

**Understanding childhood trauma as a strong epigenetic factor contributing to co-occurring addiction and post traumatic stress disorder**



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**What is the intersection of childhood trauma and later addiction or PTSD?**

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**The Adverse Childhood Events Study (ACE)**

- Landmark study published 1998
- N-17,337 adults – who joined Kaiser San Diego between 1995-1997
- 80% white including Hispanic, 10% Asian, 10% African-American.
  - 75% attended college, 40% basic or some higher ed., all insured average, age 57, 50% male & female, Most had jobs.
- Volunteered to fill out ‘standard medical questionnaire’ that asked about childhood experiences

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**Questionnaire**

- 10 types of child abuse (score 1 for each)
  - Three types of *abuse*: sexual, physical, emotional
  - Two types of *neglect*: physical and emotional
  - Five types of *family dysfunction*
    - Having a mother who was treated violently
    - Household member (HM) who is drug user or alcoholic
    - HM has been imprisoned
    - HM has diagnosed mental illness
    - Parents who are separated or divorced

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**Abuse**

- Emotional Abuse recurrent threats, humiliation (11%)
- Physical Abuse – beating, not spanking (28%)
- Contact sexual abuse (28% women, 16% men, 22% overall)

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**Household dysfunction**

- Mother treated violently (13%)
- Household member alcoholic or drugs (27%)
- HM imprisoned (6%)
- HM chronically depressed, suicidal, mentally ill, or in psych hospital (17%)
- Not raised by both biological parents (23%)

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**Neglect**

Physical 10%

Emotional 15%

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**Responses to Questionnaire**

- Surprised everyone
- People with six or more ACEs died nearly 20 years younger
- Trauma alters function and development of children's brains.
- Leads to risk behaviors of adolescence, but do these behaviors continue?
- Still many un-answered questions, and correlation is not causation....still....

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**Epidemiology**

- Male children with ACE score 6 or more have a 4,600% increased likelihood of later becoming an injection user compared to 0 score ACE score male child
  - Suggest that addiction experience-dependent and not substance dependent
- Higher ACE scores correlate to smoking (250%), self-defined alcoholism (500%), and self-defined injection drug use.
- <http://acestudy.org/aboutus.html>
- <http://www.cdc.gov/NCCDPHP/ACE>

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**Prevention/Intervention**

- Kaiser – increasing questions such as
  - have you ever been a combat soldier
  - Have you ever lived in a war zone
  - Who in your family has been a suicide
  - Others...
  - Expanded ROS and Past History questionnaire
    - Those with high scores saw psychiatrist, 81% found this helpful

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**Kaiser, cont'd**

- Productive response to “yes’ answer is “I see that you have... Tell me how that has affected you later in life”
- 35% decrease in MD visits after this approach initiated..
- 11% reduction in ER, 3% reduction in hospitalization

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**Broadening the definition...**

- Childhood maltreatment is...“all forms of physical and/or ill-treatment, sexual abuse, neglect or negligent treatment or commercial or other exploitation, resulting in actual or potential harm to the child’s health, survival, development, or dignity in the context of a relationship of responsibility, trust, or power.
- Butchart, Phinney, Mian & Furniss 2012 p. 9(WHO)

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**Problem....**

- Influences of childhood abuse disrupt the pathways that govern executive functioning.
  - 80 college students, given stress test, measured cortisol, heart rate, blood pressure, and subjective tension
  - Correlated results with checklist for traumatic experiences, and a depression scale
  - Regression analysis - blunted cortisol response only in male patients - similar to PTSD studies
    - Further research needed

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**ACE Categories**

- Approximately equal to others in terms of impact.
- Numbers of those with high scores distinctly higher than if the categories were independent of each other.

