
  rape in women (46% risk)
  combat in men (39% risk)
- one third of cases have duration of many years
- 88% of cases have psychiatric comorbidity

Kessler et al., 1995

Mental Health and recent wars in Iraq and Afghanistan

Up to 17% screen + for PTSD, depression, GAD

23% to 40% sought professional help

Stigma, care barriers

Redeployment

PTSD

DSM- 5 Criteria

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

- Direct experience
- Witnessing in person as it occurs to others
- Learning of accidental or violent death in a someone close
- Experiencing repeated or extreme exposure to aversive details of trauma (e.g. first responders collecting human remains; police officers exposed to details of child abuse).

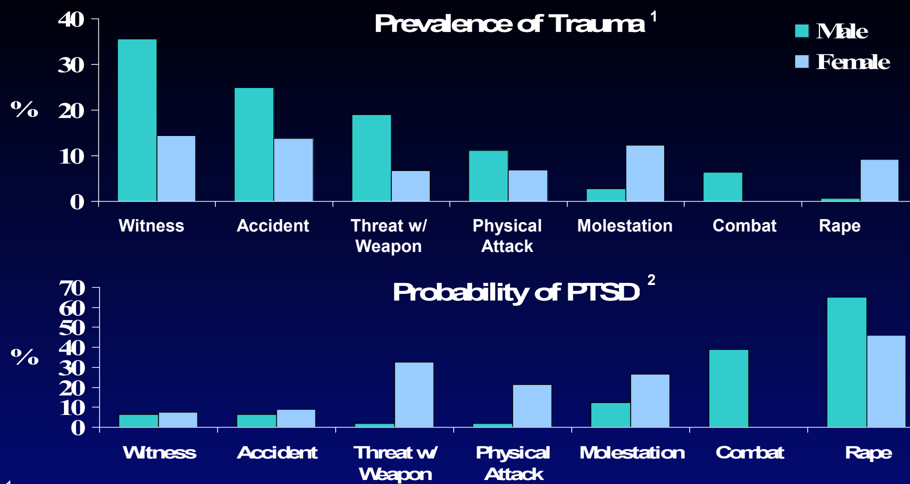
PTSD

DSM- 5 Criteria (cont.)

- Re-experiencing the traumatic event
- Persistent avoidance of stimuli associated with event
- Negative alterations in cognitions and mood (e.g. disillusionment, guilt, shame, emotional numbing, estrangement, inability to experience positive emotions)
- Symptoms of increased arousal
- At least 1 month’s duration (otherwise can diagnose Acute Stress Disorder)
- Significant distress or impairment in social, occupational, or other functioning

American Psychiatric Association. *DSM-5.*

Prevalence of Trauma and Probability of PTSD



[1] Kessler R et al. J Clin Psychiatry. 2000;61(Suppl 5):4-14.
[2] Kessler R et al. Arch Gen Psychiatry. 1995;52:1048-1060.

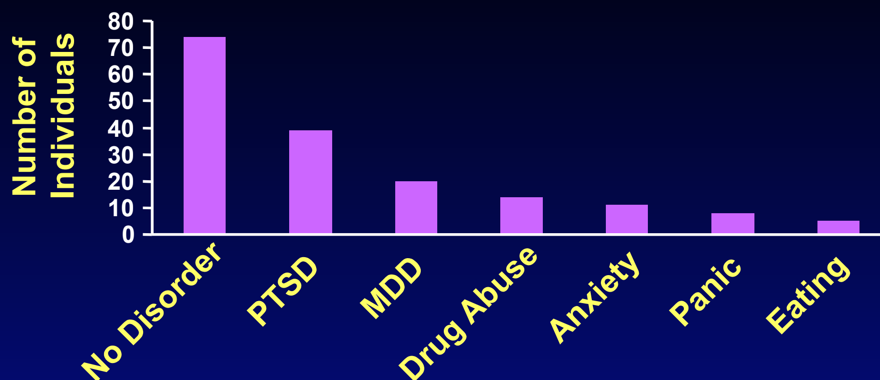
Twelve-Month Prevalence of DSM-IV Major Psychiatric Disorders

	%
Mood Disorders	
Major depressive episode	6.7
Dysthymia	1.5
Manic episode	2.6
Anxiety Disorders	
Social Phobia	6.8
Simple Phobia	8.7
PTSD	3.5
Agoraphobia without panic	0.8
GAD	3.1
Panic disorder	2.7
Substance Use Disorders	
Alcohol abuse/dependence	4.4
Drug abuse/dependence	1.8

Adapted from Kessler RC, et al. Arch Gen Psychiatry. 2005;62:617-627.

