Does Child Abuse Permanently Alter the Human Brain?

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Maltreatment and Trauma Studies Support

NIMH
RO1 MHT3636 (1997-2001)
RO1 MH66222 (2003-2008)
RO1 MH91391 (2010-2015)

NIDA
RO1 DA16934 (2003-2007)
RO1 DA17846 (2004-2009)

NARSAD (2005-2007)
Simches Family

New England Society for the Treatment of Trauma and Dissociation
Lexington, MA
April 30, 2011
What factors rob us of our mental health?

Early Adversity

Physical, Sexual, and Psychological trauma in childhood may lead to psychiatric difficulties that show up in childhood, adolescence, or adulthood.

Hypothesis

Early childhood maltreatment

Stressor

Cascade of physiological and neurohumoral responses

Trajectories of brain development

Emergence of psychiatric disorders

Hypothesis

Childhood adversity

Genetics

Age

Brain development

PTSD

Depression

Medical Disorders

Addiction

Dissociation

Cognition

Other psych disorders
Adverse Childhood Experience Study
Dr. Vincent Fellitti and Dr. Robert Anda

ACEs
- Recurrent Physical Abuse
- Recurrent Emotional Abuse
- Sexual Abuse

Growing up in a household where:
- Someone was in prison
- Where the mother was treated violently
- With an alcoholic or a drug user
- Where someone was chronically depressed, mentally ill, or suicidal
- Where at least one biological parent was lost to the patient during childhood – regardless of the cause.

Population attributable risk associated with early adversity:
- 50% for drug abuse
- 54% for current depression
- 65% for alcoholism
- 67% for suicide attempts
- 78% for iv drug use

How stressful early experience influences the developing brain.

Step 1
Early stress programs our stress hormone systems to initially have a more exaggerated and prolonged response to subsequent stressors.
How stressful early experience influences the developing brain.

Step 2

Exposure of the developing brain to stress hormones exerts consequences by affecting gene expression, myelination, neural morphology, neurogenesis and synaptogenesis.

Early stress affects the two pivotal components of postnatal brain development.

- Myelination
- Synaptogenesis

Human Brain Development

<table>
<thead>
<tr>
<th>Embryonic</th>
<th>Postnatal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week: 0 6 12 18 24 30 35</td>
<td>Month: 0 6 12 18 24 30 36 Year: 4 8 12 16 20 24</td>
</tr>
</tbody>
</table>

Nerve Cell Structure

- Signals travel away from the cell body, down the axon.
- Myelin sheath produced by glial cells
- Nerve terminals synapses

Cell body, Dendrites, Axon
Impact of early stress on the developing brain depends on timing, vulnerability of specific brain regions, and genetic factors.
VulnerabilityResilience

Genes
Timing (developmental stage when abuse occurs)
Type of abusive experience
Protective factors

Role of Genotype in the Cycle of Violence in Maltreated Children
Depression with Early Trauma/Loss

Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene

Avshalom Caspi,1,2 Karen Sugden,1 Terrie E. Moffitt,1,2* Alan Taylor,1 Ian W. Craig,1 Honalee Harrington,2 Joseph McClay,1 Jonathan Mill,1 Judy Martin,3 Antony Braithwaite,4 Richie Poulton3


Polymorphisms Associated with Gene x Environment Interactions

Complex Overlapping Associations
Epigenetics

DNA methylation
Methyl markers added to certain DNA bases repress gene activity.

Histone modification
A combination of different molecules can attach to the ‘tails’ of proteins called histones. These alter the activity of the DNA wrapped around them.

First Neuroimaging Findings
Myelinated regions, such as the corpus callosum (CC) are potentially vulnerable to the impacts of early exposure to excessive levels of stress hormones, which suppress glial cell division critical for myelination.

### Table: Comparison between abused/neglected boys, non-abused psychiatric control boys (contrast group), and healthy boys.