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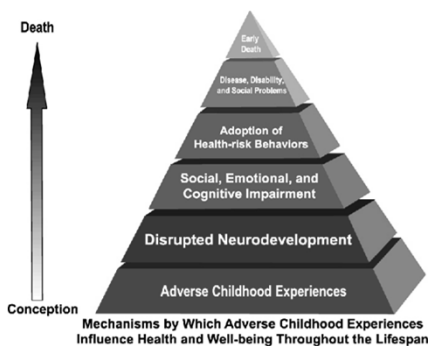
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**ACE pyramid ( Felitti, 1998)**



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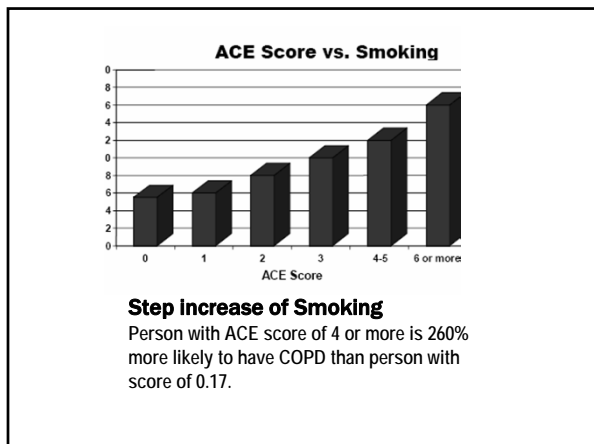
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**Addiction caused by adverse life experiences (ACE study conclusion)**

- Short term emotional benefits
- Long term risks and chronic disease
- “Cause and effect lie within a family”

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**Finding Your ACE Score**

**While you were growing up, during your first 18 years of life:**

1. Did a parent or other adult in the household **often** or **very often** ... Swear at you, insult you, put you down, or humiliate you? **or**  
 Act in a way that made you afraid that you might be physically hurt? Yes No If yes enter 1 \_\_\_\_\_

2. Did a parent or other adult in the household **often** or **very often** ... Push, grab, slap, or throw something at you? **or**  
 Ever hit you so hard that you had marks or were injured? Yes No If yes enter 1 \_\_\_\_\_

3. Did an adult or person at least 5 years older than you **ever**... Touch or fondle you or have you touch their body in a sexual way? **or**  
 Attempt or actually have oral, anal, or vaginal intercourse with you? Yes No If yes enter 1 \_\_\_\_\_

4. Did you **often** or **very often** feel that ... No one in your family loved you or thought you were important or special? **or**  
 Your family didn't look out for each other, feel close to each other, or support each other? Yes No If yes enter 1 \_\_\_\_\_

5. Did you **often** or **very often** feel that ... You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you? **or**  
 Your parents were too drunk or high to take care of you or take you to the doctor if you needed it? Yes No If yes enter 1 \_\_\_\_\_

6. Were your parents **ever** separated or divorced? Yes No If yes enter 1 \_\_\_\_\_

7. Was your mother or stepmother: **Often** or **very often** pushed, grabbed, slapped, or had something thrown at her? **or**  
**Sometimes, often, or very often** kicked, bitten, hit with a fist, or hit with something hard? **or**  
**Ever** repeatedly hit at least a few minutes or threatened with a gun or knife? Yes No If yes enter 1 \_\_\_\_\_

8. Did you live with anyone who was a problem drinker or alcoholic or who used street drugs? Yes No If yes enter 1 \_\_\_\_\_

9. Was a household member depressed or mentally ill, or did a household member attempt suicide? Yes No If yes enter 1 \_\_\_\_\_

10. Did a household member go to prison? Yes No If yes enter 1 \_\_\_\_\_

**Now add up your "Yes" answers: \_\_\_\_\_ This is your ACE Score.**

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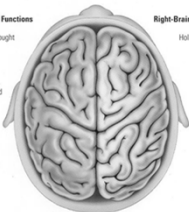
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**Left and Right Brain Functions**

**Left-Brain Functions**

- Analytic thought
- Logic
- Language
- Science and math



**Right-Brain Functions**

- Holistic thought
- Intuition
- Creativity
- Art and music

**What is the intersection between child maltreatment and brain development**

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**Cascade of effects of the trauma of abuse and neglect**

- Changes in stress hormones
- Changes in neurotransmitters
- Affect development of vulnerable brain regions
- Landmark study using brain imaging of children and adults
- Adult survivors of abuse and neglect vs adults not abused (Teicher et al 2004)

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**Cascade of effects on brain development (Teicher, 2004)**

- 4 types of brain abnormalities in adults abused as children
- 1. Smaller corpus callosum & poor integration of hemispheres
- 2. Abnormal development of left hemisphere (depression and memory)
- 3. Risk of seizures from change in limbic system (sadness, embarrassment, anger, intense laughter, serenity, fear)
- 4. Abnormal EEGs (aggression, self destructive behavior)