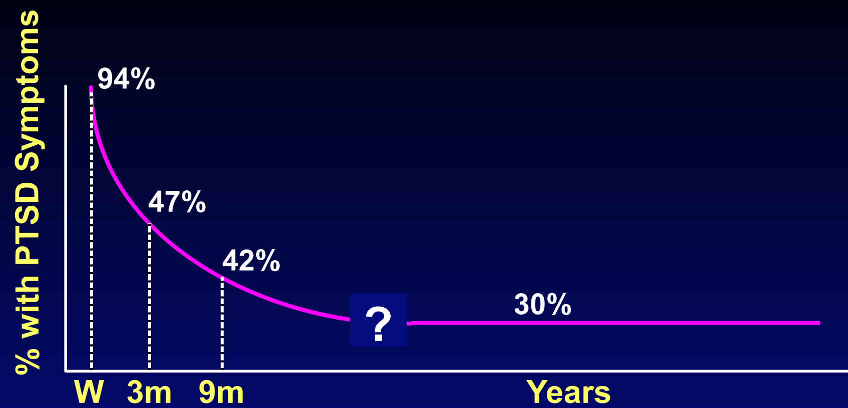
Primary Psychiatric Disorder 6 Months Following Trauma

Responses to Trauma Are Heterogeneous



McFarlane, Atchison, Yehuda. Ann N Y Acad Sci. 1997(June);821:437-441

Longitudinal Course of PTSD Symptoms

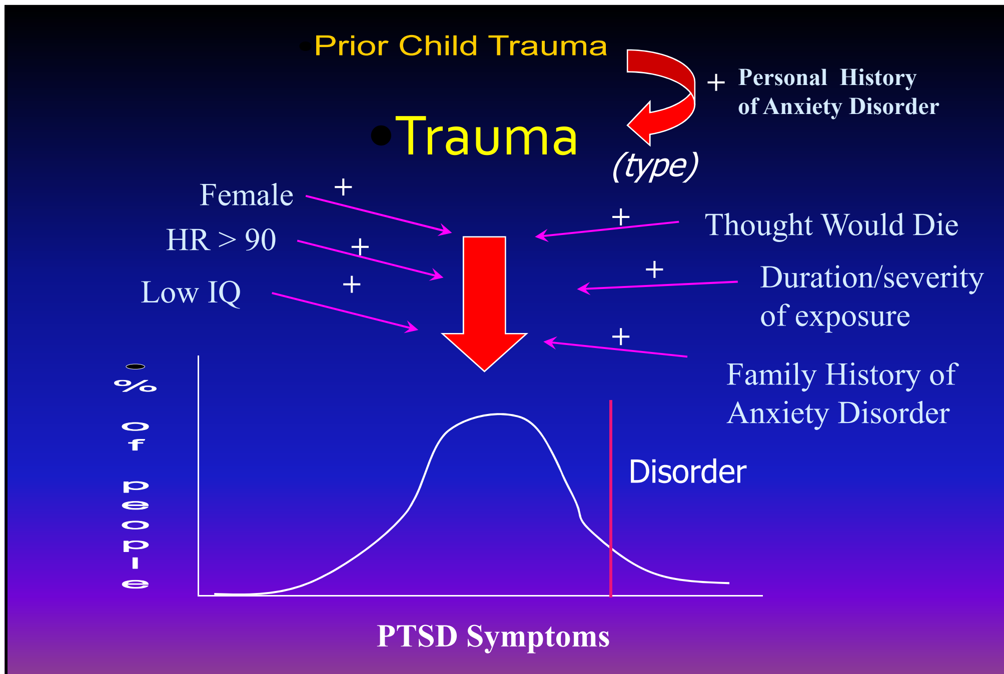


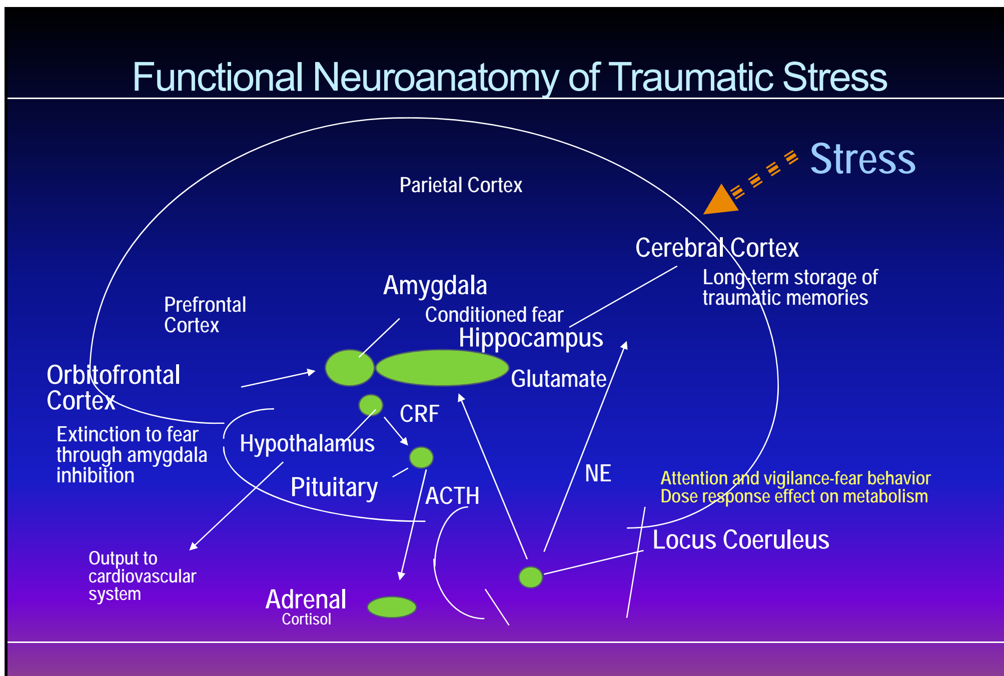
Shalev & Yehuda, 1999

PTSD

Risk Factors for PTSD

- Severity of trauma (ie, threat, duration, injury, loss)
- Prior traumatization
- Gender
- Prior mood and/or anxiety disorders
- Family history of mood or anxiety disorders
- Education

