

# Neuropsychological Functioning and PTSD

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*“It is strange to think how to this very day I cannot sleep a night without great terrors of fire ...”*



-From the diary of Samuel Pepys, 1666

Quoted in Daly, 1983; Saigh & Bremner, 1998

# Overview

- I. Definitions
- II. Epidemiology of trauma and PTSD
- III. Conceptualization of PTSD as a psychoneurobiological disorder
- IV. Neuropsychological correlates of PTSD
- V. Potential sources of deficits

# Current PTSD Criteria

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A. Traumatic event

B. Re-experiencing

C. Avoidance and Numbing

D. Increased arousal

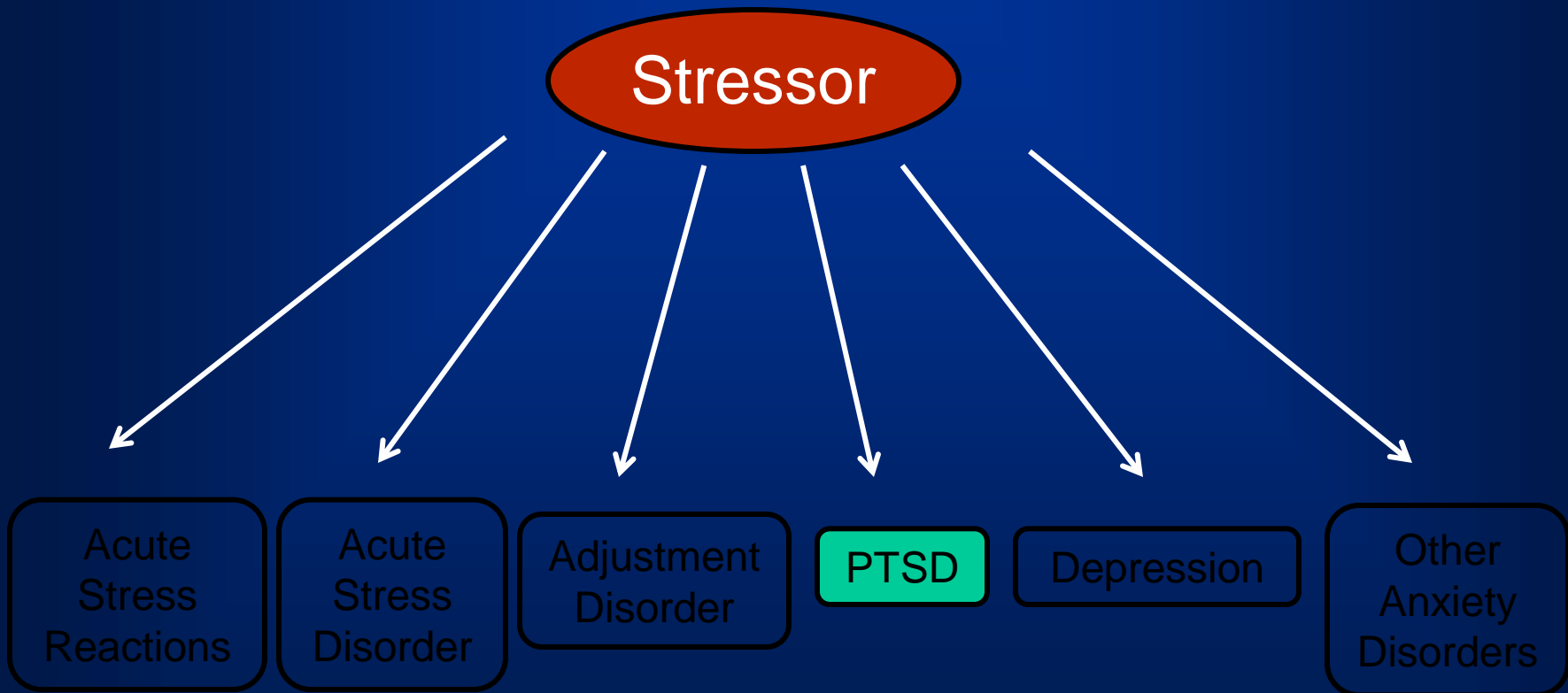
E/F. > 1 month, clinical impact

Stress  $\neq$  Trauma

Exposure  $\neq$  PTSD

Acute  $\neq$  Chronic

# Spectrum of Psychological Trauma Reactions



# Epidemiology

# Epidemiology: Trauma Exposure

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- 50-60% of general population exposed to trauma.
- 56% men; 49% women exposed to >1 trauma.

*National Comorbidity Study (Kessler et al. 1995, Arch Gen Psych)*

- 90% exposure in some high risk urban areas.

*Detroit (Breslau et al., 1998, Arch Gen Psych)*

# Epidemiology (lifetime): PTSD

- 7-8% general population

*National Comorbidity Study (Kessler et al. 1995, Arch Gen Psych)*

- Combat veterans higher (NVVRS)

- 30% using liberal estimate

(Kulka et al., 1990)

- 19% using conservative estimate

(Dohrenwend et al., Science, 2006)

