Cannabinoids and Health

Module 9

Lecture 3: Etiology of Anxiety and PTSD

Etiology of GAD

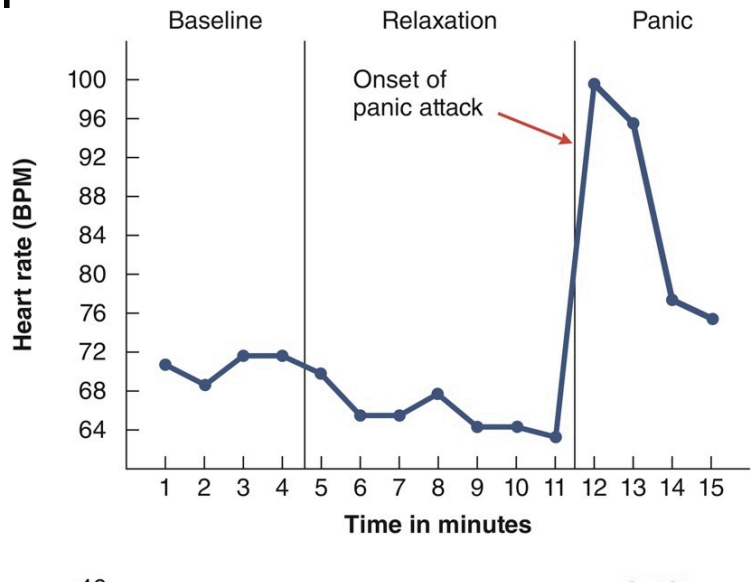
- We do not know a lot of specifics about the causes, but factors are involved
  - Family history of anxiety
  - Changes in brain neurotransmitters like GABA
  - Recent and prolonged exposure to stressful situations
  - Childhood trauma
  - Maladaptive cognitions, assumptions
    - A situation/person is unsafe until proven safe
    - It is always best to assume the worst
  - Researchers have repeatedly found that people with GAD have maladaptive assumptions, particularly about danger

Etiology of Panic: Biological Perspective

- An increase in norepinephrine from the sympathetic nervous system increases the rate of contractions in the heart

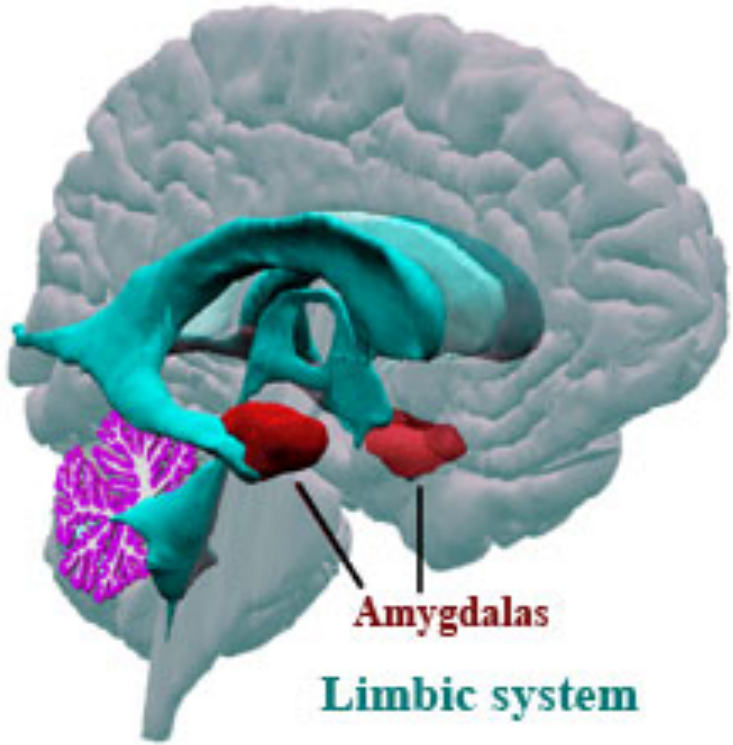
- Along with epinephrine, norepinephrine also underlies the fight-or-flight response, directly increasing heart rate

- Misfiring of fight-flight system



Etiology of Panic: Biological Perspective

- Brain structure and function likely play a role
- Brain circuits involving the amygdala
- Critical role in the circuits that control the experience of fear, both instinctive fear (like being afraid of snakes or large carnivores) and fear that is learned from life experiences.