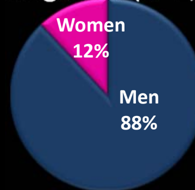

Prior Child Trauma
+ Personal History of Anxiety Disorder
Trauma
(type)
Female +
HR > 90 +
Low IQ +
+ Thought Would Die
+ Duration/severity of exposure
+ Family History of Anxiety Disorder
% of people
Disorder
PTSD Symptoms


Functional Neuroanatomy of Traumatic Stress
Stress
Parietal Cortex
Cerebral Cortex
Long-term storage of traumatic memories
Prefrontal Cortex
Amygdala
Conditioned fear
Hippocampus
Glutamate
Orbitofrontal Cortex
Extinction to fear through amygdala inhibition
CRF
Hypothalamus
Pituitary
ACTH
NE
Attention and vigilance-fear behavior
Dose response effect on metabolism
Locus Coeruleus
Output to cardiovascular system
Adrenal
Cortisol

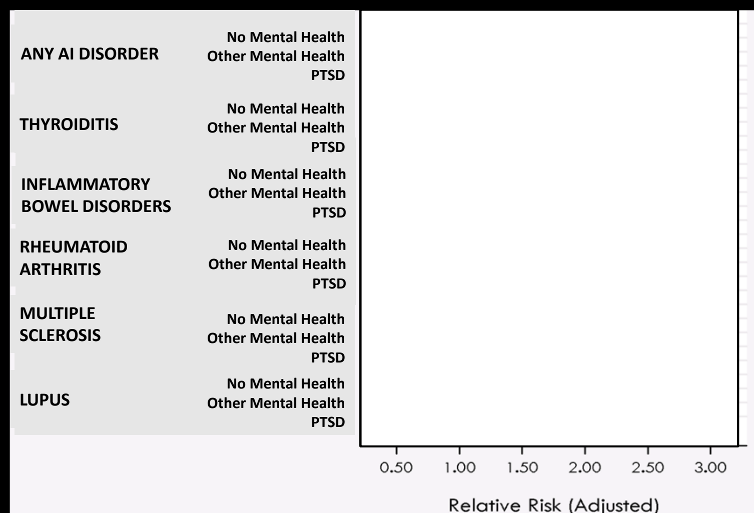
AUTOIMMUNE DISORDERS WITH PTSD

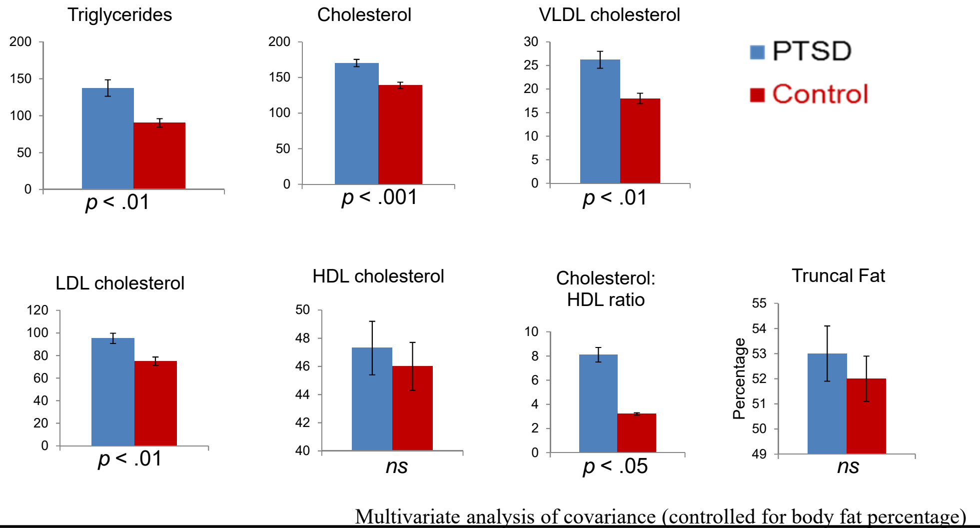
O'Donovan..Neylan. Biol Psychiatry. 2015 Feb 15;77(4):365-74