# PTSD Risk and Protective Factors

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## TRAUMA CHARACTERISTICS

Demographics

Prior trauma exposure

Personal or family psychiatric history

Social support

Genetics

Biological/neural factors

# **PTSD as a Psycho- Neurobiological Disorder**

# Stress response: Sympathetic Nervous System

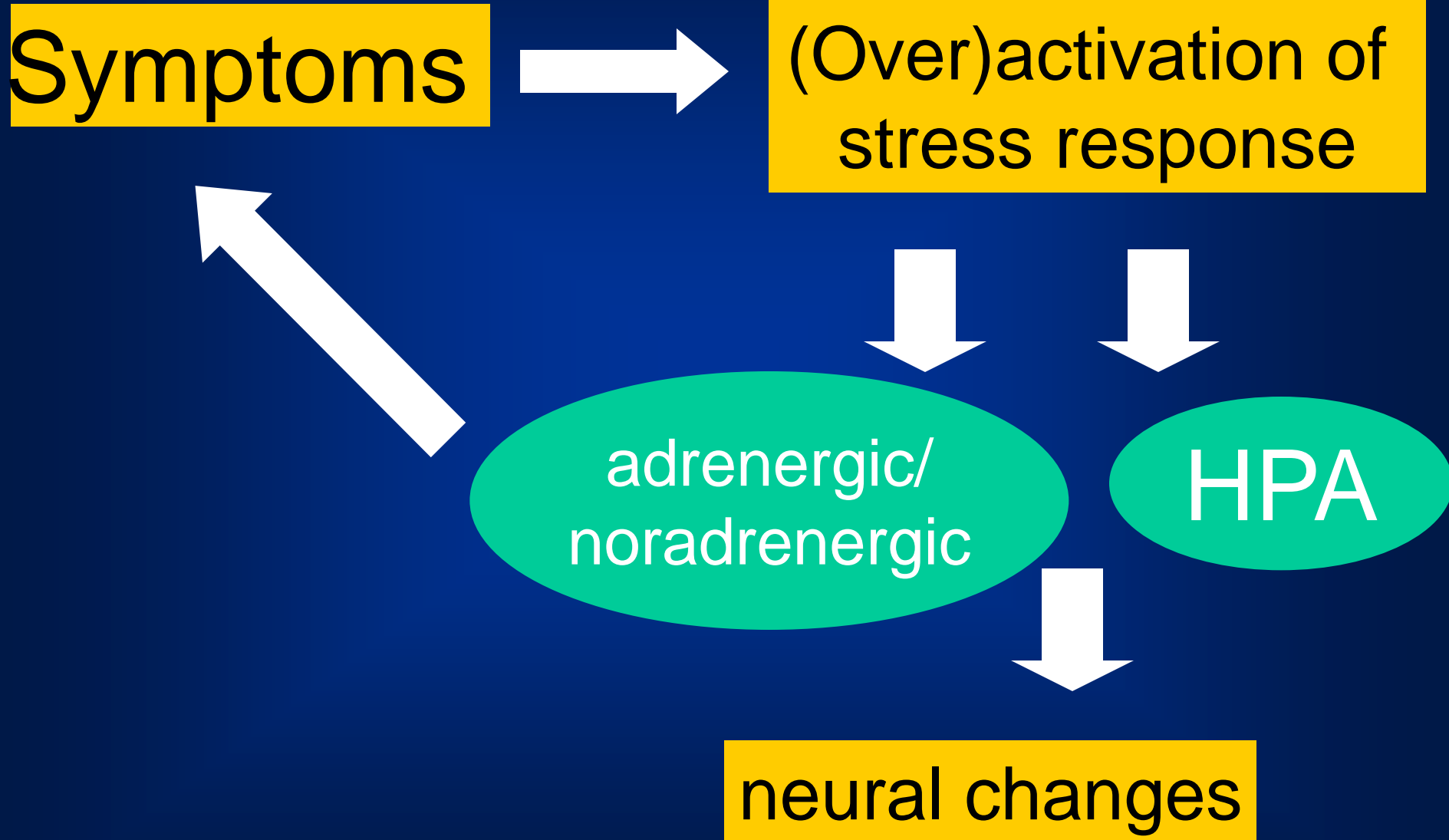


# Stress Response

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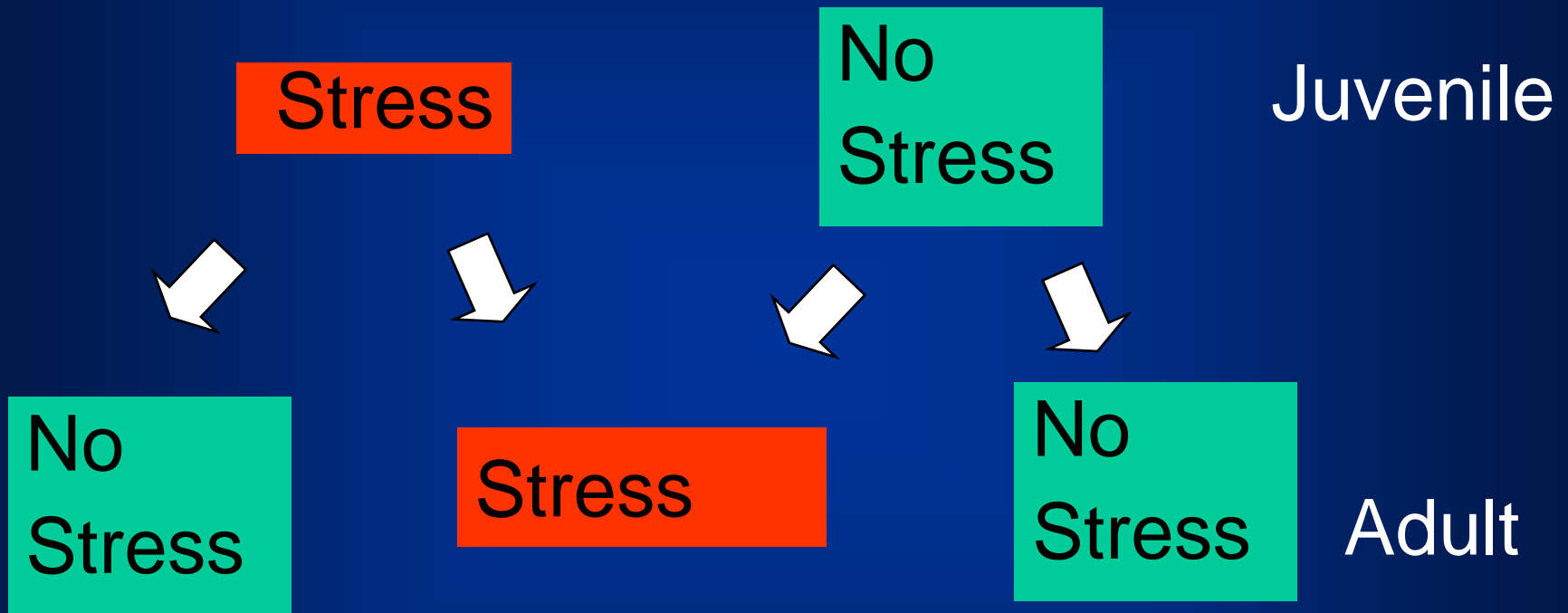
- Life saving initially
- If continues, overwhelms organism
- When maintained, potentially more damaging than the stressor

# Sensitization



# Sensitization: An Animal Model

*(Tsoory et al., 2008; Progress in Brain Research)*



Juvenile stress → enhanced startle, reduced exploration, decreased learning in response to subsequent stress

# Emotional Memories

Dual Representation Theory (Brewin):

Trauma Memory

```
graph TD; TM[Trauma Memory] --- SB[Sensation-based]; TM --- VA[Verbally accessible];
```

Sensation-based

- Perceptual
- Difficult to articulate
- Poorly controlled

Verbally accessible

- Narrative
- Controlled recall

# Fear Conditioning

Before Conditioning:

