Pediatric Post-Traumatic Stress Disorder: Risk, Resilience, and Treatment

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- “Whenever you hear anyone talking about a cultural or even about a human problem, you should never forget to inquire who the speaker really is. The more general the problem, the more he will smuggle his own personal psychology into the account he gives of it.”

Carl Jung

Limitations of PTSD Diagnosis

Conceptualized from an adult perspective

Created as diagnosis for Vietnam vets and adult rape victims

Focuses on single event traumas

Fails to recognize chronic/multiple/on-going traumas

Is not developmentally sensitive and does not reflect the impact of trauma on brain development

Many traumatized children do not meet full diagnostic criteria

Does not direct clinical attention to attachment history and attachment-related injuries and needs

Infants and young children exposed to cumulative, chronic traumatic events show disturbances and deficits in emotional, social, and cognitive competencies that are not encompassed by the existing criteria for diagnosing PTSD.

One major reason for this situation is that the existing diagnostic criteria for PTSD do not incorporate developmentally appropriate constructs of infancy and early childhood.

continued

- A second problem is that the current definition of PTSD is predicated on the occurrence of a single traumatic event, whereas pervasive and recurrent traumatization is often the norm for children living in high-risk families and communities

continued

For millions of young children, repeated exposure to traumatic events takes the form of co-occurring physical abuse, domestic violence, community violence, and accidents such as falls, burns, dog bites and near-drownings that occur as the byproduct of severe neglect. Developmental competencies are derailed in [numerous] domains.

Lieberman,Ghosh Ippen, Van Horn 2008

DSM-V PTSD

- (For ages 6 and older):
- A. Exposure to actual or threatened death, serious injury, or sexual violence
- B. Presence of intrusion symptoms after traumatic event
- C. Persistent avoidance of stimuli associated with the event
- D. Negative alterations in mood or cognition

- E. Marked alterations in arousal and reactivity
- F. Duration is more than one month
- G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of function
- H. The disturbance is not attributable to the effects of a substance or another medical condition

Criteria A

- 1. Directly experiencing the traumatic event
- 2. Witnessing in person the event as it occurred to others
- 3. Learning that the event happened to a close family member or close friend. Event must be violent or accidental
- 4. Experiencing repeated or extreme exposure to details of the aversive event
- 5. Does not apply to electronic media unless work related

Criteria B

- 1. Recurrent, involuntary and intrusive distressing memories of the event; in children older than 6 years, repetitive play may show themes or aspects of the event
- 2. Recurrent distressing dreams; in children may have frightening dreams sans overt aspect of event
- 3. Dissociative reactions or flashbacks, as if the event is happening in real time; in children trauma specific reenactment may occur

4. Intense or prolonged psychological distress when exposed to internal or external cues that symbolize or resemble aspects of the event

5. Marked physiological reactions to those same triggers or stimuli

Criteria C

- 1. Avoidance of or efforts to avoid distressing thoughts, memories, or feelings about or closely related to the event
- 2. Avoidance of or efforts to avoid external reminders, such as people, conversations, places, activities, objects, situations, that trigger distressing memories, thoughts or feelings about or closely associated with the event

Criteria D

- 1. Inability to remember an important aspect of the traumatic event
- 2. Persistent, exaggerated negative beliefs about oneself, others, the world
- 3. Persistent, distorted cognitions about the cause or consequences of the event that lead the person to blame self or others
- 4. Persistent negative emotional state: fear, shame, horror, anger, guilt, depression

- 5. Markedly diminished interest or participation in significant activities
- 6. Feelings of detachment or estrangement from others
- 7. Persistent inability to experience positive emotions

Criteria E

- 1.Irritable behavior and angry outbursts, with little or no provocation, both verbal and physical
- 2. Reckless or self destructive behaviors
- 3. Hypervigilance
- 4. Exaggerated startle response
- 5. Problems with concentration
- 6. Sleep disturbance

Specifiers

- With delayed expression

- With dissociative symptoms:
  - Depersonalization
  - Derealization

For Children under 6 years

- Criteria A: Witnessing does not include events witnessed only in electronic media
- Criteria B: Flashbacks/dissociation at the extreme can be loss of awareness of the present surroundings