Etiology of Social Anxiety Disorder

- Genetics are important – twin studies have found a significant genetic component thought the exact genes are unknown
- The family environment is another important factor.
  - Having an anxious parent
  - Growing up in an environment characterized by frequent criticism
- Learning from specific traumatic or humiliating social events, such as traumatic experience with public speaking, being bullied

Etiology of PTSD: Developmental Risk Factors

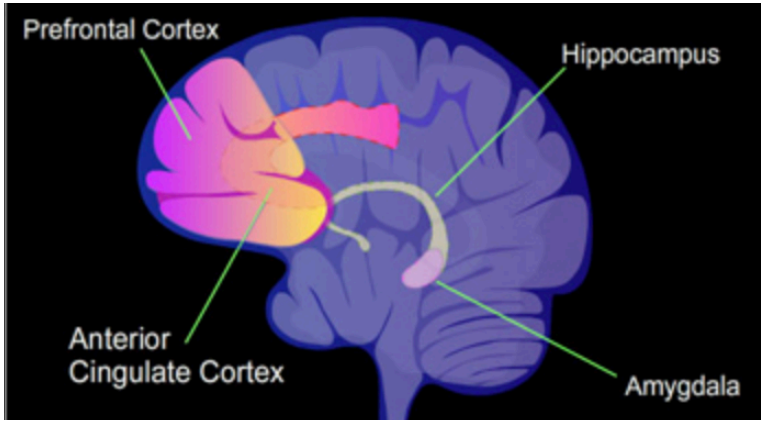
- Relatively small but significant effects on risk for PTSD for individual characteristics and environmental factors:
  - pre-trauma psychological adjustment
  - child abuse, general childhood adversity, family instability

- Support for both “stress vulnerability” and “stress sensitization” models for development of PTSD

Koenen, 2006, *Annals of NY Acad Sci*

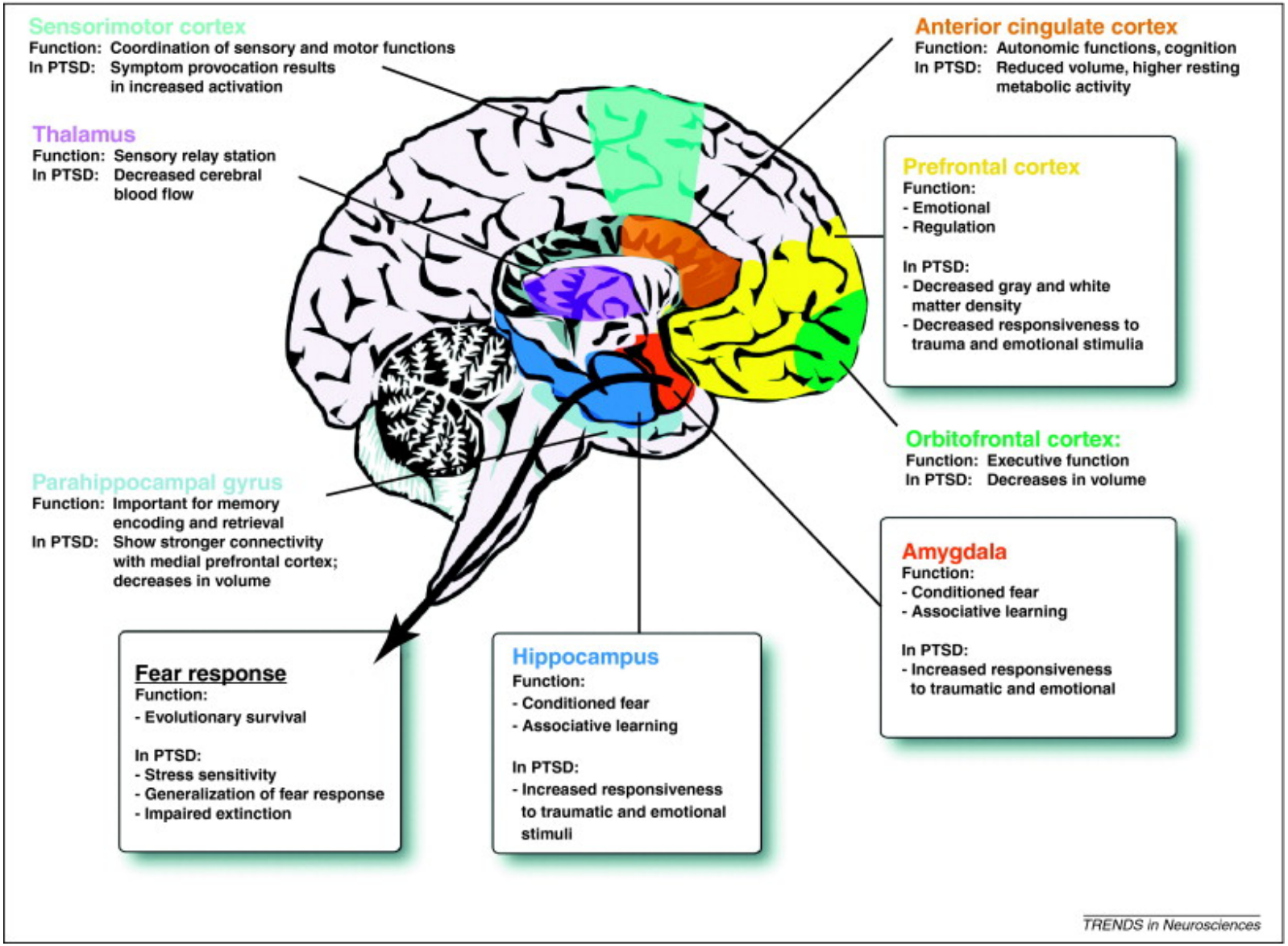
Etiology of PTSD: The Role of Self-Regulation

