OVERVIEW OF POST-TRAUMATIC STRESS DISORDER

CANNABIS RESEARCH BOARD
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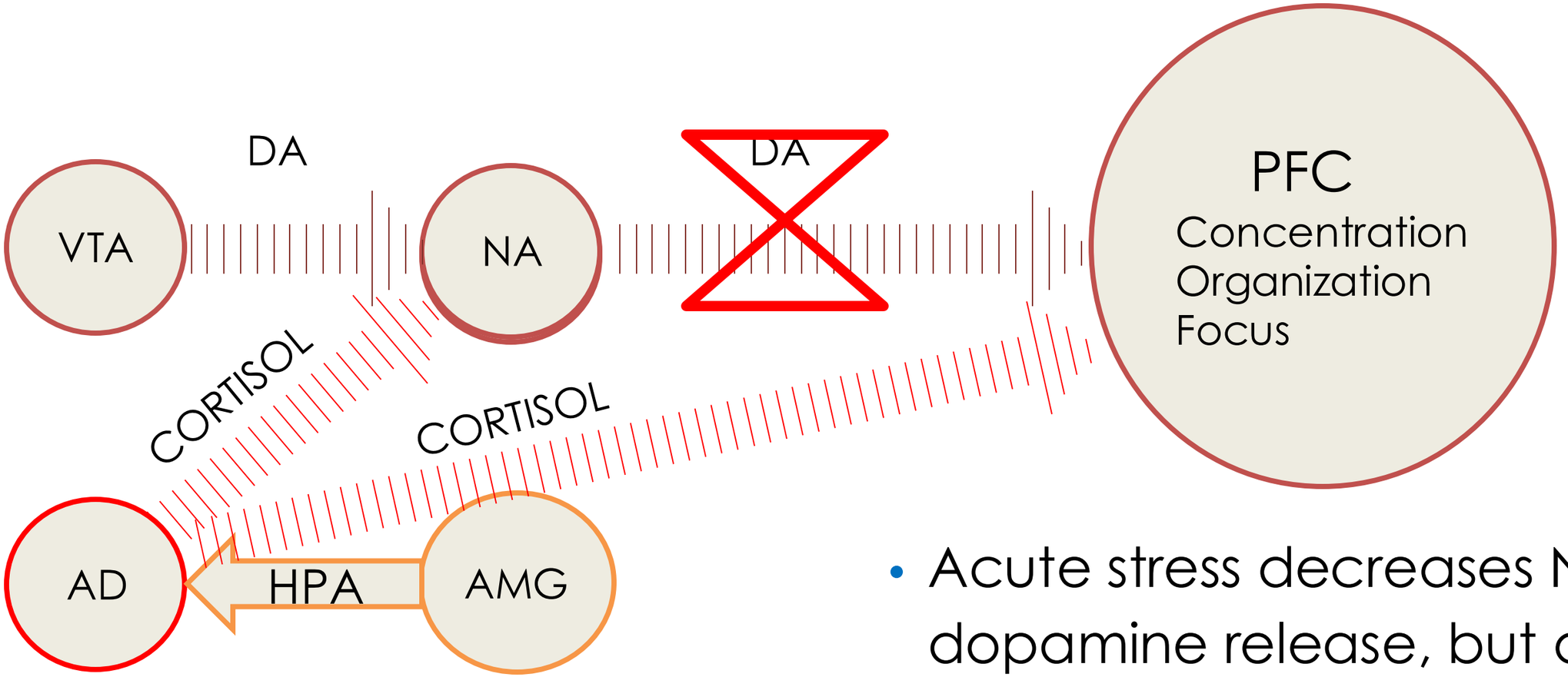
LEARNING OBJECTIVES

- Understand the growing public health impact of PTSD
- Recognize the importance of neuroinflammation in the development of PTSD symptoms
- Explain how lifestyle psychiatry can expand the window of tolerance and improve PTSD symptoms