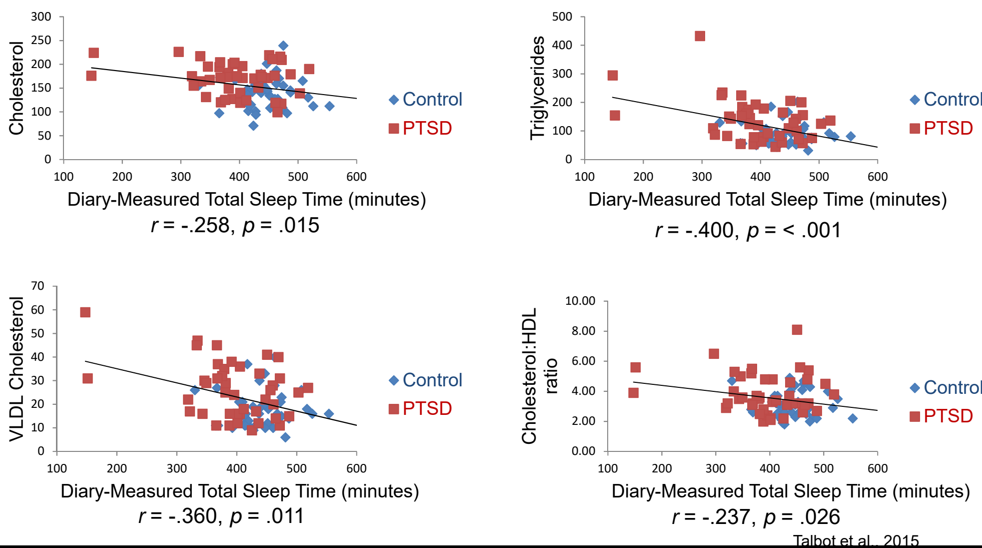
- VA OEF/OIF Roster
  - Includes OEF/OIF veterans who have separated & accessed VA care (Seal et al., 2007)
  - <u>TREATMENT-SEEKING POPULATION</u>
- N=670,338 (October 2005 – March 2012)
  - Aged < 55 years
  - No AI diagnosis before MH diagnosis (n=2,939)
- M age = 31.3±8.7
- N = 80,361 women



INCREASED PREVALENCE OF AUTOIMMUNE DISORDERS WITH PTSD



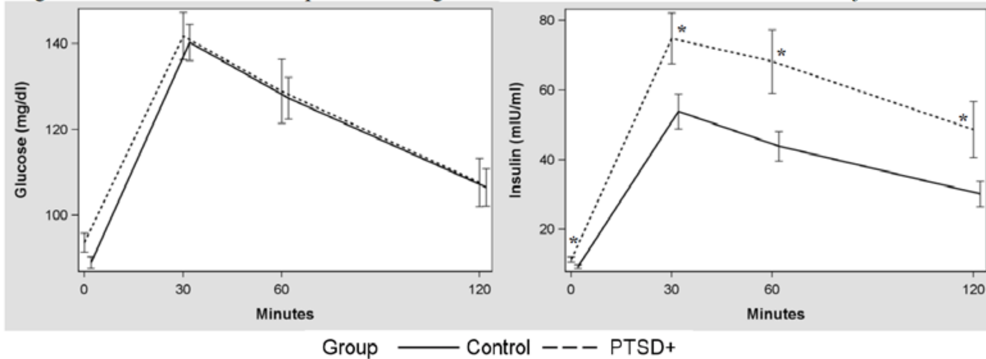

Sleep and Metabolic Risk Factors in PTSD
Lisa Talbot et al. Psychosomatic Medicine 2015 May;77(4):383-91
Triglycerides
p < .01
Cholesterol
p < .001
VLDL cholesterol
p < .01
PTSD
Control
LDL cholesterol
p < .01
HDL cholesterol
ns
Cholesterol:
HDL ratio
p < .05
Truncal Fat
Percentage
ns
Multivariate analysis of covariance (controlled for body fat percentage)


Sleep and Lipids
Cholesterol
Diary-Measured Total Sleep Time (minutes)
r = -.258, p = .015
Control
PTSD
Triglycerides
Diary-Measured Total Sleep Time (minutes)
r = -.400, p = < .001
VLDL Cholesterol
Diary-Measured Total Sleep Time (minutes)
r = -.360, p = .011
Cholesterol:HDL ratio
Diary-Measured Total Sleep Time (minutes)
r = -.237, p = .026
Talbot et al., 2015

Evidence for insulin resistance in PTSD

Madhu Rao et al., Psychoneuroendocrinology. 2014 Jul 23;49C:171-181.

Figure 1. Glucose and insulin responses to oral glucose tolerance test in PTSD+ and control subjects†



Does Treatment for PTSD Affect Other Outcomes?

- Brain Structure (e.g. hippocampal volume)
- Metabolism
- Inflammation
- Long-term risk for dementia

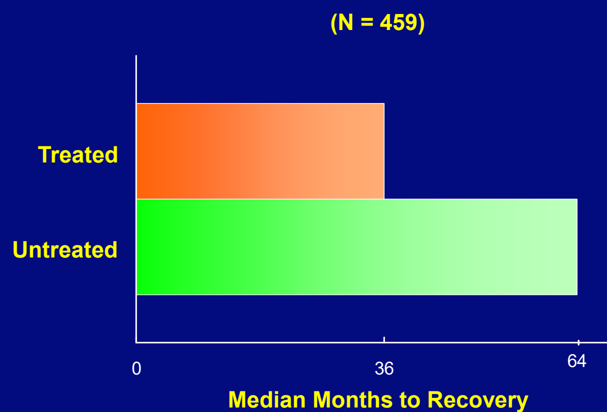
PTSD Treatment Options

- Psychotherapy
- Pharmacotherapy
- Complementary Alternative Interventions
  - Yoga
  - Exercise
  - Meditation
- Multimodal treatment

PTSD

Impact of Treatment on Recovery

(N = 459)



Kessler RC et al. *Arch Gen Psychiatry*. 1995;52:1057.

