

PTSD: TARGETED DIRECTIONS IN TREATMENT

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OBJECTIVES

- Describe the precipitants of PTSD and the role of premorbid risk factors
- Correlate the neurobiological effects of trauma with specific symptoms
- Describe the pharmaco/psycho-therapeutic approaches to treatment and rationales for application
- Translate the science to help the individual with PTSD understand the “how’s and why’s” of treatment while promoting self-care



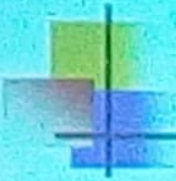
PREVALENCE OF PTSD

- 60% of women and 50% of men will experience a traumatic event, in Nairobi, by the time one reaches 18 years, 99 will have been exposed to a traumatic event
- 9.7% of women and 3.6% of men will develop PTSD (5-15% will have developed PTSD)
- 30% of these will develop a chronic form- these will include comorbid mental disorders



RISK FOR DEVELOPING PTSD INCREASES IF PEOPLE:

- Were directly exposed to the traumatic event as a victim or a witness
- Were seriously injured during the trauma
- Experienced a trauma that was long-lasting or very severe
- Saw themselves or family member in imminent danger
- Had a negative reaction during the event
- Felt helpless during the trauma and were unable to help themselves or a loved one



INDIVIDUALS ARE MORE LIKELY TO DEVELOP PTSD IF THEY:

- Have experienced an earlier life-threatening event or trauma
- Have a current mental health issue
- Have less education
- Are younger
- Lack social support
- Have recent, stressful life changes



DSM 5 CRITERIA FOR PTSD

- Criterion A: Stressor
 - Person has experienced, witnessed, or been confronted with an event or events that involve actual or threatened death or serious injury, or a threat to physical integrity of oneself or others
 - Person's response involved intense fear, helplessness, or horror (or disorganized or agitated behavior in children)




DSM 5 SYMPTOM CLUSTERS

- Criterion B: Re-experiencing symptoms
- Criterion C: Avoidance and numbing symptoms (DSM V proposal is to separate these two into separate cluster)
- Criterion D: Hyperarousal symptoms



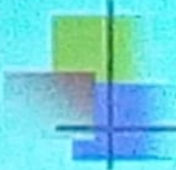
REEXPERIENCING SYMPTOMS

- Intrusive/distressing thoughts
- Recurrent bad nightmares
- Experience flashbacks
- Intense emotional upset at reminder
- Intense physical reactions at reminder
- Person must experience at least *one* of the above




AVOIDANCE AND NUMBING SYMPTOMS

- Avoid thoughts/feelings
- Avoid activities/situations/places
- Can't recall important aspects
- Loss of interest in activities
- Detached/cut-off from others
- Impaired range of emotions
- Changed future plans/hopes
- At least *three* must be experienced



HYPERAROUSAL SYMPTOMS

- Difficulty sleeping
- Irritable/anger outbursts
- Difficulty concentration
- Overly alert
- Jumpier/easily startled
- At least *two* must be experienced

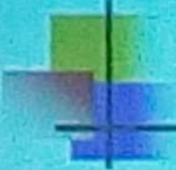


DURATION AND FUNCTIONAL SIGNIFICANCE


- Criterion E: Duration of symptoms in B, C, and D is more than one month
- Criterion F: The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

NEUROBIOLOGY OF PTSD:

HPA AXIS

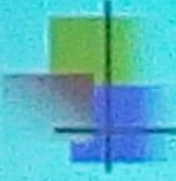


- Hypothalamus secretes corticotropin-releasing factor (CRF), which stimulates the Pituitary to produce and release adrenocorticotropin (ACTH), which stimulates release of glucocorticoids from the Adrenal cortex
- In "Fight or Flight," sustained glucocorticoids have adverse effects on hippocampal neurons