Introduction

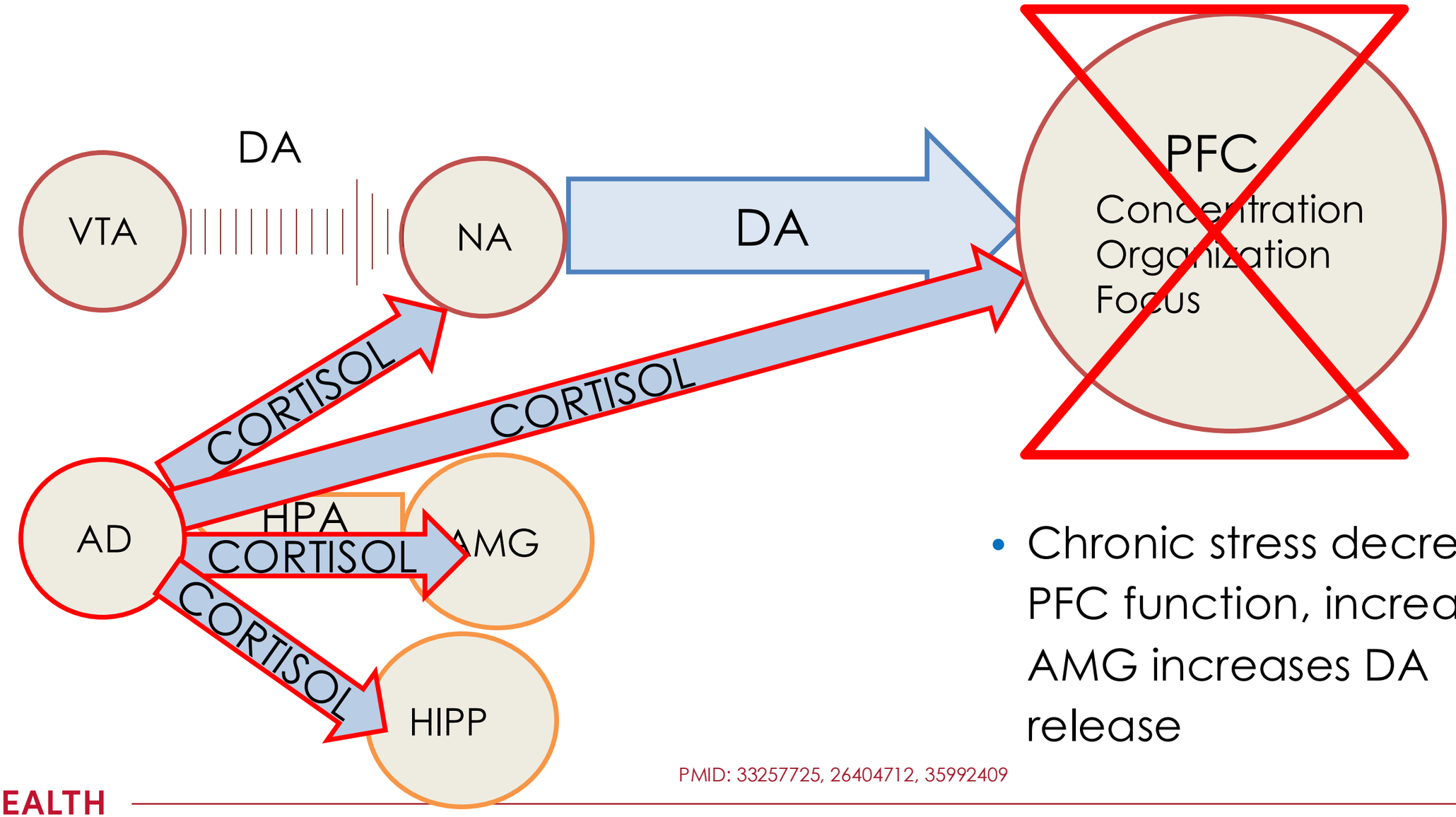
ACUTE STRESS REACTION



- Acute stress decreases NA dopamine release, but acts on PFC to improve focus

PMID: 33257725, 26404712

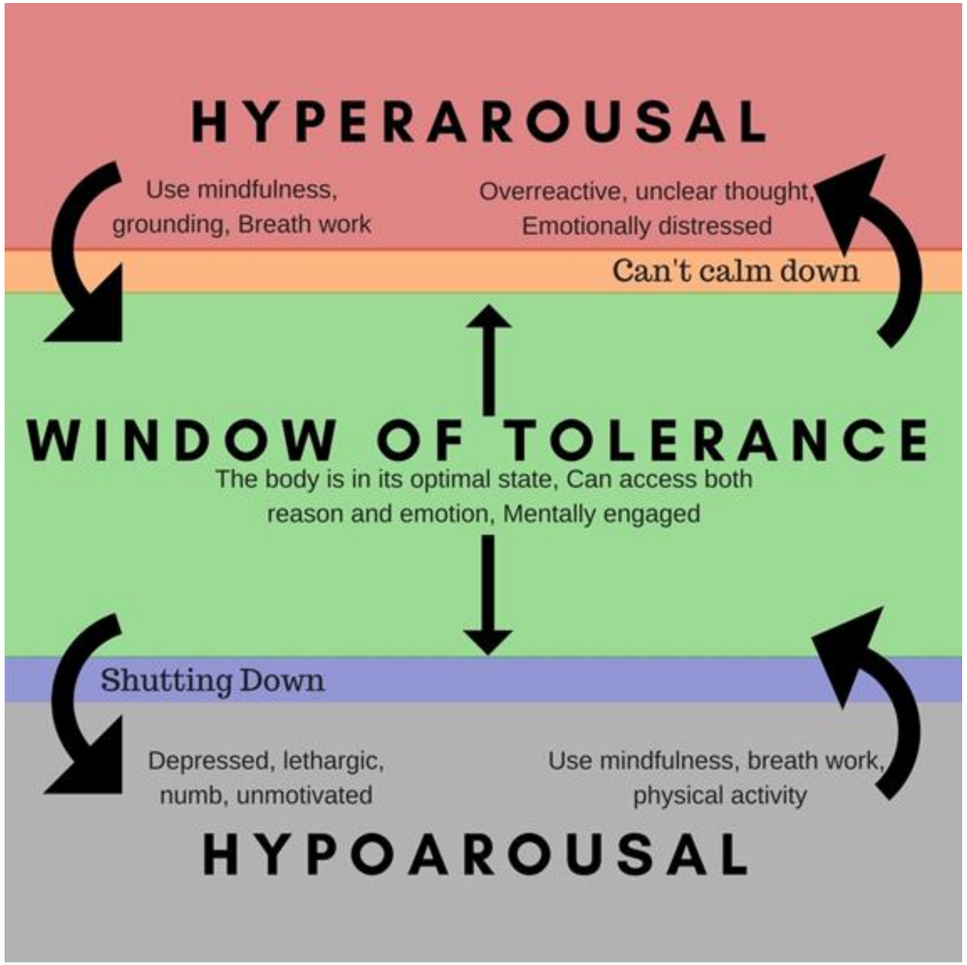
CHRONIC STRESS REACTION



- Chronic stress decreases PFC function, increases AMG increases DA release

PMID: 33257725, 26404712, 35992409