<table>
<thead>
<tr>
<th>Region</th>
<th>Abused/neglected</th>
<th>Contrast</th>
<th>Healthy</th>
<th>Group diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (rostrum)</td>
<td>0.305</td>
<td>0.103</td>
<td>0.128</td>
<td>0.1000</td>
</tr>
<tr>
<td>2 (genu)</td>
<td>0.761</td>
<td>0.900</td>
<td>0.864</td>
<td>0.1300</td>
</tr>
<tr>
<td>3 (rostral body)</td>
<td>0.463</td>
<td>0.615</td>
<td>0.606</td>
<td>0.0020</td>
</tr>
<tr>
<td>4 (ant. midbody)</td>
<td>0.361</td>
<td>0.486</td>
<td>0.523</td>
<td>0.0001</td>
</tr>
<tr>
<td>5 (post. midbody)</td>
<td>0.331</td>
<td>0.416</td>
<td>0.429</td>
<td>0.0055</td>
</tr>
<tr>
<td>6 (isthmus)</td>
<td>0.889</td>
<td>1.100</td>
<td>1.152</td>
<td>0.0043</td>
</tr>
<tr>
<td>7 (splenium)</td>
<td>0.403</td>
<td>0.466</td>
<td>0.496</td>
<td>0.5450</td>
</tr>
<tr>
<td>(n)</td>
<td>13</td>
<td>13</td>
<td>61</td>
<td></td>
</tr>
</tbody>
</table>

Overall differences between groups, MANCOVA, p < 0.0001

### Table: Association of Early Experience and Age on Regional Anatomy of Corpus Callosum in Boys, Based on Step-wise Regression.

<table>
<thead>
<tr>
<th>Region</th>
<th>Physical Abuse</th>
<th>Sexual Abuse*</th>
<th>Neglect*</th>
<th>Age**</th>
<th>PTSD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (rostrum)</td>
<td>--</td>
<td>--</td>
<td>-41.7%†</td>
<td>7.4%ζ</td>
<td>--</td>
</tr>
<tr>
<td>2 (genu)</td>
<td>--</td>
<td>--</td>
<td>-29.2%γ</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>3 (rostral body)</td>
<td>--</td>
<td>--</td>
<td>-33.2%γ</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>4 (ant. midbody)</td>
<td>-9.6%†</td>
<td>--</td>
<td>-30.7%γ</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>5 (post. midbody)</td>
<td>--</td>
<td>--</td>
<td>-40.2%γ</td>
<td>1.5%†</td>
<td>--</td>
</tr>
<tr>
<td>6 (isthmus)</td>
<td>--</td>
<td>--</td>
<td>-45.7%γ</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>7 (splenium)</td>
<td>--</td>
<td>-18.3%†</td>
<td>-24.2%ξ</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

†p < 0.10, ‡p < .05, §p < .01, ¶p < .001
*Values are expressed as % change in volume associated with positive history
**Values are expressed as % change in volume per year of age.
The morphology of the corpus callosum is significantly affected by early neglect (as well as physical abuse and sexual abuse).

*Teicher et al. (2004) Biological Psychiatry 56, 80-85*

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44 maltreated children and adolescents with PTSD and 61 matched controls underwent comprehensive assessments and MRI.

Most significant finding was reduced midsagittal area of corpus callosum in PTSD subjects.

There was a greater corpus callosum area reduction in maltreated males than maltreated females with PTSD.

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Infant male monkeys raised individually in a nursery from 2 to 12 months were compared to age-matched infants raised in a semi-naturalistic social environment. Although overall brain volumes did not differ, the corpus callosum was significantly decreased in the nursery group.
Reduced area or integrity of the corpus callosum is the most consistent neurobiological finding in children and adults with histories of exposure to childhood abuse.

Using Diffusion Tensor Imaging we found that the integrity of the middle portion of the corpus callosum correlated inversely with degree of exposure (ACE score) to childhood abuse in young adults (n = 191).