- Criteria C:
- 5. Socially withdrawn behaviors
- 6. Persistent reduction in expression of positive emotions

- Criteria D:
- 1. Includes extreme temper tantrums

NIMH RDoC

- New approach to understanding mental illness, being studied in maltreated children
- Looks at brain circuits involved, such as the fear circuit: amygdala, vmPFC, and hippocampus, and
- Genetics and epigenetic modifications from experience

Kaufman et al JACAP 54:8

Risk Factors

- There is no such thing as an event in the genesis of PTSD when children are involved.
- Sub-threshold damaging developmental failures of nurturance, attachment, and stable family functioning, as well as other factors are frequently identified in those children who go on to develop PTSD; in fact for children in active treatment for PTSD, the great majority (70%) have suffered two or more explicit severe traumatic events

Stolbach et al, NCTSN, 2009

Children with PTSD

- 90% experienced at least one form of interpersonal trauma
- 63% experienced at least one form of family violence
- 58% experienced ongoing traumatic stress (chronic stress)
- 54% had an impaired caregiver
- 37% had severe neglect
- 30% had been in foster care

NCTSN

- 26% had experienced the death of a significant other
- 24% of the caregivers had unresolved trauma history
- 23% witnessed drug use and criminal activity in their home; 16% had incarcerated family member
- 22% were emotionally abused or neglected
- 18% were exposed to prostitution or other sexual activity in the home
- 7% were homeless


Children found
in homes with
meth labs

Adverse Childhood Experiences

Conjoint study by Kaiser Permanente and CDC of 17337 adult HMO members:

11% reported emotional abuse

30.1% reported physical abuse

19.9% reported sexual abuse

23.5% reported exposure to family alcohol abuse and 18.8% to family mental illness

12.5% witnessed their mothers being battered

4.9% witnessed family drug abuse

Felitti VJ,1998, AM J PrevMed

Emotional Abuse and Emotional Neglect: understudied and underreported but leads to shame, distorted sense of self and others, and more damaging to resiliency under chronic stress and abuse than other forms of trauma: pathological schemas about how the world works and person's competency in own life

Shame (shunning, rejecting, devaluing) is a highly aversive affective experience for children

O' Daugherty-Wright; Child Abuse Neglect;33:1,2008

2014 Census for KY: 1,015,095 children under 18 (23.1%)

Jefferson Co.: 173,282 under age 18, with 37,600 living in poverty; 10,156 CPS reports, 3016 substantiated; 9% Homeless per JCPS; 66,000 children homeless in KY

2007: KY #1

2014 for KY: 58,114 CPS reports; 80,241 children; 14,911 substantiated, affecting 22,926 children

PCAKY, CY2014

2015

National census: 321,738,000 adults and children, with 248,000,000 adults

Estimated adults with Borderline Personality Disorder: (.02-.06) 496,000 to 1,488,000

PTSD: (.007) 173,000

Major Depression: (.06) 1,488,000

Bipolar I and II: (.014) 347,000

Substance Abuse: (.078) 1,934,000

Any anxiety disorder: (.057) 1,413,600

NIMH 2014 12 month prevalence data

Normal Stress Response

- Perceived and/or experienced threat (stressor) activates the brain to release epinephrine and norepinephrine; via HPA axis glucocorticoids (cortisol) and AVP: classic fight or flight response, with negative feedback “turning off” the process when noxious event passes

Acute Stress

- Stressor within 2-3 seconds leads to epinephrine release via Locus Ceruleus (LC), and norepinephrine within 15-30 seconds
- CRF via amygdyla and paraventricular nucleus of hypothalamus, (with AVP), releasing ACTH from the pituitary, leading to GC (cortisol) release from the fascicular layer of the adrenal

Acute stress takes the normal PFC and hippocampus “off line”, increasing amygdala function, allowing for quicker reaction time; one PFC function is to inhibit amygdala activity

Active in utero: fetus at late stage of development has the ability to have startle response, especially to noise

Noise greater than 60db acutely triggers stress response (cheap dishwasher): females much more responsive than males at all ages