CHRONIC STRESS AND WINDOW OF TOLERANCE



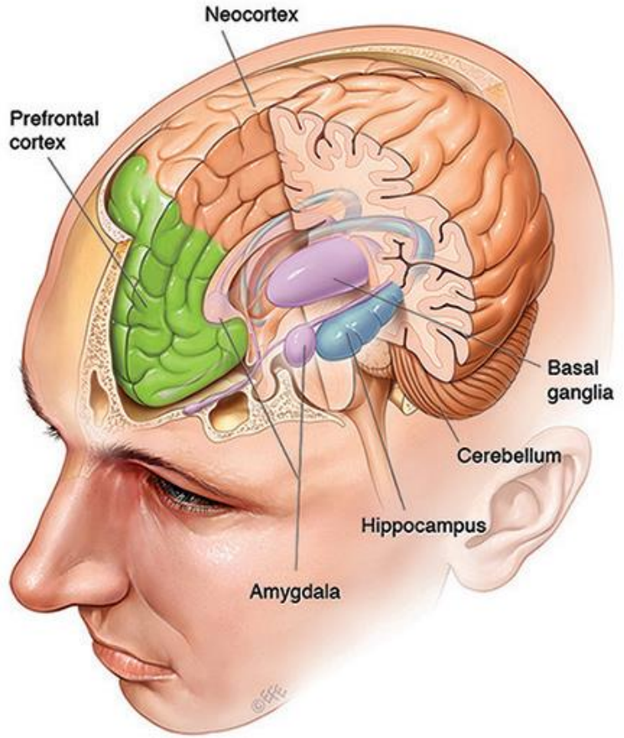
Sympathetic-dominant Hyperarousal:
Emotionally flooded, reactive, impulsive, hypervigilant, fearful, angry.
Intrusive imagery and affects, racing thoughts
Flashbacks, nightmares, high-risk behaviour
Efforts to reduce this state may include suicide planning, self harm,
compulsive cleaning, abuse of alcohol or opiates