Psychological Treatments for Chronic PTSD

First-Line Psychotherapies

- Prolonged Exposure therapy
- Cognitive processing therapy

Additional treatments

- Stress Inoculation Training
- Eye Movement Desensitization and Reprocessing (EMDR)
- Interpersonal Psychotherapy (IPT)
- Mindfulness-based stress reduction

PTSD involves Fear Conditioning

- Pairing of neutral stimuli (contextual cues) and traumatic stimulus (combat) leads to fear responses to neutral cues
- After combat, neutral cues leads to fear response
- PTSD maintained by avoidance behavior

Exposure Therapy and Extinction of Fear Conditioning

- Animal model: Repeated exposure to neutral cue (light) without shock decreases fear conditioning
- Involves active learning and is mediated by the neurotransmitter glutamate
- Extinction is the basis for exposure therapy in PTSD
  - Patients learn to confront their feared memories and situations under safe circumstances with the goal of extinguishing fear

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Cognitive Processing Therapy

- 12 structured sessions with assignments
- Targets 5 core schemas: safety, trust, power/control, esteem, intimacy
- Goal is to identify and modify "stuck points" or problem areas in thinking about the event, process trauma

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DoD/VA Guidelines for Treatment of PTSD

VA and DoD 2017 guidelines have a set of recommendations for the management of PTSD:

First-line: manualized trauma-focused psychotherapy

If these are not available, other pharmacologic and nonpharmacologic interventions are recommended for PTSD.

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Phase-Based Treatment: Stabilization

-Teaching patients about PTSD, a.k.a. "psychoeducation"
  -i.e., causes, symptoms, effects on functioning in various domains

-Teaching patients basic skills for managing common symptoms
  -"grounding" techniques, anger management, assertiveness...review series info

Format:
-Cohort-based group treatment: The 101-102-103 series
  -3 12-week once-weekly groups which veterans complete as a cohort

-Drop-in groups:
  -focused on skills development, patients can attend as desired

-Brief individual therapy "stabilization"
  -~6-12 week interventions, often for veterans unwilling or unable to participate in group treatment

-Dialectical Behavioral Therapy Program
  -comprehensive program for patients with pronounced features of borderline personality disorder, *especially* pronounced self-harm behaviors (e.g. cutting, suicidal behaviors)

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Phase-Based Treatment: “Adjunctive” Therapies

Medication Clinic

Family Therapy

Mindfulness/Meditation Groups

Strength and Wellness ??

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FDA-Approved Medications

SSRIs

- Sertraline
- Paroxetine

Medications Studied for PTSD

- Antidepressants
  - SSRIs (Sertraline and Paroxetine FDA approved)
  - SNRIs (Venlafaxine, Duloxetine)
  - SARIs (Nefazodone and Trazodone)
  - NaSSA (Mirtazapine)
  - TCAs & MAOIs
- Adrenergic inhibiting agents
- Anxiolytics
- Anticonvulsants
- Atypical antipsychotics

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α-1 Antagonists

•Agent
- Prazosin (multiple RCTs, large VA Coop study was negative

•Molecular Target
- α-1 post-synaptic adrenergic receptor (antagonist)

•Clinical Significance
- α-1 receptors widely distributed in brain, including amygdala and hippocampus
- α-1 receptors modulate sleep and startle responses
- Adverse reactions: syncope, dizziness, drowsiness, decreased energy, headache

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Antianxiety Agents: *Benzodiazepines*

Acute stress disorder: alprazolam * or clonazepam *

- Did not prevent development of PTSD
- Gelpin, et al. J Clin Psych 1996; 57:390–394.

Chronic PTSD: alprazolam vs placebo

- Improves anxiety, no effect for core symptoms of PTSD
- Braun P, et al. J Clin Psychiatry. 1990;51:236-8.

May interfere with exposure-based desensitization

Adverse reactions include: drowsiness, light-headed, dependency

Shalev AY, Bonne E. In: Shalev AY et al, eds. *International Handbook of Human Response to Trauma*. New York, NY: Klumer/Plenum Publishers; 1999.

Anti-Psychotic Agents

Not routinely used

Indications (Not FDA approved):

- Reduce disorganizing hyperarousal, paranoid ideation, and aggressive impulsivity
- Co-morbid psychotic disorder
- Adjunctive for chronic treatment resistant PTSD
- Open trials for aripirazole*, olanzapine*, quetiapine*,
- Risperidone positive RCTs, however, large multisite VA trial was negative

CBT-I IN PTSD: A RANDOMIZED CONTROLLED TRIAL

http://dx.doi.org/10.5665/sleep.3408

Cognitive Behavioral Therapy for Insomnia in Posttraumatic Stress Disorder: A Randomized Controlled Trial

Lisa S. Talbot, PhD[1,2]; Shira Maguen, PhD[1,2]; Thomas J. Metzler, MA[1]; Martha Schmitz, PhD[1,2]; Shannon E. McCaslin, PhD[1,2,3]; Anne Richards, MD[1,2]; Michael L. Perlis, PhD[4]; Donn A. Posner, PhD[5]; Brandon Weiss, BA[1]; Leslie Ruoff, BS[1]; Jonathan Varbel, BA[1]; Thomas C. Neylan, MD[1,2]