Rat  
(Neutral  
Stimulus) → No Reponse

Loud Noise  
(US) → Crying,  
attempting to  
crawl away  
(UR)

During Conditioning:

Rat  
(Neutral  
Stimulus) → Crying,  
attempting to  
crawl away  
(UR)

Loud Noise  
(US) → Crying,  
attempting to  
crawl away  
(UR)

After Conditioning:

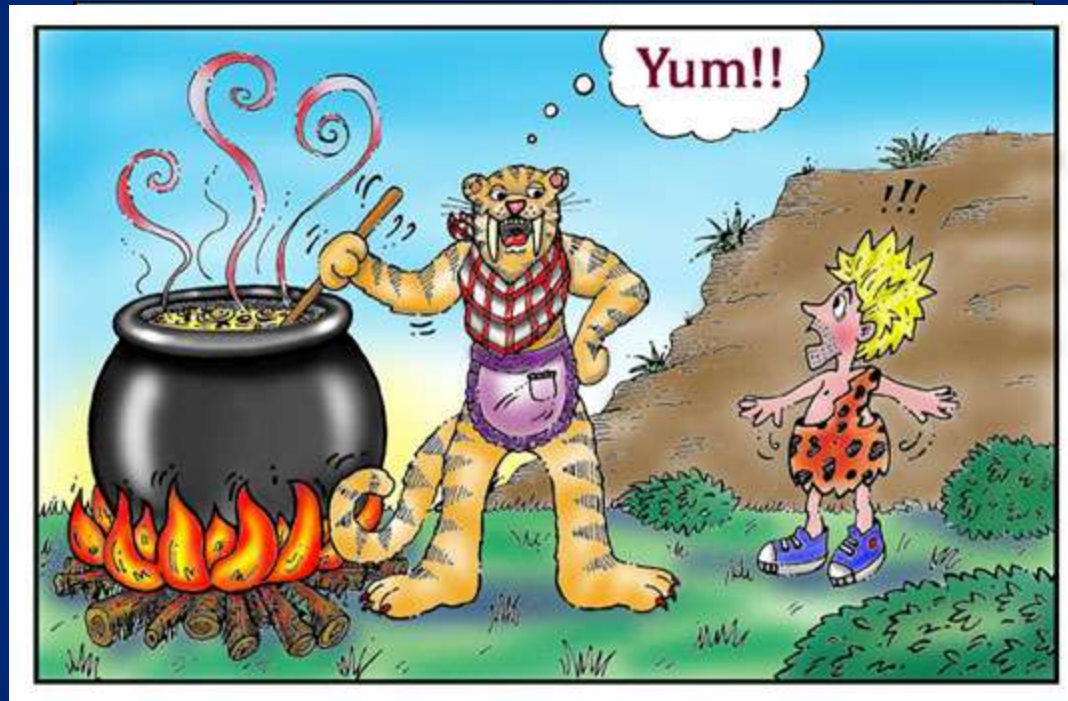
Rat  
(Previously  
Neutral Stimulus)  
(CS) → Crying,  
attempting to  
crawl away in  
response to the  
rat  
(CR)

Psychobiolog. Abnormality	Possible Clinical Behavior
Adrenergic hyper-reactivity	Hyperarousal, re-experiencing, dissociation, aggression/anger, information processing/memory abnormalities, panic, anxiety
HPA enhanced negative feedback	Stress intolerance, emotional numbing
Elevated CRF levels	Hyperarousal, re-experiencing, panic/anxiety
Sensitization/kindling	Hyperarousal, re-experiencing

Adapted from “PTSD, Allostatic Load, and Medical Illness,”  
VA Natl. Center for PTSD