Parasympathetic-dominant Hypoarousal:
*F*lat affect, numb, "empty," or "dead"
Cognitively dissociated, inability to think
Collapsed, disabled defensive responses
Helpless and hopeless
Efforts to reduce may include suicide planning, self-harm, compulsive

https://neurodivergentinsights.com/blog/window-of-tolerance; Corrigan et al 2011

CHRONIC STRESS: NEUROINFLAMMATION

- Neuroinflammatory response: microglia & blood-brain-barrier
  - Interferon-gamma
  - Interleukin 6
  - Interleukin 1 beta
  - Tumor necrosis factor-alpha
- Decrease hippocampal volume
  - Failures to process
  - Unable to record explicit memories (?)
- The hippocampus is unable to check the amygdala (neuroception)
- It affects gut microbiota and alters digestion



PMID: 26544749, 19042779, 32074311, https://qbi.uq.edu.au/brain-basics/memory/where-are-memories-stored

CHRONIC STRESS: TRIFECTA ACTIVATED

- Abnormal learning conditions
- Affective dysregulation
- Altered cognitive cues of social circumstances via classically conditioned responses
- These implicit memories develop patterns to protect the individual from encountering the same fear response

PMID: 8659645, 8564271

CHRONIC STRESS: ROLE OF SYMPTOMS

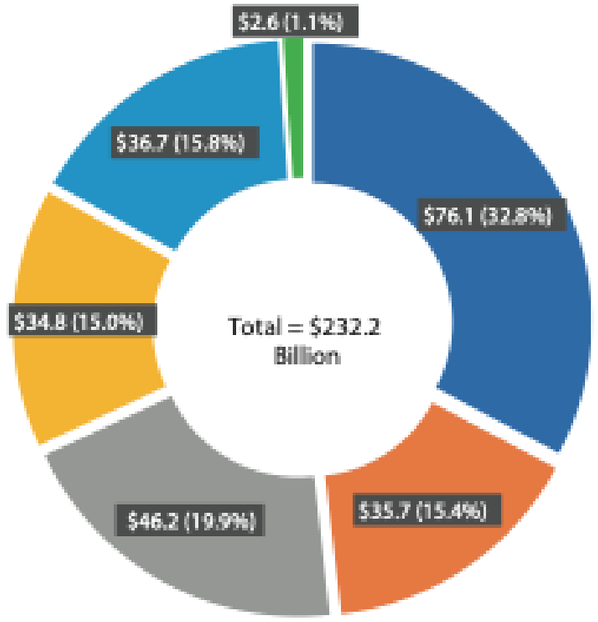
- Flashbacks and hypervigilance
  - Keeps the individual on guard
- Depression, despair, and hopelessness
  - Helps the individual to be seen but not heard
- Fear
  - Restricts relationships and the freedom to act
- Shame
  - Pushes the individual into invisibility

Fisher J. Transforming the Living Legacy of Trauma: A Workbook for Survivors and Therapists. 2021; https://drwinnieymaduro.com/f/traumatic-stress-%E2%80%93-pathologies-%E2%80%93-recovery-the-body-keeps-the-scor

Impact of PTSD

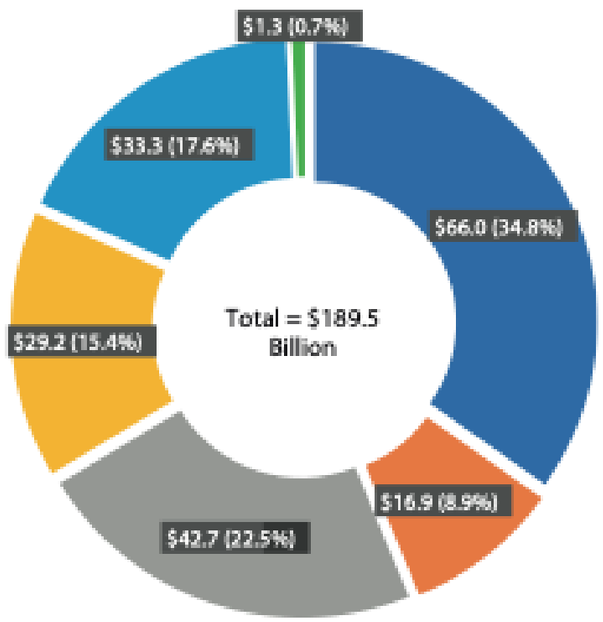
IMPACT OF PTSD

Figure 1. Excess Economic Burden of PTSD in the Overall US Population in 2018, Billion USD



Abbreviations: PTSD = posttraumatic stress disorder, USD = United States dollars.