Corpus Callosum and Hemispheric Laterality

- Hemispheric brain activity was measured in adult subjects under two conditions: first, during recall of a neutral memory, and then during recall of an unpleasant affectively-laden early experience.
Deficient Hemispheric Integration

Our discoveries that abused patients have diminished right-left hemisphere integration and a smaller corpus callosum suggest an intriguing model for the emergence of borderline splitting.

With less integrated hemispheres, they may shift between logical and rational state to highly emotional state.

Deficient Hemispheric Integration

Lack of integration between the hemispheres may also be a factor in the genesis of dissociation and multiple distinct identities.

Time is of the essence

Sensitive Periods
Sensitive Periods

The brain is molded by experiences that occur throughout the lifespan. However, there are particular stages of development when experience exerts either a maximal (sensitive period) or essential (critical period) effect.

* Hubel and Wiesel - Nobel Prize Medicine 1981

Corpus Callosum - Rostral Body

Abused at index age vs abused at other ages

CC area reduced 22.4% in subjects who experienced abuse at age 10 (n=5).
Exposure to stress can affect:

- Development of synapses
- Birth of new neurons
- Dendritic branching of neurons
- Survival of neurons in the hippocampus.

Hippocampus plays a critical role in memory consolidation and retrieval, and is believed to be a key region involved in the generation of dissociative states*.

Recent theories postulate that impaired hippocampal function (particularly suppressed neurogenesis) is involved in the pathophysiology of depression.


Hippocampal volume reduced 13.2% in subjects who experienced abuse at age 4 (n=7).
The frontal lobes are important for

- Attention
- Executive Function
- Working Memory
- Motivation
- Behavioral Inhibition.

They are important in

Planning and anticipating outcomes.

Self-monitoring and self-awareness - necessary for appropriateness of behavior.
Prefrontal Cortex

Abused at index age vs abused at other ages

PFC GMV reduced 5.8% in subjects who experienced abuse at age 14 (n=4).

Sensitive Periods and Psychopathology

If stress exposure targets different brain regions based on ages of exposure, then exposure at different ages may lead to different clinical outcomes.

Translational Support

If stress exposure targets different brain regions based on ages of exposure, then exposure at different ages may lead to different clinical outcomes.
Reduction in both prefrontal cortex and hippocampal volume have been reported in subjects with depression, and depression is the most common adult psychiatric consequence of exposure to childhood sexual abuse.

These studies suggest that there may be two separate types of depression associated with early stress.

- early childhood abuse, hippocampus affective regulation
- adolescent abuse, subregions of prefrontal cortex, more cognitive consequences.
Delayed Effects

Childhood exposure sensitizes the individual to later emergence of depression during adolescence.

On average, 9 year gap between exposure to childhood sexual abuse and emergence of depression and emergence of PTSD.

Possibility to preempt.
Delayed Effects – Silent Period

Childhood abuse has been associated with reduced hippocampal size in adulthood.

<table>
<thead>
<tr>
<th>Study</th>
<th>Groups (n)</th>
<th>Reduction / Side</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bremner et al 1997</td>
<td>PTSD (17), NL (17)</td>
<td>-12% L</td>
</tr>
<tr>
<td>Stein 1997</td>
<td>PTSD/DID (21), NL (21)</td>
<td>-5% L</td>
</tr>
<tr>
<td>Dreissen et al 2000</td>
<td>Borderline (21), NL (21)</td>
<td>-16% L,R</td>
</tr>
<tr>
<td>Vythilingam et al, 2002</td>
<td>Depressed (21), NL (14)</td>
<td>-15% L</td>
</tr>
<tr>
<td>Vermetten et al, 2006</td>
<td>DID (15), NL (23)</td>
<td>-19.2% L,R</td>
</tr>
<tr>
<td>Andersen et al, 2008</td>
<td>Abused (26), NL (17)</td>
<td>-6.8% L,R</td>
</tr>
</tbody>
</table>

Delayed Effects – Silent Period

... but not in childhood.