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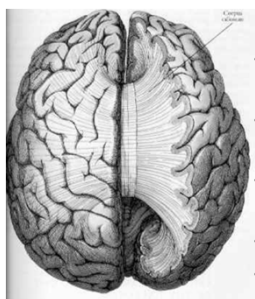
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**Corpus collosum (tough body)**



- Largest white matter in the brain
- Wide flat bundle of neural fibers beneath the cortex
- Connects left and right cerebral hemispheres
- Facilitates interhemispheric communication
- 200-250- axonal projections
- Abnormal in autism also

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**Adolescents exposed to neglect or abuse (physical or emotional)**

- Reduction in grey matter (brain cells)
- Boys lose impulse control more than girls and are more prone to substance abuse
- Girls more prone to depression

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**Role of Genetics and Epigenetics<sub>cs</sub>**

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### DNA is keyboard

- Genes are the keys
- Epigenetics determine when and how each key can be played, changing the tune
- Methylation makes expression of genes stronger or weaker
- E.g. Stress during pregnancy can cause epigenetic changes in fetus, causing behavior problems (rat research)
- Random epigenetic changes can occur also



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### Hereditability

- Hereditability: measures extent to which differences among people in a population can be explained by differences in their genetics.
- Hereditability of Intelligence 75% from genetics

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### No one is born an addict

- "Susceptibility does not mean inevitability"
- "You got to be careful"
- Environment is large factor in risk - maltreatment as child /other trauma
- Chances are greater than most people if inherit genes
- Most likely 50-100 genes influencing addiction



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**The choices you make can change your genes and those of your kids**



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**Addiction is complex genetic illness  
.... genetics influence**

- Initiating drug use
- Activation of reward system
- Continuing drug use
- Addiction process (frontal cortex)

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**Gene Variants in childhood trauma and SUDS**

- Serotonin Transporter Gene (SERT) with childhood trauma increase risk of suicide
- 5-HTTLPR S allele + Dopamine Transporter Gene (DAT) and early childhood trauma
- Gene polymorphism and HPA Axis increase risk of substance use disorders
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**Epigenetic influence..**

- “early experiences can have profound long-term effects on the biological system that govern responses to stress...Disturbances [in neuron-development] at a critical time early in life may exert a disproportionate influence, creating the conditions for childhood and adult depression, anxiety, and post-traumatic stress symptoms

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**Gene-stress Interaction markers for brain arousal profile and risk of depression**

- Genetic (BDNF val66met & Serotonin Receptor gene 3A (HTR3A) genotypes) & early life stressors associated with EEG asymmetry, emotion elicited heart rate, and negativity bias (correlates of risk for depression)
- Step towards biological markers for risk before symptoms of depression
- Used data from database from BRAINnet (N=36)
- (Gatt et al, Biological Psychiatry, 2010)

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**Fear processing & memory in PTSD**

- Amygdala- hyperactive
- Hippocampus- reduction in size
- Medial prefrontal anterior cingulate networks fail to reduce amygdala activity
- Results in hyper-reactivity to threat.
- “Oversensitive negative feedback system”
- Low levels of cortisol inhibit production of ACTH by anterior pituitary gland
- Can't slow sympathetic response causing CONSOLIDATION OF TRAUMATIC MEMORIES

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**Women and quality of life**

- Study of 305 women with SUD 1 month and 6 months after treatment
- Trauma Symptom Checklist-40
- Recovery instruments to measure social support
- WHO Quality of Life – BREF form
- Trauma symptoms predicted physical and psychological quality of life.
- Supports trauma informed services to women with substance abuse problems. (Tracy et al, 2012)

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**“Poly victimization”**

- National Sample of Adolescents 12-17(N=4023)
- Over 2/3 endorsed a traumatic experience
- Poly victimization in 1/3 of sample leading to
- 2x risk of depression
- 3 x risk of PTSD,
- 3-5 x risk of Substance Use Disorder
- 5-8 x risk of comorbidities.
- Assault witness and accident/disaster groups had 2-3x MDD and ETOH abuse if had trauma history &
- 5-30 times more for poly victimization group. (Ford et al, 2010)

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**Neuroimaging Studies of Trauma**

- Brain scans of children exposed to physical abuse or domestic violence same as soldiers exposed to combat
- Heightened activity in anterior insula & amygdala when stimulated
- Develop a “hyperawareness of their environment” =watch for DANGER
- Risk factor for mental health and substance abuse problems
- Remain vulnerable.. (Hood, 2011 Internal Medicine)

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**PTSD**

- Always an external causative factor
- Threat of death, serious injury, threat to physical integrity present
- Psychiatric history, lower intelligence, female gender, prior exposure to trauma ↑ risk
- Emotional processing theory: fear structures in memory → reactions when activated → alter beliefs about world and self → misinterpret
- Dual representation theory: Verbally accessible & situational accessible memories (triggered) → flashbacks..