- Emotion processing (EP) and executive function (EF) systems are key
  - Adults with PTSD show deficits in both
- Central role of amygdala—fear processing
  - amygdala overactivation (EP) in response to threat AND/OR
  - frontal (EF) deficits resulting in the lack of amygdala inhibition
  - deficits in EP and EF mediated by interconnections between limbic (amygdala) and frontal brain regions



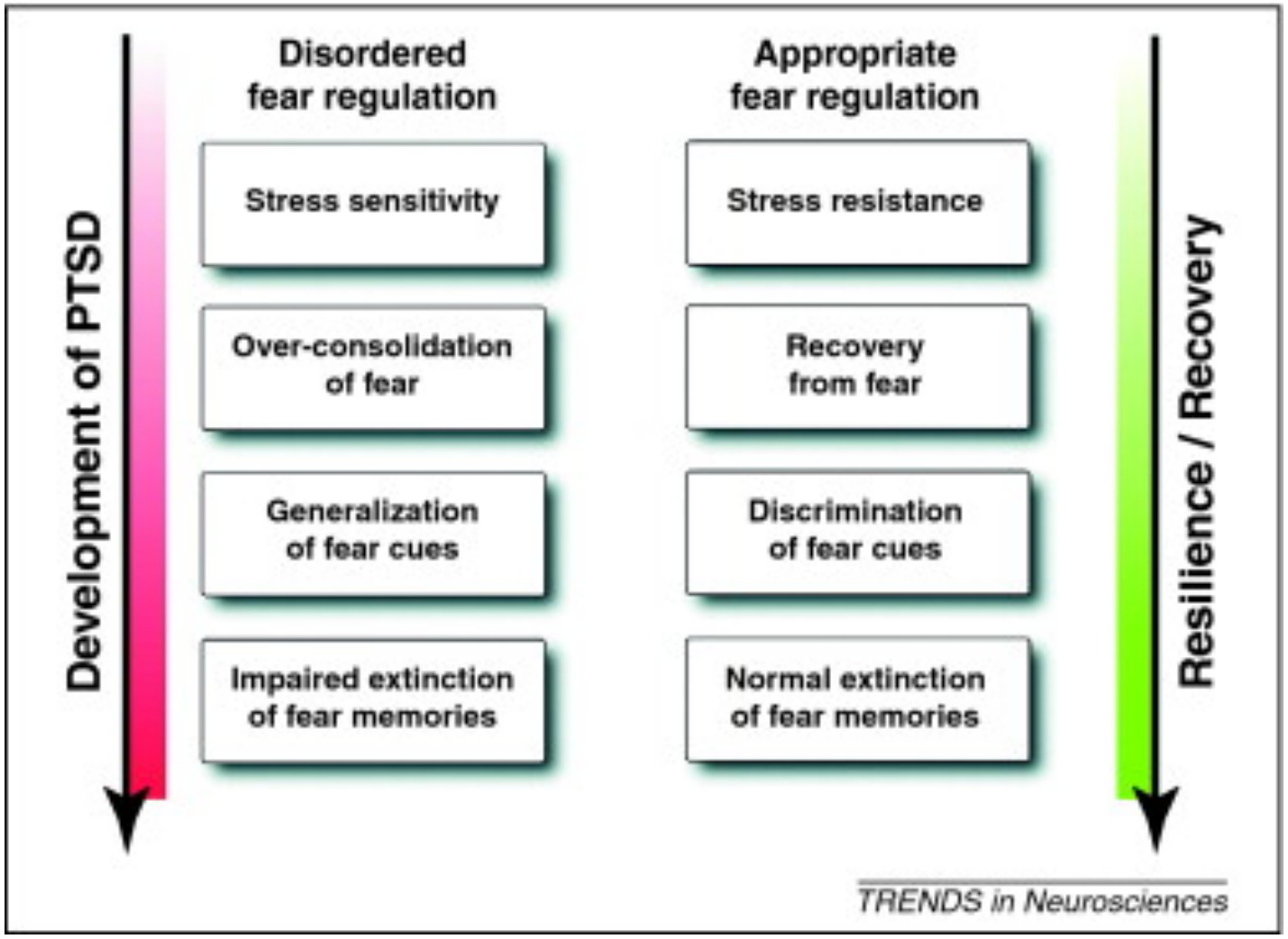
Koenen, 2006, *Annals of NY Acad Sci*

Etiology of PTSD: Fear Conditioning Model



Mahan & Ressler, 2012, *Trends in Neurosciences*

Etiology of PTSD: Fear Conditioning Model



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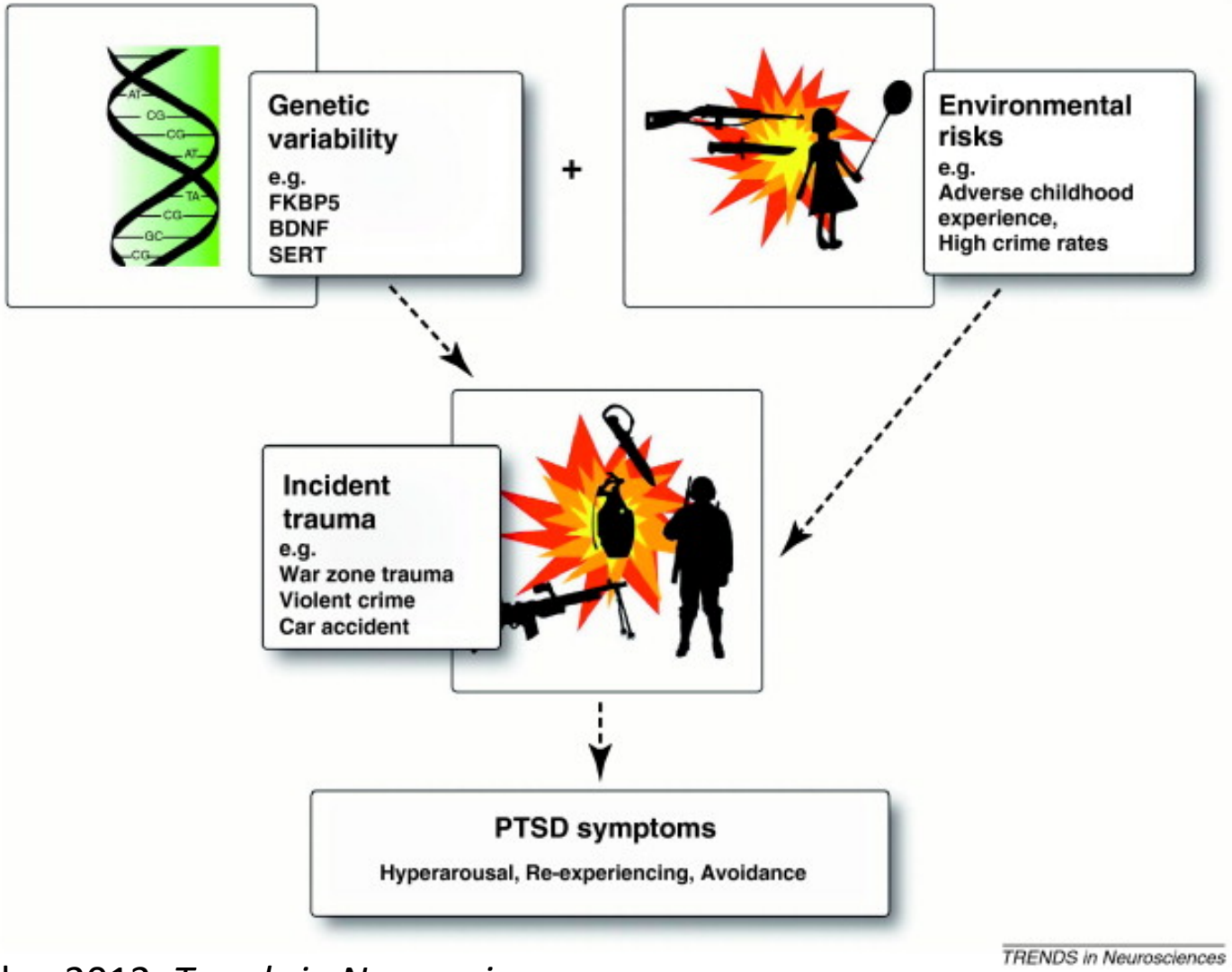
Etiology of PTSD: Genes + Environment