Figure 2. Excess Economic Burden of PTSD in the US Civilian Population in 2018, Billion USD



Abbreviations: PTSD = posttraumatic stress disorder, USD = United States dollars.

Davis et al. 2022

IMPACT OF PTSD

SCIENTIFIC INVESTIGATIONS

JCSM
Journal of Clinical Sleep Medicine

pii: jc-00285-14
http://dx.doi.org/10.5664/jcsm.4692

Obstructive Sleep Apnea and Posttraumatic Stress Disorder among OEF/OIF/OND Veterans

Peter J. Colvonen, PhD[1,2]; Tonya Masino, MD[1]; Sean P.A. Drummond, PhD[1,2,3]; Ursula S. Myers, MS[3]; Abigail C. Angkaw, PhD[1,2,3]; Sonya B. Norman, PhD[1,2,3,4]

[1]VA San Diego Healthcare System and Department of Psychiatry, University of California, San Diego, CA; [2]Center of Excellence for Stress and Mental Health (CESAMH), VA San Diego Healthcare System, San Diego, CA; [3]San Diego State University/University of California, San Diego Joint Doctoral Program, San Diego, CA; [4]National Center for PTSD, White River Junction, VT

Objectives: This study examined: (a) the relationship between self-reported posttraumatic stress disorder (PTSD) symptoms and risk of obstructive sleep apnea (OSA) in a younger, Iraq and Afghanistan (OEF/OIF/OND) veteran sample seeking treatment for PTSD; and (b) the relationships between PTSD symptom scores and each risk factor of OSA (snoring, fatigue, high blood pressure/BMI).

Methods: Participants were 195 Iraq and Afghanistan veterans presenting to a VA outpatient PTSD clinic for evaluation. Veterans were 21 to 59 years old (mean 33.40, SD 8.35) and 93.3% male (n = 182). Logistic regressions were run to examine whether veterans with greater PTSD symptom severity had an increased probability of screening as high risk for OSA, even after controlling for known risk factors (older age, positive smoking status, and use of CNS depressants).

Results: Of 159 veterans screened, 69.2% were assessed as being at high risk for OSA. PTSD symptom severity increased the risk of screening positive for OSA. PTSD symptom severity increased risk of screening positive for snoring and fatigue, but not high blood pressure/BMI.

Conclusions: OEF/OIF/OND veterans with PTSD screen as high risk for OSA at much higher rates than those seen in community studies and may not show all classic predictors of OSA (i.e., older and higher BMI). This study is the first to suggest that the Berlin may be a useful screener for OSA in a younger OEF/OIF/OND veteran population with PTSD. Screening of younger veterans with PTSD for OSA should be standard care, and polysomnography and OSA interventions should be readily available to younger veterans.

Keywords: OEF/OIF/OND, veterans, obstructive sleep apnea, PTSD

Citation: Colvonen PJ, Mosino T, Drummond SP, Myers US, Angkaw AC, Norman SB. Obstructive sleep apnea and posttraumatic stress disorder among OEF/OIF/OND veterans. *J Clin Sleep Med* 2015;11(5):513–518.

Colvonen et al, 2015

IMPACT OF PTSD

- Relative to veterans with chronic pain alone, those with co-occurring chronic pain and probable PTSD were more likely to screen positive for psychiatric disorders (odds ratios [ORs]=2.59-9.88).
- Relative to veterans with probable PTSD only, those with co-occurring chronic pain and probable PTSD were more likely to have attempted suicide (OR=4.79; 95%CI, 1.81-12.69).

J Gen Intern Med. 2024 Aug;39(11):2009-2016. doi: 10.1007/s11606-024-08803-w. Epub 2024 May 23.

Co-occurring Chronic Pain and PTSD Among US Military Veterans: Prevalence, Correlates, and Functioning

David E Reed 2nd [1 2], Ian C Fischer [3 4], Rhonda M Williams [5 6], Peter J Na [3 7], Robert H Pietrzak [3 4 8]

Affiliations

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DOI: 10.1007/s11606-024-08803-w

Abstract

Background: The prevalence of co-occurring chronic pain and posttraumatic stress disorder (PTSD) has yet to be established in a nationally representative sample of US veterans, and little is known about the individual contributing roles of these disorders to the psychiatric and functional burden of this comorbidity.