Acute Stress Response

Stressful sound stimulates the auditory cortex and amygdyla; amygdyla stimulates the Superior Colliculus to orient gaze to source of sound

Central Nuclei of amygdyla releases CRF

Amygdyla stimulates the caudate and reticular pons leading to startle response

Stimulates the periaqueductal gray area to "freeze"

Stimulates the Parabrachial nn. to increase respiratory rate, increasing O2

Inhibits OPFC, augments CRF release via PVnn of hypothalamus

Viamontes,G.,Psych.Annals 2009

Chronic Stress and Immunity

- Initial increase in GC inactivates nuclear factor kappa B (NFKB)[a good thing]causing decreases in inflammatory cytokines, esp. IL-6 and C reactive protein
- If chronic stressors, NFKB elevated [not so good thing], leading to increased IL-6 and CRP, and increased vulnerability to infection and poor healing and depression

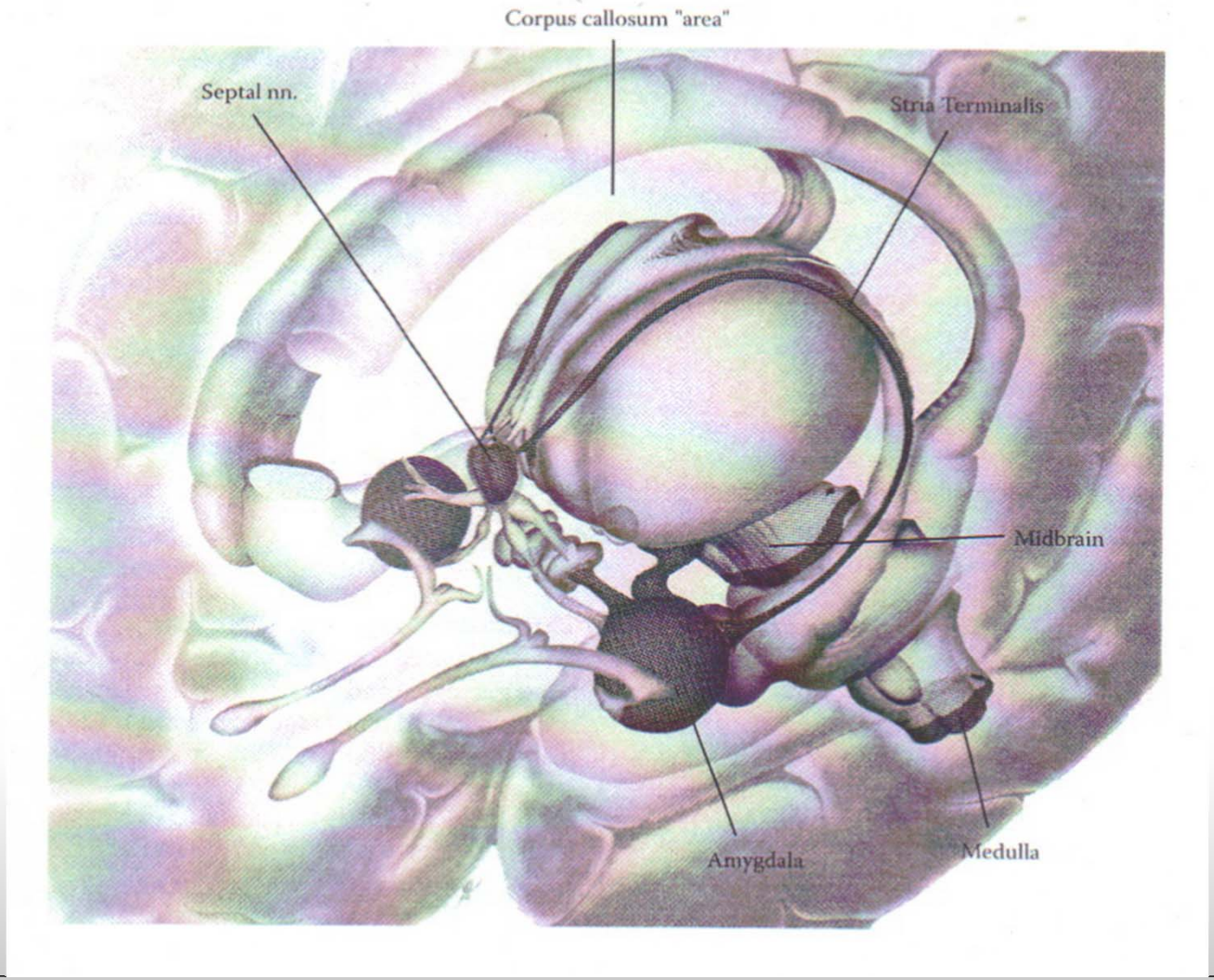
Viamontes 2009

Inflammation

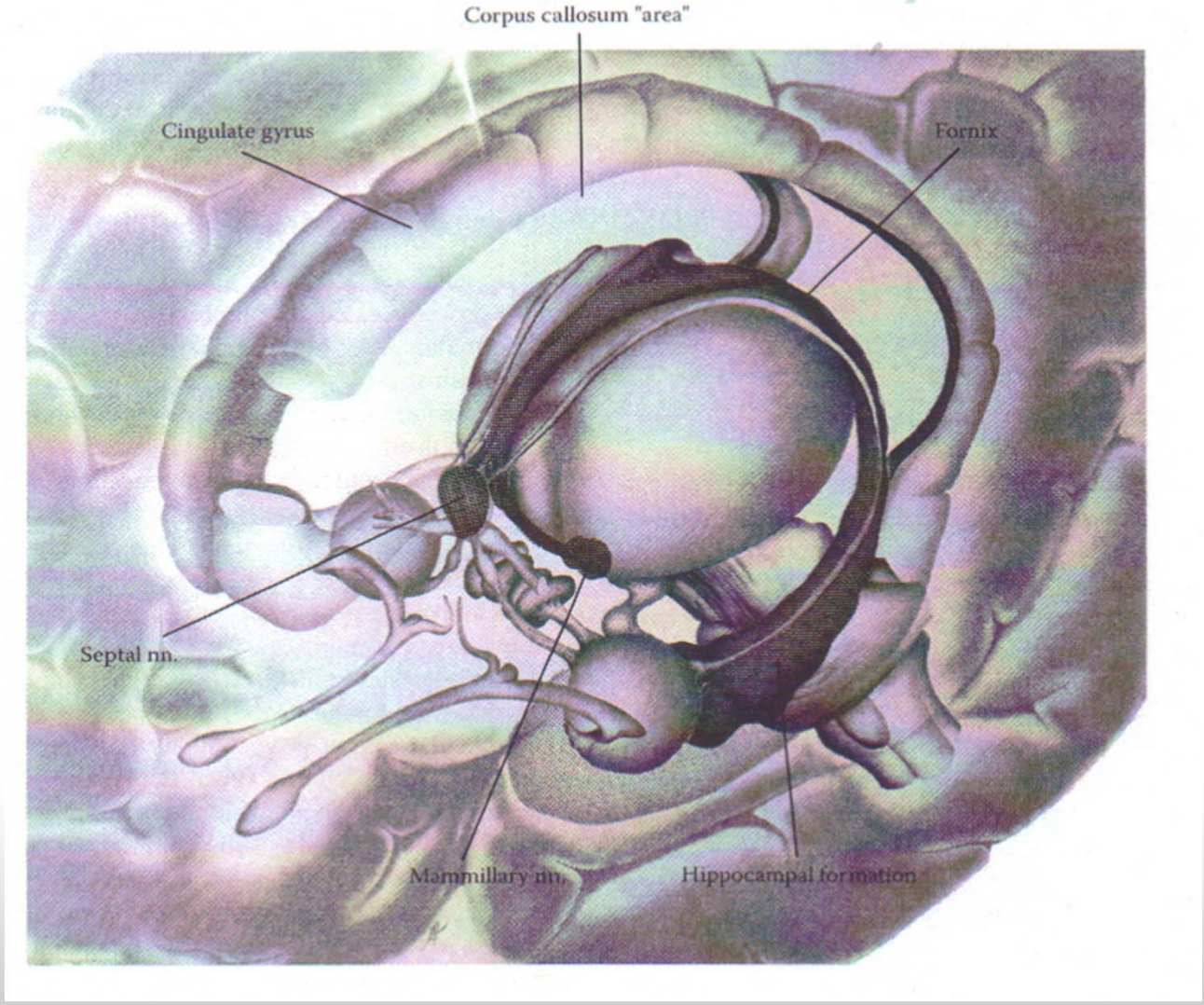
- Microglial activation, releasing CRF and glutamate
- NSAIDS, minocycline, penicillin's, SRI, SNRI, TCAs, NMDA antagonists all inhibit microglial activation and specifically inhibit glutamate release
- Can decrease chronic inflammatory response, decrease apoptosis (cell death) and improve neurogenesis in vulnerable systems via BDNF, especially hippocampus