[1]San Francisco VA Medical Center, San Francisco, CA [2]Department of Psychiatry, University of California, San Francisco, CA; [3]National Center for PTSD, VA Palo Alto Health Care System, Palo Alto, CA; [4]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA; [5]Department of Psychiatry and Human Behavior, Brown University, Providence, RI

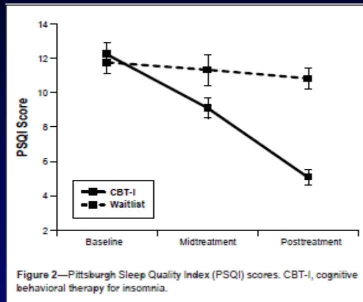


Figure 2—Pittsburgh Sleep Quality Index (PSQI) scores. CBT-I, cognitive behavioral therapy for insomnia.

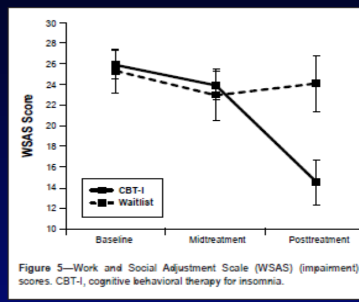
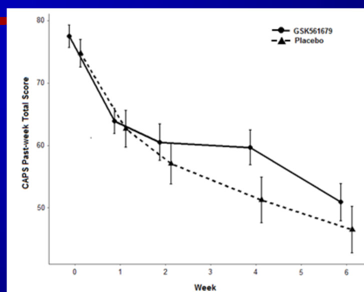


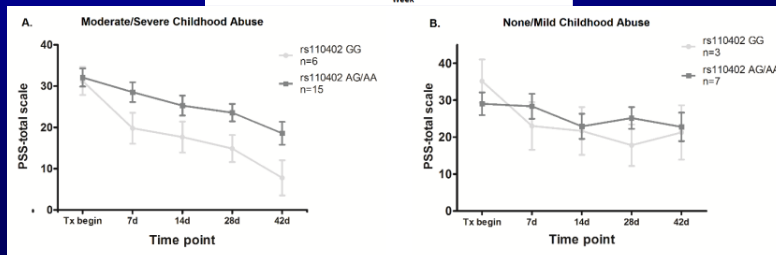
Figure 5—Work and Social Adjustment Scale (WSAS) (impairment) scores. CBT-I, cognitive behavioral therapy for insomnia.

Sleep. 2014 Feb 1;37(2):327-41

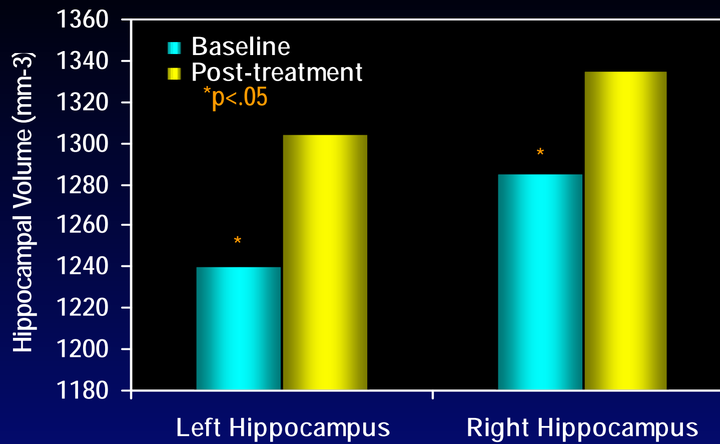
CRF Receptor Antagonist for PTSD



Dunlop et al. Biol Psychiatry. 2017 Dec 15;82(12):866-874



Increased Hippocampal Volume With Paxil in PTSD

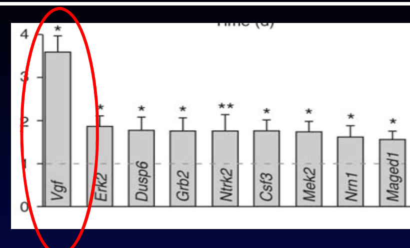


Effects of 9-12 months of treatment with 10-40 mg paroxetine.
Vermetten et al. *Biol Psychiatry*. 2003.

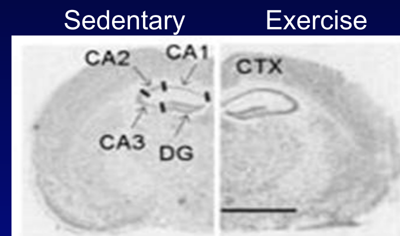
Exercise and Neurogenesis?

Growth factor signaling genes upregulated by exercise

VGF involved in energy balance & synaptic activity; increased by ECS



Exercise increases VGF mRNA in the hippocampus



Slide adapted from D. Shin

VGX
VETERANS GROUP EXERCISE

MIND-BODY GROUP EXERCISE FOR VETERANS

Paid Research Study Offering 12 weeks of Exercise

VETERANS GROUP EXERCISE

MIND-BODY GROUP FITNESS FOR VETERANS WITH SERVICE-RELATED STRESS

Veterans between the ages of 18-69 years old may be eligible for a 12-week group exercise trial.