# PTSD: Survival Gone Awry?

A *normal* response ... to an abnormal situation



.... perpetuated

# Functional Neuroanatomy

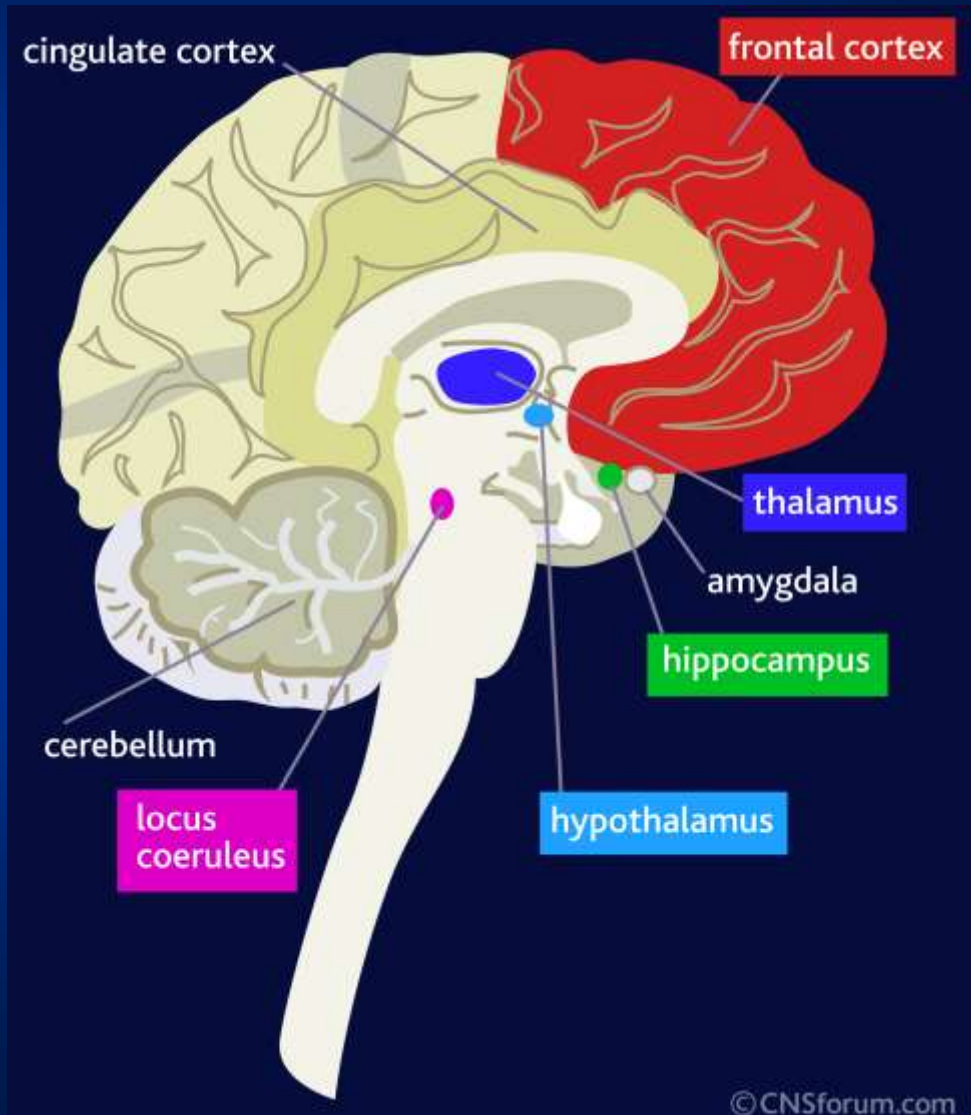
# Neuroimaging in PTSD

## Structural

- ↓ hippocampus
- ↓ medial PFC

## Functional

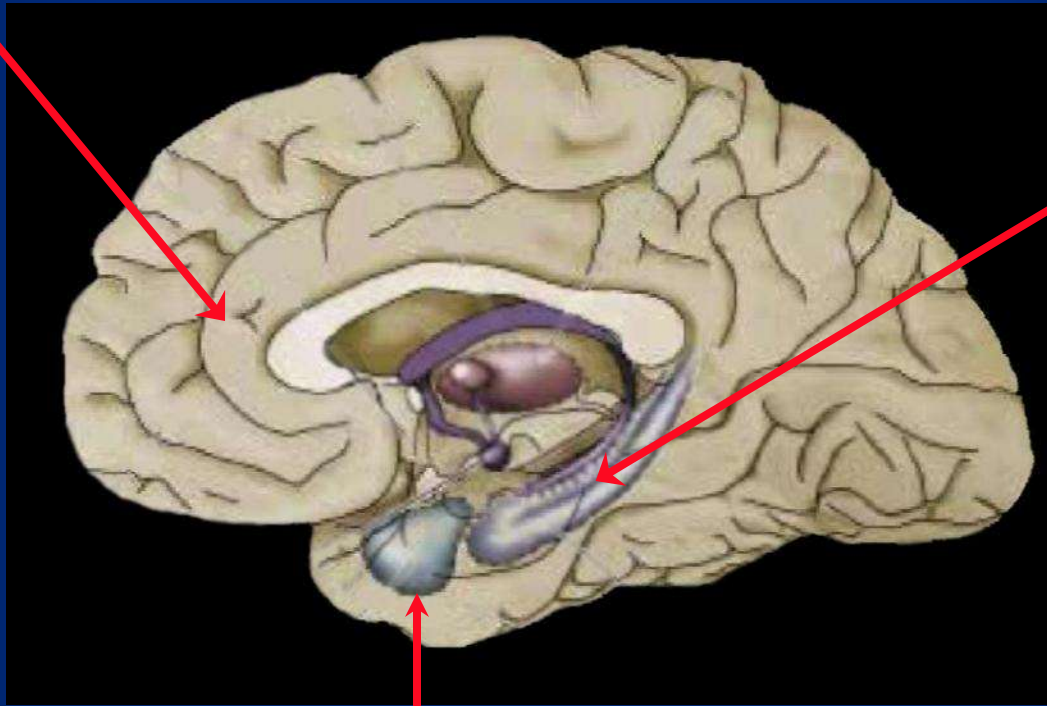
- ↑ amygdala
- ↓ medial PFC



# Functional Neuroanatomy of PTSD

MEDIAL PFC & Ant Cingulate

HIPPOCAMPUS



AMYGDALA

# **Neuropsychological Correlates of PTSD**

# Types of PTSD-Related Neurocognitive Abnormalities

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- Emotionally neutral information
- Emotionally relevant information

Emotionally Neutral Information:

Deficits on Neuropsychological  
Performance Tasks

# PTSD-related Neuropsychological Deficits

- ✓ Verbal intellectual
- ✓ Sustained attention
- ✓ Working memory
- ✓ Inhibition
- ✓ New learning/memory



# Inhibition/Gating

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- Ability to direct attention
- Ability to filter irrelevant stimuli
- Ability to inhibit thoughts and/or actions

# Inhibition/Gating

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- *Leskin & White (2007; Neuropsychology)*

Administered Attentional Network Task, Trails

Results:

No diffs: alerting, orienting, Trails

Response inhibition impaired on ANT

# 1991 Gulf War Study

- N = 43 GW veterans:

**PTSD Group (n = 19):**

**No – PTSD Group (n = 24):**

- Equivalent for age, education, SES, and average alcohol intake

**Vasterling, Brailey, Constans, & Sutker (1998)**

*Neuropsychology*

# Attention Components (Mirsky et al., 1991)

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- **Focus-execute** -the ability to focus on relevant stimuli and respond appropriately to them
- **Sustain** - the ability to maintain optimal levels of attention or vigilance over time
- **Shift** - the ability to change the focus of attention
- **Encode** - the capacity to register, recall, and mentally manipulate information sequentially

# New Learning and Memory

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- **Modality**

  - auditory/verbal

  - visual/spatial

- **Processes**

  - learning v. retention

  - sensitivity to interference

  - monitoring (intrusions, perseverations)

  - recall v. recognition

# Attentional Performances

	PTSD	No-PTSD
<b>Focus-Execute</b>		
Letter cancellation omissions	1.6 (2.1)	1.2 (1.6)
Stroop interference	46.8 (9.6)	47.3 (8.6)
<b>Sustain</b>		
CPT omissions	2.9 (4.2)	1.5 (1.9)
<b>CPT commissions</b>	<b>7.7 (12.5)</b>	<b>1.6 (5.6)*</b>
<b>Shift</b>		
WCST % correct	62.8 (15.6)	70.8 (12.4)
WCST % categories achieved	4.5 (1.7)	5.2 (2.3)
<b>Encode</b>		
WAIS-R Digit Span	10.4 (2.7)	9.5 (2.2)
<b>WAIS-R Arithmetic</b>	<b>8.3 (2.2)</b>	<b>10.3 (1.9)**</b>

\* p < .05 \*\* p < .01

# Verbal Memory Performances: AVLTL

	PTSD	No-PTSD
Total recall, Trials 1 – 5	44.3 (7.9)	49.7 (7.3)*
Savings ratio	0.9 (0.2)	0.9 (0.2)
Proactive Interference ratio	0.9 (0.5)	0.9 (0.4)
Retroactive Interference ratio	0.8 (0.2)	0.9 (0.2)*
Recognition, hits	13.0 (1.9)	13.3 (1.8)
Recognition false positives	3.8 (3.6)	1.8 (2.1)