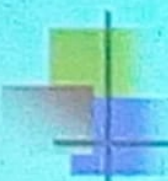
PTSD AND THE HIPPOCAMPUS

- Sustained exposure by glucocorticoids (primarily cortisol) to hippocampal neurons leads to reduction in dendritic branching and reduced hippocampal volume, a finding in PTSD
- Paradoxically, in combat vets, holocaust victims, and abuse victims, there are *decreased* blood/urine cortisol levels



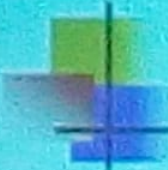
CRF AND CORTISOL

- Corticotropin-Releasing Factor – increased CRF concentrations in lumbar puncture despite low cortisol concentration
- Increased CRF in the CNS may promote increased startle reactivity and hyper-arousal



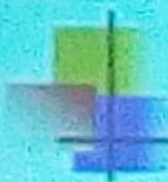
NEUROTRANSMITTERS: THE CATECHOLAMINES

- Norepinephrine and epinephrine are released from the adrenal medulla during exposure to a stressor
- Increased urinary excretion of NE is found in PTSD patients, who also exhibit increased heart rate, BP, and NE levels when challenged with traumatic reminders



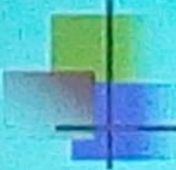
NEUROTRANSMITTERS: SEROTONIN

- Serotonin. Serotonergic neurons originate in the brainstem and project to brain regions including the amygdala, hippocampus, and pre-frontal cortex (PFC)
- It helps to regulate sleep, appetite, sexual behavior, aggression/impulsivity, and analgesia



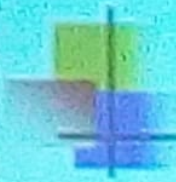
NEUROTRANSMITTERS: GABA/BNZ SYSTEM

- GABA is the primary inhibitory transmitter in the CNS
- PET scans reveal decreased BNZ receptor binding in the cortex, hippocampus, and thalamus of persons with PTSD
- Treatment with BNZs after exposure to psychological trauma, however, doesn't prevent PTSD




NEUROTRANSMITTERS: GLUTAMATE/NMDA SYSTEM

- Glutamate is the primary excitatory transmitter in the CNS and exposure to stress increases glutamate release
- Glutamate binds to several receptors, one of which is NMDA(N-Methyl-D-aspartate **receptor**)
- The glutamate/NMDA receptor system is implicated in learning, memory, and enhanced neuronal communication
- Overexposure to glutamate is associated with excitotoxicity and may cause loss of neurons in the hippocampus and prefrontal cortex



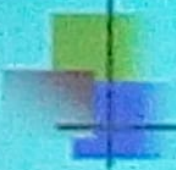
CHANGES IN STRUCTURAL AND FUNCTIONAL NEUROANATOMY

- Decreased volume in the **HIPPOCAMPUS**. The hippocampus controls stress responses, declarative memory, and contextual aspects of fear conditioning
- Functional imaging studies show hypersensitivity of the **AMYGDALA** in PTSD. The amygdala is involved with the acquisition of fear responses
- The **PREFRONTAL CORTEX** exerts inhibitory control over stress responses including fear acquisition



CONNECTING FINDINGS WITH SYMPTOMS: STRUCTURE

- Decreased hippocampal volume can lead to memory impairments and impair the ability to distinguish between safe and unsafe contexts
- Changes in the amygdala leads to exaggerated responses and promote the activation of stress responses
- PFC impairments may cause deficits in suppressing fear responses and interfere with extinction



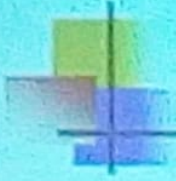
CONNECTING FINDINGS WITH SYMPTOMS: FUNCTION

- Norepinephrine enhances the encoding of *fearful memories*
- Glucocorticoids block the retrieval of emotional memories
- Together these actions could cause encoding of traumatic memories and lack of inhibition of memory retrieval which might cause intrusive memories