Activities include aerobic conditioning, muscle strengthening, and controlled breathing.

Compensation up to $480.

CONTACT

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www.StressAndHealthResearch.org

NCIRE

STRESS & HEALTH

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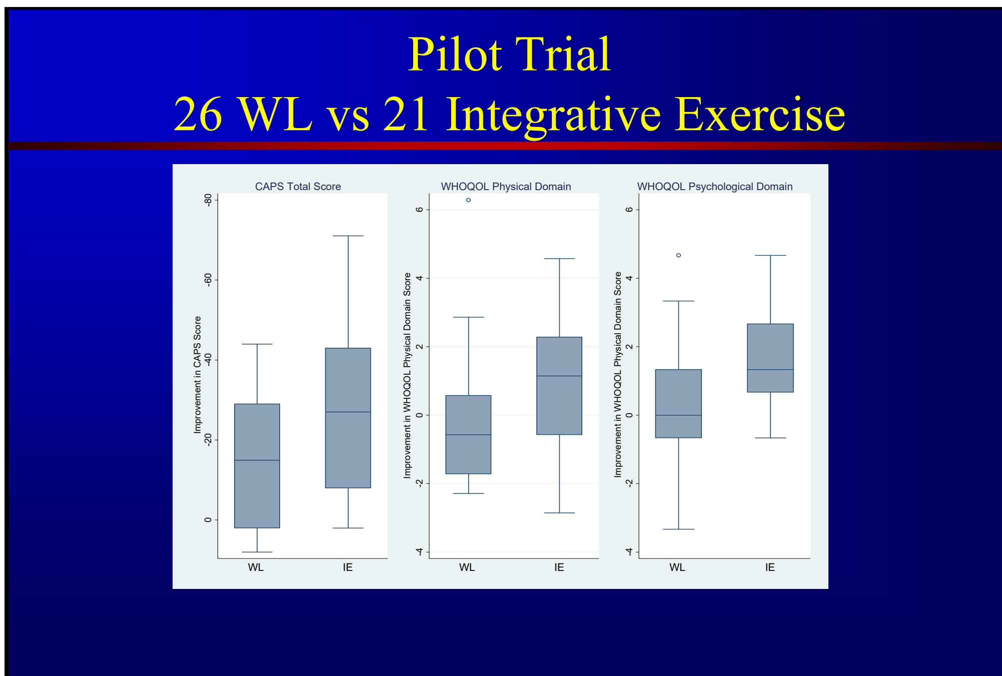
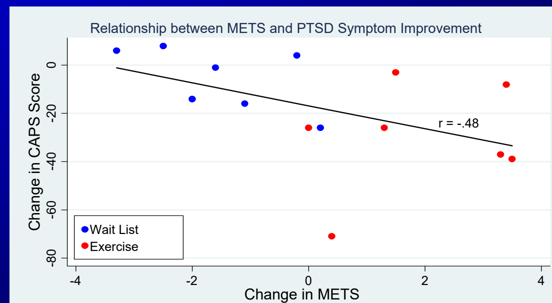
Pilot Trial
26 WL vs 21 Integrative Exercise