Wager-Smith,K. 2010 NeurosciBehavRev

Amygdala - Location



Hippocampal Formation



PTSD with ECA

Early Childhood Abuse and PTSD: 30% dissociative, 70% hyperarousal; fMRI study

Dissociative: marked elevated activity in dorsal ACC, medialPFC: decreased amygdala and Right Insula (emotionality) activity

Hyperarousal: increased activation of amygdyla, insula, decreased dACC and mPFC

Hippocampus function inhibited in both types

Lanius, 2010,AJP

Chronic stress and depression

- One possible cause is stress-induced methylation of N. Acumbens GDNF gene: epigenetic decreased transcription of glial-derived neurotropic factor
- Leads to increased depression via decreased N. Acumbens activity: anhedonia, lack of reward seeking

Uchida,S.,Neuron,2011

Chronic elevation of GC leads to inhibition of synthesis of TSH, T4, estrogen, progesterone, and growth hormone

Chronic elevation of CRF down-regulates GC receptors at the pituitary via epigenetic methylation, disinhibiting ACTH release and continuing high levels of GC

Miller,L.,J.Neuro Psych. 2005

Chronic hypercortisolemia (GC) leads to adrenal exhaustion; pregnenalone shunts to produce more GC, with severe deficits in DHEA, aldosterone, testosterone, estrogen (Na, water retention

Causes decreased insulin sensitivity, with decreased glucose utilization (including CNS)

Decreased secretory IgA, increased IgG, decreased NK activity and certain interleukins, decreased T-lymphocyte function

Sher,L "PTMood" 2008 Minerva

Poverty is the main risk factor for CAA; co-occurring factors are domestic violence and substance abuse

80% of CPS substantiated cases that lead to loss of parental rights have caregivers with substance abuse/addiction

60% of cases have associated severe domestic violence histories

Complex Developmental Trauma

Severe trauma and attachment failures at critical developmental times

Consistent with early onset PTSD but significant overlay with Borderline Personality Disorder, Dissociative Disorder, Reactive Attachment Disorder, and mood and anxiety disorders

Adults may have many of these diagnoses, none of which by itself adequately defines the interpersonal aspect of causation at those same critical developmental windows

Adult Psychiatric Illness

Lifetime first episode of DSM-IV disorders screened in 9282 adults (National Comorbidity Survey Replication) found 44.6% of all childhood onset disorders and 29-32% of all adult onset disorders associated with child abuse (CA), taking into account recall bias

Strongest association was CA (physical and sexual abuse) in context of parental mental illness, substance abuse, criminality, and family violence

Green,JG, 2010 Arch Gen Psych

Biopsychosocial model of schizophrenia: stress/vulnerability model of Zubin and Spring 1977 reconsidered; analysis of >80 studies

Findings revealed child physical or sexual abuse in 55% of patients dx with schizophrenia/psychotic disorder when screened; emotional abuse or neglect as child in 40-60% of patients:

Noted the similar abnormalities of CA victims and schizophrenics: brain volume changes, abnormalities of HPA, hippocampal damage, abnormalities of serotonin, dopamine, and catechol functioning.