Mahan & Ressler, 2012, *Trends in Neurosciences*

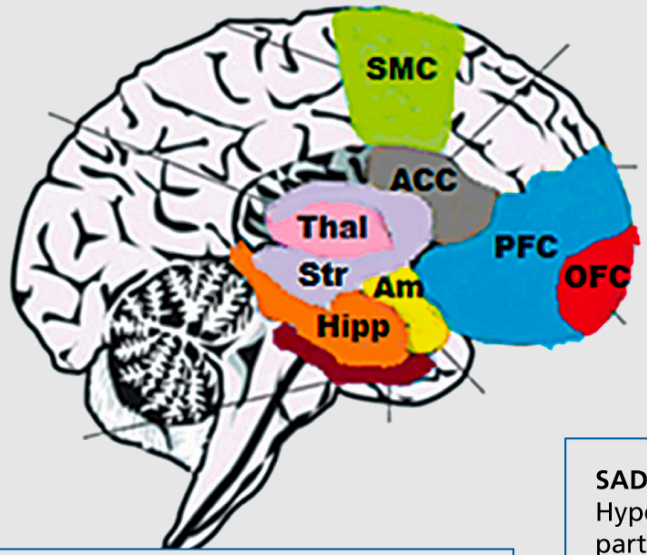
Shared Components Across Anxiety Disorders

- Fear stimulus/trigger
  - Anxiety is almost always cued
- Misinterpretation of threat
  - Overestimating the likelihood of negative outcome
  - Catastrophizing
- Avoidant coping
  - Primary avoidance – avoiding triggers altogether
  - Secondary avoidance – engaging in safety behaviors when complete avoidance is not possible
- Absence of corrective learning
  - New learning does not occur and the fear is maintained (and often strengthened)

Shared Neurobiology

Anxiety disorders:
Hyperactivation of the "fear network" incorporating the thalamus, amygdala, hippocampus, ACC, striatum, sensory-motor cortex and insula (not shown in diagram); hypoactivation of the PFC

PTSD:
Hyperactivation of the lateral and basal amygdala for fear consolidation and expression, insula, as well as hypoactivation and inefficient regulation of limbic activation by the ACC and PFC



PD:
Hyperactivation of the fear network, as well as the brain stem and hypothalamus for excessive panic symptoms, insula for bodily sensations of panic and inefficient regulation of limbic activation by the ACC, PFC and overevaluation of threat by the OFC and contextual fear processing by the hippocampus

GAD:
Hypoactivation of ACC and PFC to perceived threat, hyperarousal to emotion via ineffective PFC processing

SAD:
Hyperactivation of the limbic system, particularly amygdala, in response to social stimuli; disfunction between corticolimbic circuitry, hyperactivation of insula and PFC circuitry in response to social emotion

OCD:
Inefficiency within the cortico-striato-thalamo-cortical loops for inhibitory or excitatory behaviours; interplay between these loops may underlie symptom dimensions (eg, hoarding, checking, counting, contamination fears)

Dialogues Clin Neurosci. 2015;17(3):261-279

Special Topics: The Veteran Population

- PTSD is one of the most common conditions in returning military veterans in the U.S
- PTSD commonly co-occurs with chronic pain, traumatic brain injury and opioid use disorder
- These disorders all increase suicide risk
- VA National Suicide Data Report released in 2018:
  - More than 6,000 Veteran suicides each year from 2008 to 2016
  - In 2016, the suicide rate was 1.5 times greater for Veterans than for non-Veteran adults, after adjusting for age and gender

Special Topics: The Veteran Population

In a 2018 study of 667 veterans with chronic pain:

- 18.14% of veterans had both PTSD and TBI in addition to pain
- 20.69% reported chronic pain and TBI
- 17.39% reported chronic pain and PTSD

Another study of veterans with PTSD between 2004-2013 (N=731,520)

- 2.7% had opioid use disorder in addition to PTSD
- Comorbid opioid use disorder + PTSD diagnoses increased from 2.5% in 2004 to 3.4% in 2013

Blakey et al., 2018, *Journal of Pain*

Shiner et al., 2017, *Journal of Dual Diagnosis*

Summary

- Genetics play a role in anxiety disorders broadly
- Maladaptive learning has a causal role
- Maladaptive cognitions play a role in anxiety disorders
- Rumination plays a role in anxiety disorders
- Biological factors have a causal role
  - Overactivation of fear network – limbic system (same area with high numbers of CB1 receptors)