\*  $p < .05$

# Visual Memory Performances: CVMT

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	PTSD	No-PTSD
Total correct, learning	71.1 (6.1)	77.2 (6.9)**
Total correct, delay	3.2 (1.3)	4.3 (1.8)
False positives, learning	19.0 (7.1)	20.6 (7.1)*

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\*  $p < .05$  \*\* $p < .01$

# Inhibition/Gating

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- Created inhibition factor from:
  - intrusions on memory recall tests
  - false positives on recognition tests
  - commissions errors on vigilance test (CPT)
- Inhibition: PTSD < no-PTSD
- Poorer inhibition → more re-experiencing symptoms

# Memory Meta-Analysis

*Brewin et al. (2007; J Abn Psychol)*

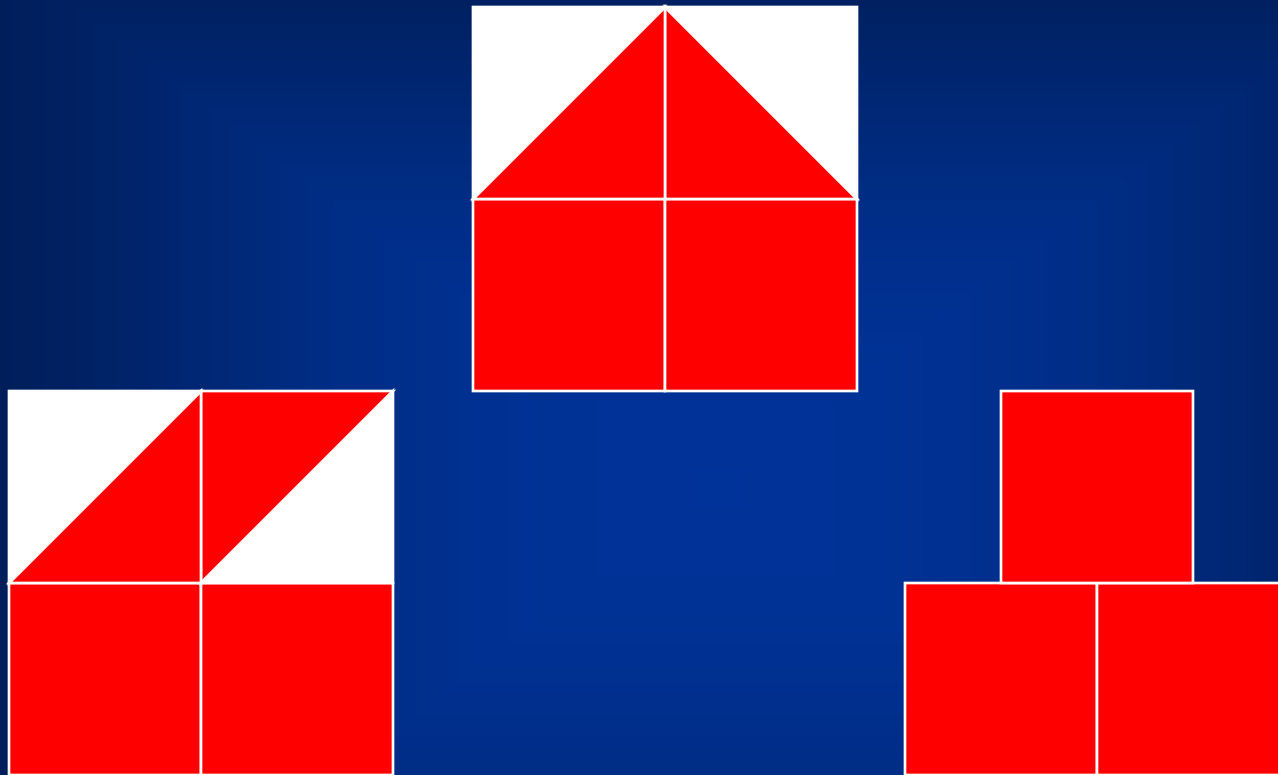
$n = 27$  studies; 660 indiv w/ PTSD; 812 controls

- Findings:
  - PTSD diagnosis → less proficient memory
  - small to moderate effect size
  - more impairment of verbal memory
  - no effect for immediate vs. delayed recall
  - could not be explained by TBI

# Interhemispheric Differences?



# Block Design



Vasterling , Rogers, Kaplan (2000). *Assessment*

# Global-Local Processing in PTSD

*(Vasterling, Duke, Lowery, Tomlin, & Kaplan, 2003, JINS)*

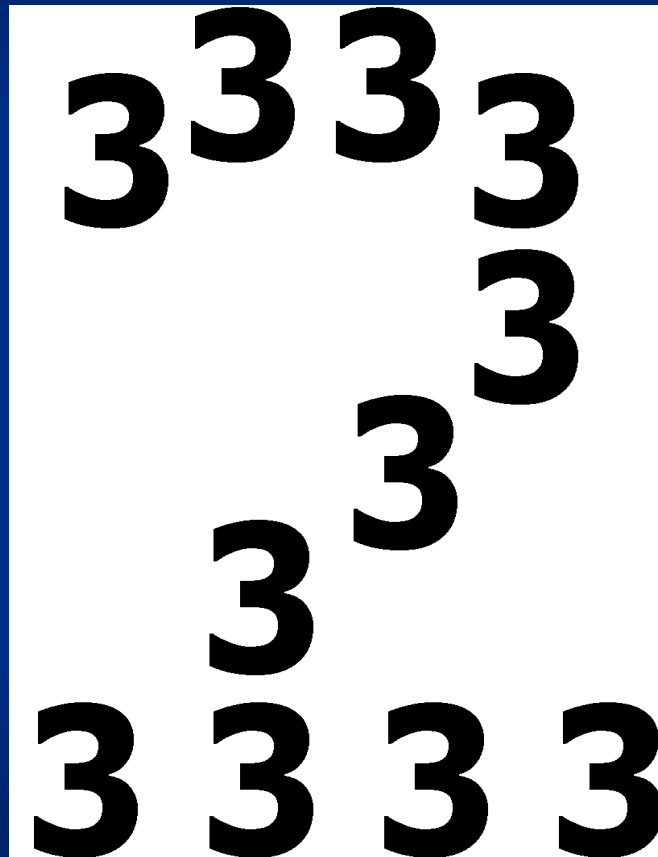


Figure adapted from Fileteo et al. (1992; 1995)