Reed, J. 2008; ClinSchz Related Psych

In twin study of 2232 children interviewed at ages 5,7,10 and 12 years, those who had abuse or bullying were much more likely to have reported psychotic symptoms (relative risk 3.16 and 2.47) than those without abuse

Associated with poverty, lower IQ, early onset of pathology, genetic loading

Arseneault,L;2011 AM J Psy

PTSD Sleep

Disrupted REM, increased REM arousals, increased nightmares

Can cause or worsen metabolic dyscontrol, leading to obesity, with secondary obstructive sleep apnea (OSA)

Inherent sleep problems causing vicious cycle of secondary symptoms

Germaine,A. 2009, Sleep

CFS, aka Systemic Exertion Intolerance Disease or SEID

CFS associated with hypercortisolism

Chronic fatigue syndrome (CFS) strongly associated with childhood trauma sampled from 19381 persons in general population in Georgia: CFS patients had marked elevations of all five scales of the CTQ

Sexual abuse and emotional abuse best indicators of CFS

Interpreted that hypercortisolism is risk factor for CFS, not due to CFS itself

Heim, C. 2009 ArchGenPsych

Bulemia Nervosa

999 young women in Australia:

121 reported at least one episode of childhood sexual abuse (12%), and 82 reported two or more events (8%)

Those with more than one event had 4.9 times the risk for bulimic behaviors than those with no CSA; with one episode had 2.5 times risk

CSA not associated with Anorexia Nervosa

Sanchi,L; 2008 Arch Ped Adol Med

Effects of nurturing

Increased grooming and nurturing in rat pups during the first week of life led via increased NGF1-A which increased gene transcription by decreasing methylation to up-regulation of GR (glucocorticoid receptors) in hippocampus and PFC which decreased ACTH activity

Decreased HPA over-activity that lasted life of rat:

Nurturing experience in critical window of life led via epigenetic processes to lifelong health benefits, improved stress resistance, decreased anxiety, even in rats with poor genes

Ogren,M.,2008,JAACAP

“My mom loved me”

Protective Alleles et al

1. Serotonin transporter gene: 5-HTTLPR
2. GABA A receptor gene: GABRA2
3. FKBP5 gene: protein that binds with cortisol receptor, alters risk for PTSD
4. NMDA (GRIN 1) receptor if abnormal: worsens extinction learning (reversed with D-cycloserine)
5. Mitochondrial mRNA 33: partially binds RNA and prevents transcription, preventing memory consolidation, and the underlying mechanism for state specific memory

- NPY: Neuropeptide Y, inhibits continued release of norepinephrine, bringing ANS back to baseline
- DHEA: under extreme stress, decreases impact of cortisol; soldiers with greater release before and during stress better overall performance and less dissociation
- DOD 2012

- CRF receptor variants may be protective of long term HPA dysfunction and depression and anxiety in the context of child abuse
- In study of women with hx of significant abuse and ELS (early life stress) without depression and anxiety, had significant increase frequency of protective alleles (2 specific out of 15 identified)

Bradley,RG,2008 ArchGenPsych

Resilience

- 1. Positive Social Support (teacher, relative, neighbor)
- 2. Music training
- 3. Mindfulness training
- 4. Meditation
- 5. Yoga, Tai Chi
- 6. Spiritual and religious practices

These conscious activities can directly modify circuit activity by epigenetic modifications

Barriers: depression, anhedonia, poverty and lack of caregiver support

(Write a prescription for this, is not soft science)

- Find a role model
- Practice relaxation techniques first
- Realistic Optimism: positive emotions, weed out negative schemas, don't catastrophize
- Learned Optimism: specific training
- Use humor; part of improving cognitive flexibility
- Altruism, helping others; sharing, or reciprocal altruism: improves dopamine release in N. Acumbens and
- Pet therapy, with oxytocin release

Exercise

1. Decreases depression
2. Improves memory and self esteem
3. Enhances brain plasticity and neurogenesis, especially in hippocampus
4. Increases physical and emotional resilience to future stress

DOD 2012

Acute Care

- Psychological First Aid: Safety, Calming, Connect, Self-efficacy, Hope
- Meet the child's basic needs
- Psychoeducation
- Normalization
- Find or create social and spiritual support