Objective: To determine the prevalence of chronic pain, PTSD, and co-occurring chronic pain and PTSD, and psychiatric comorbidities and psychosocial functioning in these groups.

Design: Data were analyzed from the National Health and Resilience in Veterans Study, which surveyed a nationally representative sample of US veterans.

Participants: Veterans (n=4069) were classified into four groups: control (i.e., no PTSD or chronic pain), chronic pain only, PTSD only, and co-occurring chronic pain and PTSD.

Main measures: A probable PTSD diagnosis was established using the PTSD Checklist for DSM-5, and a chronic pain diagnosis using a self-report item that queried health care professional diagnoses. Psychiatric and functional status were assessed using the Patient Health Questionnaire-4, Alcohol Use Disorders Identification Test, Screen of Drug Use, Suicide Behaviors Questionnaire-Revised, Short Form Health Survey-8, Brief Inventory of Psychosocial Functioning, and Medical Outcomes Study Cognitive Functioning Scale.

Key results: A total of 3.8% of veterans reported both probable PTSD and a diagnosis of chronic pain. Relative to veterans with chronic pain alone, those with co-occurring chronic pain and probable PTSD were more likely to screen positive for psychiatric disorders (odds ratios [ORs]=2.59-9.88) and scored lower on measures of psychosocial functioning (Cohen's ds=0.38-1.43). Relative to veterans with probable PTSD only, those with co-occurring chronic pain and probable PTSD were more likely to have attempted suicide (OR=4.79; 95%CI, 1.81-12.69).

Conclusions: Results underscore the importance of whole health care that considers a broad range of health and functional domains in the assessment and treatment of co-occurring chronic pain and PTSD in veterans.

Reed et al, 2024

IMPACT OF PTSD

- Traumatic stress increases the risk for inflammation-related somatic diseases and early mortality.
- The metabolic syndrome reflects the increased health risk associated with combat stress and PTSD.
- Obesity, dyslipidemia, hypertension, diabetes mellitus, and cardiovascular disease are prevalent among PTSD patients.

Turning Basic Research into Clinical Success

CARDIOLOGY

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Posttraumatic Stress Disorder and Cardiometabolic Disease

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Key Words
Cardiovascular disease · Hypothalamic-pituitary-adrenal axis · Inflammation · Insulin resistance · Metabolism · Sympathetic nervous system

Abstract
The need for addressing posttraumatic stress disorder (PTSD) among combat veterans returning from Afghanistan and Iraq is a growing public health concern. Current PTSD management addresses psychiatric parameters of this condition. However, PTSD is not simply a psychiatric disorder. Traumatic stress increases the risk for inflammation-related somatic diseases and early mortality. The metabolic syndrome reflects the increased health risk associated with combat stress and PTSD. Obesity, dyslipidemia, hypertension, diabetes mellitus, and cardiovascular disease are prevalent among PTSD patients. However, there has been little appreciation for the need to address these somatic PTSD comorbidities. Medical professionals treating this vulnerable population should screen patients for cardiometabolic risk factors and avail themselves of existing preventive diet, exercise, and pharmacologic modalities that will reduce such risk factors and improve overall long-term health outcomes and quality of life. There is the promise that cardiometabolic preventive therapy complementing psychiatric intervention may, in turn, help improve the posttraumatic stress system dysregulation and favorably impact psychiatric and neurologic function.

Introduction

Exposure to traumatic stressors is widespread. Short-term severe traumatic stress may severely compromise an individual's long-term psychological health. However, there is increasing evidence that posttraumatic stress disorder (PTSD) is not just a 'mental illness' but is also associated with an increased risk for somatic diseases and early mortality [1, 2].

Current management of PTSD focuses on the psychiatric parameters of this condition with little emphasis on addressing the comorbid cardiometabolic risk factors that impair overall long-term health outcomes.

Posttraumatic Stress Disorder

PTSD is a severely disabling neuropsychiatric anxiety disorder that develops in civilians, police officers, combat soldiers, and others as a result of experiencing horrifying trauma/stress [3].