Emotionally Relevant Deficits:

Abnormalities on Information  
Processing Tasks

# Standard Stroop

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Blue

Red

Green

Blue

Green

# Emotional Stroop

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chair

lonely

bodybags

# Why is attention poor for neutral information but enhanced for threat-relevant information?

- **Information processing models of PTSD:**

Enhanced attention and sensitivity to perceived threat stimuli perceived to be threatening

- **Resource allocation model:**

Diminished availability of finite cognitive resources for non-threatening stimuli

# Potential Sources of Deficits

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Motivational factors

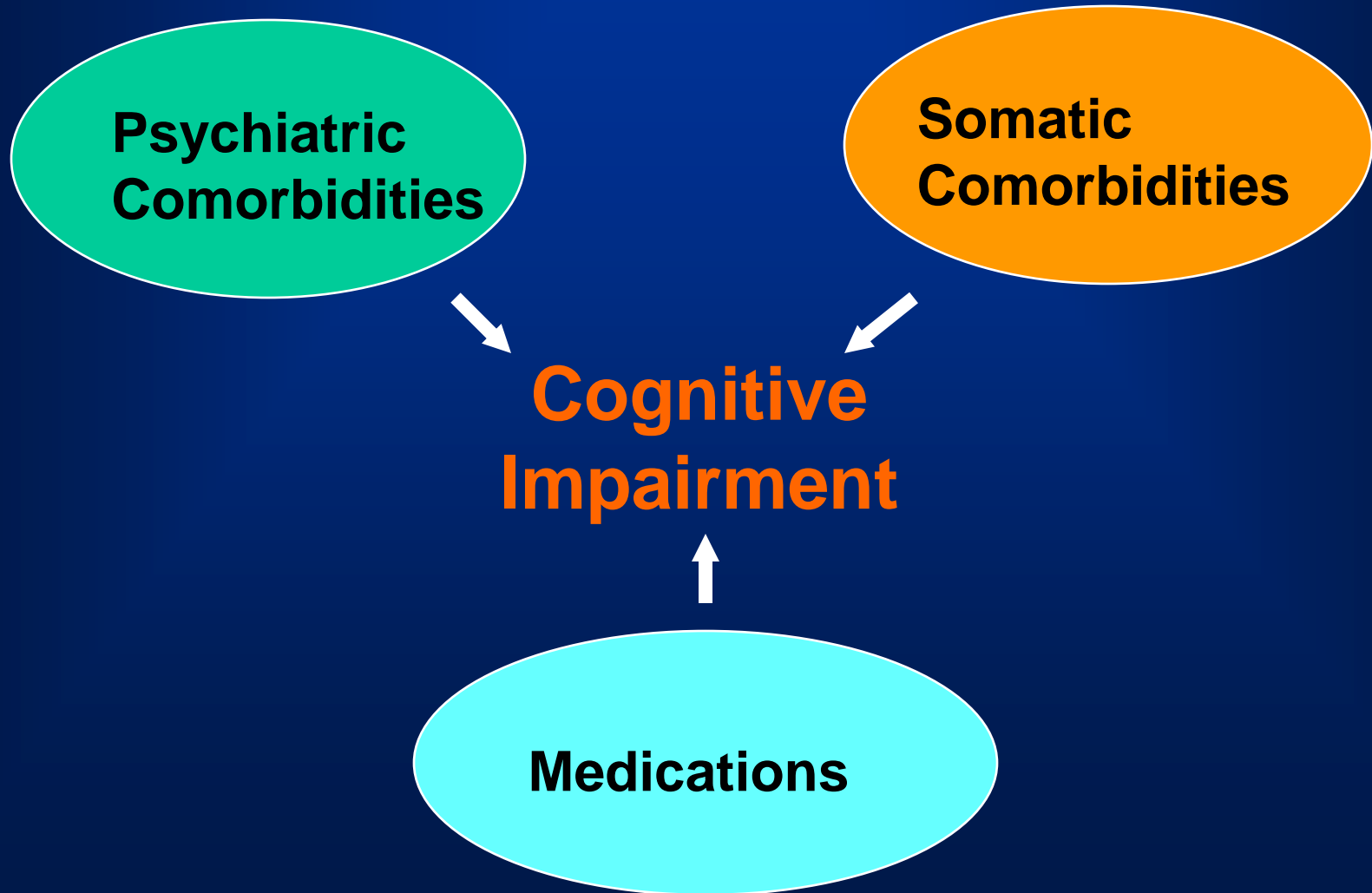
Stress exposure v. emotional response

Acquired neurobiological changes

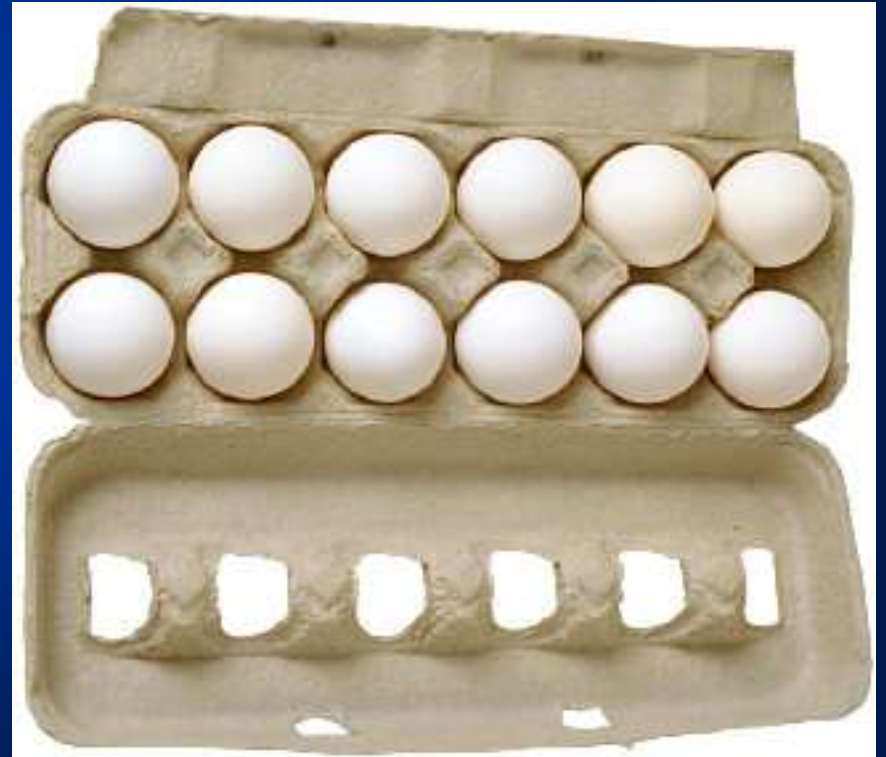
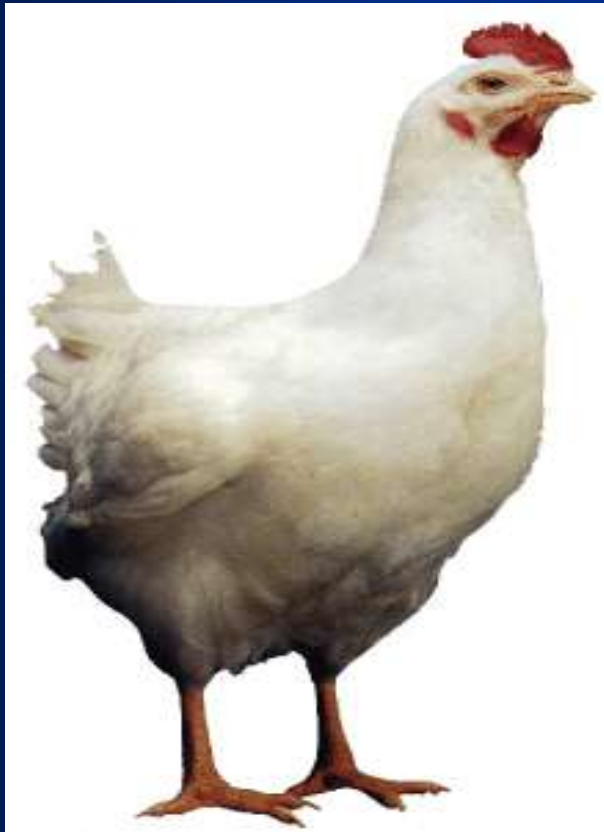
Pre-trauma functioning

Factors not specific to PTSD (e.g., sleep, co-morbidities)

# How Specific are Deficits to PTSD?



# Neuropsychological Abnormalities in PTSD: Cause or Effect?



# PTSD/Stress → Neuropsychological Decrements

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Subjective appraisals

Animal studies

Elite military training studies

*(Lieberman et al., 2005; Biol Psychiatry, 57, 422-429; Morgan et al., 2000; 2001; 2002)*

# PTSD/Stress → Neuropsychological and Neural Alterations

- Longitudinal work

Memory (*Yehuda et al, 2006, Biol Psychiatry*)

Fronto-temporal atrophy (*Cardenas et al., 2011*)

- Twin Studies (prefrontal (ACC) volume)

(*Kasai et al., 2008, Biol Psychiatry*)

- Associations with duration of PTSD

Attention (*Marx et al., 2009; Arch Gen Psych*)

Hippocampal volume (*Felmingham et al., 2009; Neuroreport*)

# The Brain as a Predictor of PTSD

- Vietnam veterans twins (*Gilbertson et al.; 2006, Nature Neuroscience; 2007, J Abnormal Psychol*)

Neuropsych performance and hippocampal volume most closely associated with familial relationships

- IQ and PTSD (*e.g., Thompson & Gottesman; 2008*)

Interaction between combat and pre-induction cognitive skills measured by Army entrance exams

- TBI as predictor of PTSD

How else can we address this question?



Prospective research in at-risk populations

# Parslow & Jorm (2007) Am J Psychiatry

- > 1500 people exposed to major fire; evaluated before and after
- Results:
  - Re-experiencing and arousal sx → poorer word recall over time
  - Pre-trauma scores on 5 measures (memory, digit span, coding speed, vocab) → re-exp and arousal sx