NCTSN and DOD, 2014

Therapy

- First and foremost: TFCBT with children (trauma focused cognitive behavioral therapy) AFTER first teaching relaxation and general psychoeducation to pt and cargivers, or
- Alternative therapies, to include EMDR
- Cognitive Processing Therapy
- Prolonged Exposure Therapy

TFCBT (ages 4-18)

TARGET BEHAVIORS:

PTSD

Depression

Anxiety

Sexualized behaviors

Externalizing behaviors

Shame

Trust

Social Competence

- Establish therapeutic relationship with child and parent
- Psychoeducation about trauma and PTSD
- Emotional Regulation skills
- Individualized stress management skills
- Connecting thoughts, feelings, and behaviors related to the trauma
- Assisting the child in developing a narrative about the trauma (verbal, written, artistic)
- Cognitive and affective processing of the event
- Teaching parents skills
- Joint parent-child sessions for skills practice

- Personal safety skills training
- Coping with future trauma related reminders (flashback preparation)

- Healthy living innoculation: importance of sleep, exercise, good food in helping boost resistance to future stressors

Medication Interventions for insomnia

- For insomnia: trazodone seems most effective, followed by mitrazapine and last, low doses of TCA, such as doxepin or amitriptyline
- For initial insomnia: diphenhydramine and hydroxyzine
- For nightmares: prazosin (consider Kapvay)
- Do not use benzodiazepines or the “Z drugs”
- Do not use atypical antipsychotics

DOD, NCTSN

Medications for PTSD

- EBT for children, teens and adults
- DOC are the SRI medications, with the best studied and with best risk/benefit ratio: fluoxetine, sertraline and paroxetine (but not in children); citalopram and escitalopram
- Separate from placebo, but still with significant placebo effect
- Mitrazapine, nefazadone, venlafaxine, TCA's also studied, possible use as second line treatments
- Hi dose trazodone
- May benefit from targeted polypharmacy

- With PTSD and comorbid anxiety disorders in children and teens, go slower and start lower than you might with depression
- Initial SRI effect is to saturate the 5-HT1A receptor, initially decreasing release of serotonin
- After a brief period of time the receptor is maximally stimulated and can do no more, allowing normal to increased serotonin in the synapse

- Alpha2 agonists, beta blockers, prazosin to help moderate excessive concomitant excessive autonomic arousal
- Other medicines when clinically indicated: Lithium in traumatized pt with Bipolar illness and PTSD, atypical antipsychotics as clinically indicated, ADHD medications, including stimulants

New Thoughts

- D-cycloserine, an NMDA receptor modifier, improves learning with CBT and prolonged exposure
- Given one hour before the session, brief half-life
- NAC (N-acetyl cysteine) does same thing
- CRF blockers to blunt cortisol effects

What Doesn't work for PTSD

- Benzodiazepines
- Seroquel
- Risperdal, other atypical antipsychotics
- Cyproheptadine
- Buspirone
- Buproprion
- Guanfacine

- Antiepileptic drugs with mixed results at best in adults with PTSD
- Valproate, Topiramate, Carbamazepine all failed RCTs
- Lamotrigine, Tiagabine, Vigabatine failed initial open label
- Use only if child has concomitant seizure disorder or bipolar disorder
- Again, no benzodiazepines or gabapentin

Pathological self-treatment

In the context of depression with active chronic stress mechanisms, increased GC increases abdominal fat and decreases catecholamines and insulin function; increasing abdominal fat sends messenger to decrease hypothalamic expression of CRF and partially decrease circulating cortisol levels in the context of loss of negative feedback inhibition

Overeating decreases the anxiety and dysphoria of the stress related state

Dallman MF;2003 PNAS

Pathological self-treatment

Persons suffering from Borderline Personality Disorder (Complex Developmental Trauma) have elevated limbic activation to facial photographs of strong positive and negative emotions, including amygdyla activation (very similar to mothers with insecure attachment to their infants)

Simultaneous physical pain inhibited this excessive amygdyla activation, minimizing the severe emotional/physiological dysphoria and cascade of pathological behaviors

(Not subtyped for dissociative v hyperarousal types)

Physical pain does make these patients feel better by feeling less, with less subjective loss of control, and "doing something about it"

Niedtfeld,I. 2010 Biological Psychiatry

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