History

Combat-related stress responses have been mentioned as early as in the 19th century BCE by an Egyptian named Hori, in the 5th century BCE by the Greek historian Herodotus [4], and in the 11th century by the *Anglo-Saxon Chronicle* [5]. Lady Percy's soliloquy in *Henry IV*, written around 1597, appears to describe PTSD symptoms

Levine et al, 2014

IMPACT OF PTSD: ACE SCORES

- Scores greater than 5 were 7-10 X more likely to report a substance use disorder
- Scores greater than 5 had a greater likelihood of developing a substance use disorder before the age of 14
- A strong linear relationship between ACE and negative health outcomes, homelessness, violent crime, and additional trauma

Souglas et al, Addict Behav. 2010 January ; 35(1): 7–13.

Interventions

FEAR MEMORY

- Explicit memory: the conscious recollection of facts or experiences
- Implicit memory: the form of long-term memory that allows an individual to perform a task without recalling the experience
- Research has explored three aspects of fear (implicit) memory
  - (1) dampening the cue-elicited fear (implicit memory)
  - (2) blocking the reconsolidation of the fear (implicit) memory
  - (3) facilitating the extinction of the (implicit) memory

Loflin et al, 2017

TREATMENT STRATEGIES

- Potential strategies under investigation for PTSD management are to uncover/develop a safe method to uncouple, attenuate, or even erase the negative valence associated with aberrant and enduring aversive memories underlying the core of this psychiatric condition.
- Research on rats has shown that injection of CBD/THC following fear conditioning tempers cued responses and results in a reduction in freezing behavior in response to conditioned fear cues
- Administration of CBD/THC to rats following memory retrieval disrupted fear memories on the following day
- Neurobiological studies have demonstrated that antagonists of the cannabinoid receptor type 1 (CB1) decrease extinction learning in rats

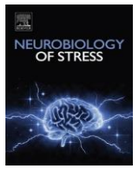
Loflin et al, 2017

TREATMENT STRATEGIES

Contents lists available at ScienceDirect

Neurobiology of Stress

journal homepage: www.elsevier.com/locate/ynstr



Endocannabinoid and neuroplasticity-related changes as susceptibility factors in a rat model of posttraumatic stress disorder

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Keywords:
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Rat
Resilience
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ABSTRACT

Traumatic experiences result in the development of posttraumatic stress disorder (PTSD) in 10–25% of exposed individuals. While human clinical studies suggest that susceptibility is potentially linked to endocannabinoid (eCB) signaling, neurobiological PTSD susceptibility factors are poorly understood. Employing a rat model of contextual conditioned fear, we characterized distinct resilient and susceptible subpopulations based on lasting generalized fear, a core symptom of PTSD. In these groups, we assessed i.) eCB levels by mass spectrometry and ii.) expression variations of eCB system- and iii.) neuroplasticity-related genes by real-time quantitative PCR in the circuitry relevant in trauma-induced changes. Furthermore, employing unsupervised and semi-supervised machine learning based statistical analytical models, we assessed iv.) gene expression patterns with the most robust predictive power regarding PTSD susceptibility. According to our findings, in our model, generalized fear responses occurred with sufficient variability to characterize distinct resilient and susceptible subpopulations. Resilient subjects showed elevated prelimbic and lower ventral hippocampal levels of eCB 2-arachidonoyl-glycerol (2-AG) compared to resilient and non-shocked control subjects. Ventral hippocampal 2-AG content positively correlated with the strength of fear generalization. Furthermore, susceptibility was associated with i.) prefrontal, hippocampal and amygdalar neuronal hypoactivity, ii.) marked decrease in the expression of genes of transcription factors modulating neuroplasticity and iii.) an altered expression pattern of eCB-related genes, including enzymes involved in eCB metabolism. Unsupervised and semi-supervised statistical approaches highlighted that hippocampal gene expression patterns possess strong predictive power regarding susceptibility. Taken together, the marked eCB and neuroplasticity changes in susceptible individuals associated with abnormal activity patterns in the fear circuitry possibly contribute to context coding deficits, resulting in generalized fear.

- Ventral hippocampal 2-AG content positively correlated with the strength of fear generalization.
- Susceptibility was associated with
  - Prefrontal, hippocampal, and amygdalar neuronal hypoactivity
  - Marked decrease in the expression of genes of transcription factors modulating neuroplasticity
  - An altered expression pattern of eCB-related genes, including enzymes involved in eCB metabolism.

Szente et al 2024

Questions

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