# Neuropsychological Outcomes of Iraq Deployment



## Study Funding:

DoD (USAMRMC-RADIII DAMD 17-03-2-0020); VA (CS/BMR&D)

# Design (n = 1595)

## Prospective, longitudinal

Time 1: Prior to Iraq deployment

Time 2: Post-deployment

Time 3: Post-deployment Follow-Up

## Cohort-controlled design:

Iraq-deploying

Non-deploying

## Cluster Sampling: Battalion-level units

Type: combat arms, combat support, service support

Duty status: Active Duty, National Guard

# Study Procedures

- Conducted on-site at military installations



- Group-administered survey instruments (15 min)

- Individually-administered, performance-based cognitive tests/interviews (60 min)



# Results

**Covariates:** Time 1 levels of outcomes; demographics; sleep, alcohol

**Model:** GEE multi-level regressions adjusted for battalion membership

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Measure	Direction of Deployment Effects	<i>p</i>
Verbal Learning	disadvantage	.003
Visual Memory	disadvantage	.0008
Sustained Attention	disadvantage	<.0001
Reaction Time	advantage	.003

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Vasterling et al. (2006), *JAMA*, 296, 519-529

# Associations with PTSD and Depression Symptoms and TBI

- PTSD and depression symptom severity negatively correlated with performance proficiency.
- Self-reported deployment mild TBI not related to performance.
- When added as covariates, **no effect on primary outcomes in core model.**

# Survival Response: Carried Over?

- Physiological: fight or flight
- Psychological:  
Adaptive redirection of cognitive resources



# Association of Time Since Deployment, Combat Intensity, and Posttraumatic Stress Symptoms With Neuropsychological Outcomes Following Iraq War Deployment

Brian P. Marx, PhD; Kevin Brailey, PhD; Susan P. Proctor, DSc; Helen Z. MacDonald, PhD;  
Anna C. Graefe, BA; Paul Amoroso, MD, MPH; Timothy Heeren, PhD; Jennifer J. Vasterling, PhD

*Arch Gen Psychiatry.* 2009;66(9):996-1004

## Healthy warriors: self-selected to stay in Army:

N = 177 active duty deployed (13 months post-deployment)

N = 108 active duty deployed (4 months post-deployment)

## Measures:

Sustained attention

Visual memory

Verbal learning

Reaction Time

CPT omissions

WMS VR % retention

WMSIII, Paired Assoc I

ANAM Simple RT

# Results

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- Greater combat severity → more efficient reaction times
- PTSD sx severity at 1 year → poorer attention

## Conclusion:

PTSD more likely to become associated with cognitive impairment over time.