Change in Exercise Capacity- Metabolic Equivalents (METS) and PTSD Symptoms

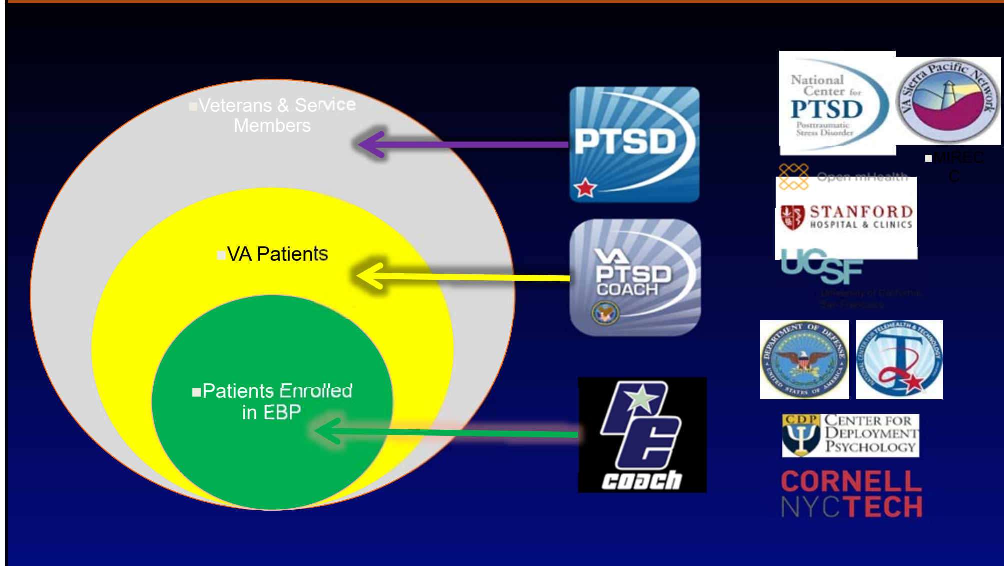


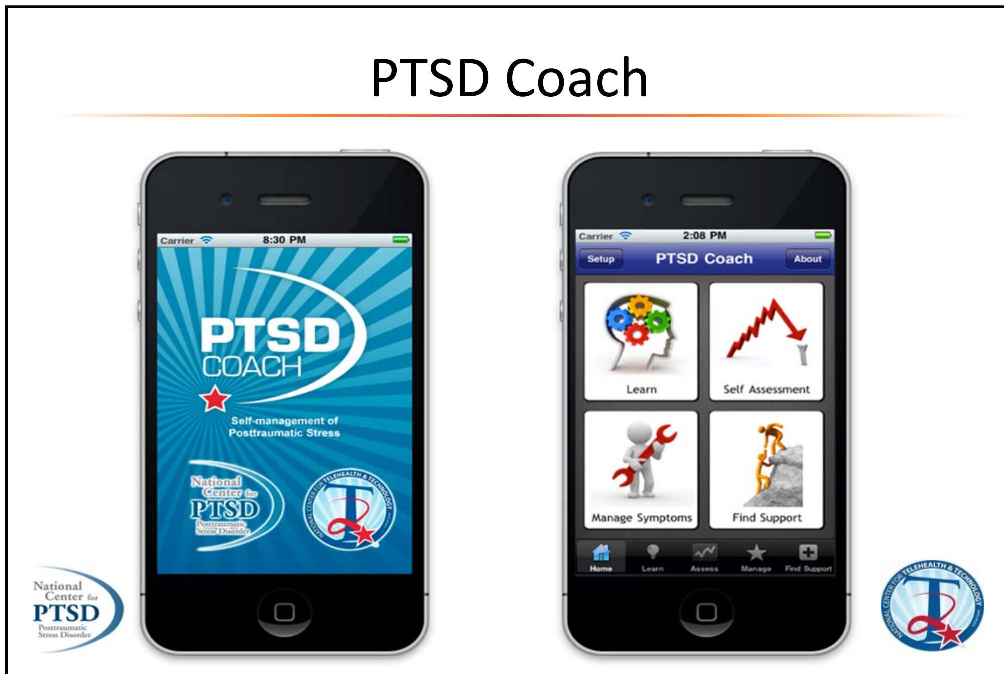
Tools and Resources

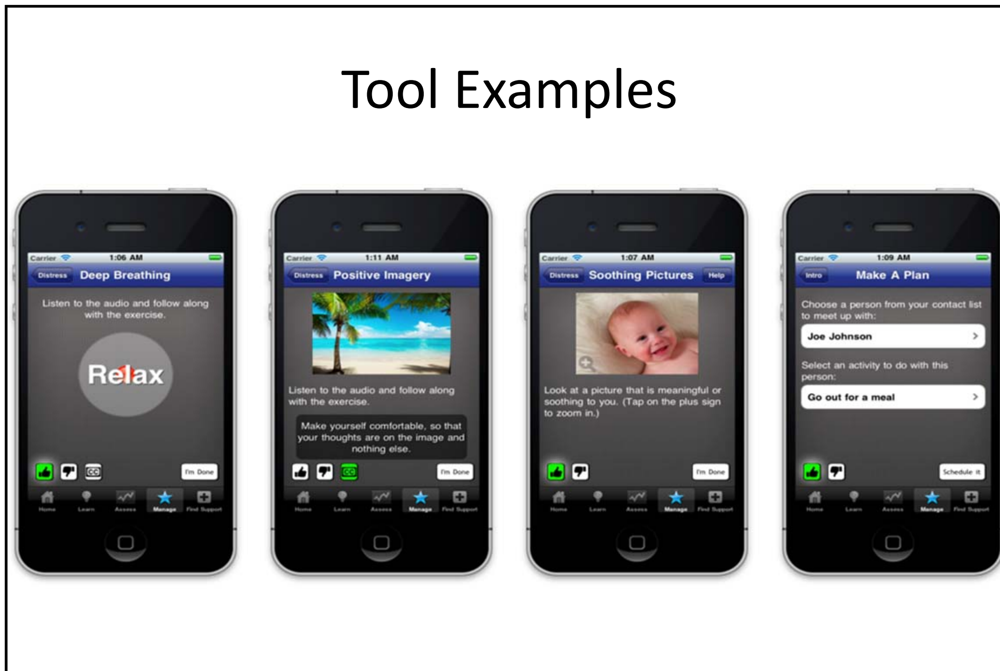
https: //www.istss.org/treating-trauma.aspx

combining recommendations with good clinical judgment

PTSD Coach


Apps for PTSD
Veterans & Service Members
VA Patients
Patients Enrolled in EBP
PTSD
VA PTSD COACH
coach
National Center for PTSD
VA Sierra Pacific Network
STANFORD HOSPITAL & CLINICS
UCSF
CENTER FOR DEPLOYMENT PSYCHOLOGY
CORNELL NYCTECH


PTSD Coach
PTSD COACH
Self-management of Posttraumatic Stress
PTSD Coach
Setup
About
Learn
Self Assessment
Manage Symptoms
Find Support
National Center for PTSD



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