CONNECTIONS: FUNCTION

- Lack of regulatory activity of GABA could increase stress responsiveness
- Lack of serotonin could lead to difficulties with impulsivity, aggression, and sleep/appetite disturbances. Serotonin projections exist in (pre-frontal Cortex (PFC) and hippocampus, and decreased volume in those areas could result in fewer serotonergic neurons



TARGETED AND NOVEL APPROACHES: THERAPY

- The gold-standard is **COGNITIVE-BEHAVIORAL THERAPY**
- Individual approaches help the patient confront altered traumatic memories while modifying negative belief systems
- Cognitive Processing Therapy (CPT) and Prolonged Exposure Therapy (PE) are types of CBT



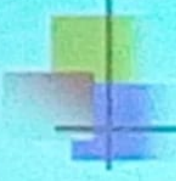
TARGETED APPROACHES: PHARMACOLOGICAL

- Pharmacological management of PTSD until recently was based on individual symptoms
- Better understanding of the neurobiological underpinnings helps in targeting the symptoms and symptom clusters




TARGETED PHARMACY: REEXPERIENCING SYMPTOMS

- SSRIs are considered the first line of defense and can help with co-morbid panic or major depression. *SSRIs have been shown to increase volume of hippocampus*
- Atypical antipsychotics risperidone, quetiapine, olanzapine decrease intrusive thoughts and flashbacks



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AVOIDANCE AND NUMBING

- Avoidance, can't recall important events, detached, impaired range of emotions
- SSRIs have been shown to reduce avoidance, especially in combination with CBT
- Lamotrigine may be helpful if SSRIs can't be tolerated
- Numbing is the most elusive symptom, and often hinders exposure therapy



HYPERAROUSAL SYMPTOMS

- Sleep disturbance, irritability and anger, difficulty concentrating, overly alert, easily startled
- Fullest range of drugs used to manage.
- SSRIs show significant efficacy in reducing hyperarousal
- Mood stabilizers lithium, olanzapine, valproic acid decrease hyperarousal
- Severe symptoms there is room for beta antihypertensive blockers



NOVEL PHARMACOLOGY

- Prazosin, an alpha-1 antagonist, is an adjunct for treatment in PTSD.
- **Prazosin** is an α_1 -blocker that acts as an inverse agonist at alpha-1 adrenergic receptors.
- It is speculated that it blocks the brain's response to norepinephrine
- Has been shown to ameliorate nightmares



CURRENT RESEARCH ON A *VERY NOVEL* APPROACH

- D-CYCLOSERINE (DCS), an antibiotic used to treat TB, is a partial NMDA glutamate agonist
- The glutamatergic NMDA receptor has been found to be critically involved in learning and memory, and learning may be augmented by DCS



CURRENT RESEARCH

- DCS has been shown to facilitate the extinction of learned fear in and reduce reinstatement of fear in rats
- Human studies have shown efficacy in facilitating fear extinction in social anxiety and other phobias
- DCS is ineffective by itself. It must be administered *during* exposure therapy



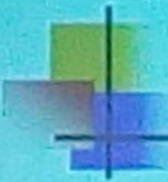
DCS RESEARCH

- DCS is thought to work cooperatively with glutamate that is released through synaptic activity associated with participation with CBT
- NIMH is currently conducting study to test effectiveness of "virtual reality" exposure therapy and DCS to treat Iraq vets with PTSD



DCS RESEARCH

- A 50 mg. dose will be administered 30 minutes before each session of virtual reality exposure therapy using a head mounted device displaying scenes of Iraq
- It's speculated that VRT will be more acceptable to vets who view talk therapy as stigmatizing. It also may be an effective way to push past numbing



FUTURE DIRECTIONS: CHICKEN OR EGG

- Research on genetic factors and PTSD
- Focus on early developmental factors
- The above can help with *predictability*, since not all who are experience trauma will develop PTSD
- 60% of women and 50% of men will experience a traumatic event, and 9.7% of women and 3.6% of men will develop PTSD
- 30% of these will develop a chronic form