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**HPA Axis and sensitization of brain circuits increase risk of SUDS**

- Higher basal plasma levels of cortisol and ACTH related to neglect
- Long term changes in multiple brain circuits caused by adverse child experiences and persistent sensitization of the CNS circuits
- May be the biological basis of increased susceptibility to SUDs

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**Biological Marker in PTSD**

- Magnetoencephalography (MEG)
- 248 sensors that record interactions in the brain by milliseconds( Georgopoulos & Engdahl, 2010))
- PTSD patients differentiated from normal brains 90% with accuracy
- Diagnose PTSD & judge severity of illness !
- (N=70 veterans and 250 mentally healthy)

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**Probing the susceptible brain  
(research)**

- What is the *brain activity* connected to emotional experiences?
- Current study-- the interactions between cognitive and emotional areas of the brain using EEG and fMRI
- Brain marking of activity after continuous stimulations designed to cause horror or sadness.
- Goal to develop portable brain monitoring machine to quantify the emotional state of people suffering from trauma (Intrator, 2012)

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**PTSD and suicide**

- Diagnosis of PTSD is a risk factor for suicidal thoughts
- With 2 or more comorbid mental disorders, more likely to be suicidal than those with PTSD alone
- 46% veterans in study had suicidal thoughts or behaviors , 3% attempted suicide (Journal of Traumatic Stress)

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**Trauma and risk of relapse**

- Individuals with PTSD believe that substance use will reduce distress of PTSD (self medication hypothesis)
- Symptoms of PTSD are a cue that triggers relapse
- Memories or traumatic event -cues that trigger relapse
- Trauma history with substance use disorder without PTSD-Risk still there for relapse
- PTSD symptoms increase the risk of relapse

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**Treatment Goal: Affect regulation**

- Reflect on trauma memories, experience the affect associated with the memories without becoming dysregulated
- Learn to self regulate
- Relationship with therapist very important: "sensitive affectively attuned relationship" in those maltreated as a child
- Helps client make sense of memories (left hemisphere), autobiographical representation and affect (right hemisphere functions)

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**Practice implications**

- Screen in medical settings for ACE
- Follow up with "how this has affect you later in life"?
- Primary prevention-Parent training, media campaigns
- "Primary prevention of ACE and improved treatment of exposed children could reduce smoking among adolescents and adults"
- Addiction treatment and trauma informed/focused approaches (healing from ACE)

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**Exposure therapy effective with PTSD and substance abuse (JAMA, 2012)**

- Trauma symptoms resurface when drug use is stopped'
- COPE (prolonged exposure) plus treatment for substance dependence (N=55) vs TAU
- 13 90 minute sessions
- Clinician Administered PTSD Scale (CAPS)
- PTSD symptom severity dropped by 38.24 points (22.14)
- Substance use didn't change : didn't need to be abstinent to find benefit (Mills and Eth)

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**EMDR vs Trauma Specific PTSD**

- Faster recovery than with trauma specific CBT(brief eclectic psychotherapy)
- 6 weeks for EMDR
- Both effective (N=140)
- EMDR rate distress every 5-10 minutes until stress level is 0 or 1, then introduce positive cognition
- (Nijdam et al, 2012)

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**Self medicating anxiety**

- Self medication of anxiety symptoms with alcohol or drugs increased risk of alcohol dependence
- 10% new alcohol and 25% new drug dependence – self medication of anxiety
- Predicted later social phobia
- More persistence of the substance use disorder if self medicated anxiety

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**Hereditability**

- Hereditability: measures extent to which differences among people in a population can be explained by differences in their genetics.
- Hereditability of Intelligence 75% from genetics

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**Adolescent brain**

- Grey matter deficits from neglect or abuse
- Boys lose impulse control more than girls

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**Resources**

- Authentic Voices International  
<http://authenticvoices.org>

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