<table>
<thead>
<tr>
<th>Study</th>
<th>Groups (n)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Bellis et al 1999</td>
<td>PTSD (44), NL (61)</td>
<td>NS</td>
</tr>
<tr>
<td>Carrion et al 2001</td>
<td>PTSD Sx (24), Hx NL (24)</td>
<td>NS</td>
</tr>
<tr>
<td>De Bellis et al 2002</td>
<td>PTSD (28), NL (66)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Translational Support

Hippocampus:CA3

- Controls
- Isolation stress
- Early adulthood
- Puberty

Synaptophysin (OD)

Age (days)
Delayed Manifestations

- Sexualized Behaviors
- Onset of Depression
- Recurrent Depressions
- Sensitive periods

Does the nature of the maltreatment matter?

Hypothesis

- Sexual Abuse
- Physical Abuse
- Witness Domestic Violence
- Verbal Abuse

Common consequences relating to the effects of stress, fear, anxiety, humiliation, etc. on the developing brain
Repeated Exposure to Childhood Sexual Abuse

Reduces gray matter volume 14.1% in left primary and secondary visual cortex.

Orbital Frontal Cortex

- The orbitofrontal cortex (OFC) is a region of association cortex of the human brain involved in cognitive processes such as decision making.
- In particular, the human OFC is thought to regulate planning behavior associated with sensitivity to reward and punishment.

Bechara, A.; Damasio, A. R.; Damasio H. & Anderson, S.W. (1994) "Insensitivity to future consequences following damage to human prefrontal cortex". Cognition 50: 7-15

Precuneus

- The interconnected medial prefrontal regions and the posteromedial parietal cortex - network through which personal identity and past personal experiences are interlinked.
- Enables us to move between representation and awareness of self.

• Autobiographical memory
• Self versus non-self representation
• Self-referential judgements
• First- versus third-person perspective
• Perceived agency
• Mind reading/social cognition.

Precuneus

Verbal Abuse
*!#$^&@

Sticks and stones may
break my bones, but
words will never
hurt me.
Effects of Verbal Abuse on Brain Structure

Fiber tracts (white matter) using diffusion tensor imaging.

Gray matter analyzed using voxel based morphometry.

Diffusion Tensor Imaging

Effects of parental verbal abuse on white matter tract integrity was assessed using Diffusion Tensor Imaging (DTI) on 16 healthy young adults exposed to parental verbal abuse (4M/12F, mean age 21.9±2.4 yrs), and 16 controls (5M/11F, 21.0±1.6 yrs).

Diffusion Tensor Imaging

Tract-based Spatial Statistics (TBSS) identified three portions of the FA white-matter skeleton with reduced FA that exceeded the preselected criteria for significance and voxel size.

Arcuate Fasciculus

Verbal IQ
Verbal Abuse: Voxel-based morphometry

Increased gray matter volume left superior temporal gyrus - auditory cortex

Peer Verbal Abuse

There is no deeper wound than humiliation. The momentary glory we may feel in humiliating someone is short-lived compared to the damage we cause. –Irwin Katsof

Power of words

Handle them carefully, for words have more power than atom bombs. –Pearl Strachan

Peer Verbal Abuse: Dose-Response

Significant Exposure: Maximal Peer Verbal Abuse Score ≥30
Substantial Exposure: Maximal Peer Verbal Abuse Score ≥ 40
Peer Verbal Abuse

Figure 5. Regions identified by TBSS in the corpus callosum (CC) and posterior corona radiata (PCR) in which there were correlations between degree of exposure to peer verbal abuse and mean diffusivity (MD), radial diffusivity (RD) and fractional anisotropy (FA) (n = 63).

Time is of the essence

somatization
depression
dissociation
drug use
anger
hostility

n = 848
Corpus callosum alterations appear to be the most consistent finding in maltreated children, and it is perhaps remarkable that they emerged in a sample of comparison subjects with no axis I disorders (resilient subjects).