# Memory → PTSD

**Table 4.** Longitudinal associations of residualized PCL scores with pre-deployment neurocognitive performances

	B	SE B	$\beta$
Model A. Verbal and visual immediate recall			
Step 1 (Autoregressor)			
PCL summary score (pre-deployment)	0.51	0.04	.48**
Step 2 (Covariates)			
Age in years	0.16	0.09	.06
Gender	3.83	1.63	.08*
DRRI Combat Experiences Scale, summary score	0.35	0.04	.28**
Test-retest interval, number of days	-0.00	0.01	-.01
Step 3 (Pre-deployment neurocognitive performances)			
WMS-III Verbal Paired Associates, immediate recall, sum of trials A-D	-0.04	0.06	-.02
WMS Visual Reproductions, immediate recall	-0.45	0.21	-.07*
Trail Making B - A (log-transformed seconds)	0.28	1.37	.01
NES3 CPT log-transformed false positives	0.41	0.85	.02
NES3 CPT log-transformed non-responses	-1.61	0.93	-.06

# PTSD/Stress → Neuropsychological and Neural Alterations

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Archival Dementia Risk Study:

N = 181,093 veterans

PTSD → almost 2x the risk of dementia

PTSD: 10.6%

No PTSD: 6.6%

*(Yaffe et al., 2010; Arch Gen Psych)*

# Neuropsychological Findings: Summary

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- Inhibitory and memory dysfunction relevant
- Attentional biases to threat relevant information
- Impairment is often mild
- Problems may broaden when dysregulation becomes chronic
- Bi-directional relationship between PTSD and brain functioning.

# Clinical Assessment

# Psychological Assessment of PTSD

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- Use of multiple methods:
  - Structured interview
  - Self-report (sx congruent, sx incongruent)
- Assessment content:
  - Traumatic event (Criterion A)
  - PTSD Symptoms
  - Comorbidities
  - Functional Impairment

# Assessment Issues: Criterion A

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- Traumatic vs. nontraumatic stress
- Current ambiguities
  - “confronted with”
  - “threat to physical integrity”
  - chronic illness
- Subjective response to the stressor (Criterion A.2)
- Amnesia for the event (e.g., car accidents)

# Assessment issues: PTSD

## Symptoms

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- Linking symptoms to trauma(s)
- Assessment of frequency, intensity, and recency
- Specificity of symptoms to PTSD
- Response bias/ motivational issues
- DSM-based diagnosis vs. severity cut-offs

# Common Psychiatric Differentials

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Acute Stress Disorder

Adjustment Disorder

Obsessive-Compulsive Disorder

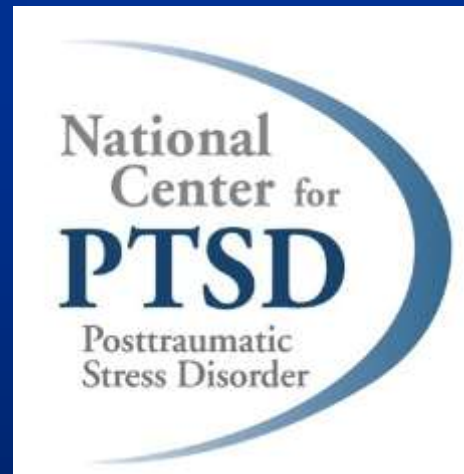
Psychotic Disorder

Mood disorder

Other anxiety disorders

Malingering (in certain contexts)

# Specific Measures



<http://www.ptsd.va.gov>

# Clinical Neuropsychological Assessment of Patients with PTSD: History/Interview

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- Routine neuropsychological risk factors and developmental history questions
- Special areas of emphasis related to PTSD

# History/Interview: Special Areas of Emphasis

- Current PTSD symptom severity
- Recent sleep patterns
- Current severity of comorbid psychiatric disorder(s)
- Observable mood disturbance
- Alteration of arousal
- Dissociative symptoms
- Current/past substance use

# History/Interview: Special Areas of Emphasis (cont.)

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- Medications, including antihistamines
- Physical injury, including TBI, related to trauma event
- Cardiovascular disease and other medical disorders
- Past suicide attempts that may have resulted in brain damage

# Neuropsychological Tests

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- Broad survey of neuropsychological domains
- Areas of special emphasis:
  - Attention (assess multiple facets)
  - Inhibition
  - Learning and memory (assess multiple facets)
  - Motivation (if possible secondary gain)
  - Mood and psychopathology

# Differential Diagnosis of Neurocognitive Deficits in PTSD

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Common differentials:

Traumatic brain injury

Sequelae of prolonged, excessive alcohol use

Medication effects

ADHD

Other psychiatric disorders (e.g., depression)

# Differential Diagnosis: Considerations

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- Onset and course of deficits
- Deficits in domains other than attention/executive and memory (e.g., visuoperceptual, language, praxis)
- Severity and nature of deficits
- Presence of unilateral signs

# PTSD Treatment

# PTSD Treatments

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- Cognitive Behavioral
  - Prolonged Exposure
  - Cognitive Processing Therapy
  - EMDR
- Pharmacological
  - SSRIs
  - Off-labels

# Threats to Treatment: General Considerations

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- Adherence
- Concentration/focus during sessions
- Group behavior

# Threats to Cognitive Interventions: Inhibition and Flexibility Deficits

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- Target distorted thoughts with goal of reappraisal
- Require inhibition of maladaptive thoughts
- Require sufficient flexibility to re-appraise

# Threats to Exposure Based Interventions: Memory Deficits

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- Require controlled retrieval of the trauma memory & assoc. emotions
- Require modification of the memory & assoc. emotions/formation of new associations

# Non-TBI Cognitive Deficits and Diminished PTSD Tx Response

- Wild & Gur (2008) (n = 23)

Lower pre-treatment verbal memory → attenuated response to CBT (for PTSD)

- Rizvi, Vogt, & Resick (2009) (n = 145)

Lower pre-treatment IQ → greater early drop out rate in CBT RCT.

# Treatment Benefits for Cognitive Impairment

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- Structure of cognitive-behavioral interventions
- Certain pharmacological therapies may enhance cognition

# Summary

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- Deficits are mild
- Typically limited to attention, inhibition, learning/  
memory
- PTSD cannot be diagnosed on the bases of  
neuropsychological tests alone
- Neuropsychological deficits may reflect both  
cause and effect

# Summary: Applications

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- Addressing functional impairment
- Ruling out more overt neurological insult
- Treatment planning

# Unresolved Questions

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- Interactions with developmental stage (i.e., children, older adults)
- How might cognitive abilities affect treatment response?
- Variation with PTSD symptom change
- Long-term risks?

Thank you!