Inferior Longitudinal Fasciculus

Sensitive Period

Random Forest Regression

Abstract: This study investigated relations between lifetime exposure to interparental aggression and (1) anxiety, depression, and anger; (2) interpersonal problems; and (3) symptoms of trauma, in a sample of young adults.

Results demonstrate that exposure to interparental violence is associated with elevations in depression, anxiety, interpersonal problems, and trauma symptoms.

Further analyses indicated that interparental verbal aggression predicted all symptom areas and was a stronger predictor than interparental violence.

WDV subjects had a 20.5% GMV reduction in right Lingual Gyrus, (BA17), 6.8% reduction in right BA18, and 16.4% reduction in left BA17.
Witnessing Domestic Violence

Witnessing Violence Toward Mother
Effects on child largely mediated by changes in maternal behavior (verbal aggression)

Witnessing Violence Toward Father
Effects on child largely mediated by exposure to maternal verbal and physical aggression

Witnessing Violence Toward Siblings
Effects are predominantly direct - not mediated by changes in sibling behavior.

Survivors guilt

Complicity - identifying with the aggressor

Corporate Punishment
Corporal Punishment

Right Medial Medial Prefrontal Cortex (BA10)
Left medial frontal gyrus (DLPFC) (BA9)
Right anterior cingulate gyrus (BA24)


Key Lessons About Abuse

Number of different types of traumatic experiences - critical factor.

Parental verbal abuse > than physical abuse (depression, anxiety, dissociation).

Parental verbal abuse = non-familial sexual abuse (depression, anxiety, dissociation).


Increased T2-RT (decreased blood flow) in right putamen
Corporal Punishment

Results: ROI analyses also indicated increased T2-RT in dorsolateral prefrontal cortex, nucleus accumbens, substantia nigra and thalamus, but not globus pallidus or cerebellum.

Stress & Drug Abuse

Stress plays a significant role in the initiation and maintenance of drug abuse and has been identified as a key factor leading to relapse to drug use.

Table 4: Correlations for the relationship between regional T2-RT in dopamine-rich regions and extent of drug and alcohol use.

<table>
<thead>
<tr>
<th>Region</th>
<th>Drug Use</th>
<th></th>
<th>Alcohol Use</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p-value</td>
<td>r</td>
<td>p-value</td>
</tr>
<tr>
<td>Anterior Cingulate Cortex</td>
<td>0.406</td>
<td>0.009</td>
<td>0.392</td>
<td>0.012</td>
</tr>
<tr>
<td>Caudate</td>
<td>0.133</td>
<td>0.412</td>
<td>0.089</td>
<td>0.584</td>
</tr>
<tr>
<td>Dorsolateral Prefrontal Cortex</td>
<td>0.416</td>
<td>0.008</td>
<td>0.444</td>
<td>0.004</td>
</tr>
<tr>
<td>Nucleus Accumbens</td>
<td>-0.225</td>
<td>0.163</td>
<td>-0.204</td>
<td>0.206</td>
</tr>
<tr>
<td>Putamen</td>
<td>0.105</td>
<td>0.521</td>
<td>0.067</td>
<td>0.682</td>
</tr>
<tr>
<td>Substantia Nigra</td>
<td>0.140</td>
<td>0.390</td>
<td>0.038</td>
<td>0.814</td>
</tr>
</tbody>
</table>

Values in bold are significant with an overall False Discovery Rate < 0.05
Corporal Punishment

Trier Social Stress Test

What may be the consequences of being unable to mount an appropriate fight/flight stress response to a routine psychosocial stressor?

Cerebellar vermis
a.k.a.
arborvitae
“the tree of life”
Physical vs. Emotional Maltreatment

- 153 young adults with 3T imaging studies
- Thin lingula, n=88 (27M/61F)
- Intermediate lingula, n=47 (20M/27F)
- Thick lingula, n=18 (8M/10F)

- Subjects exposed to emotional maltreatment had higher ratings of depression than controls \((p<0.001)\) or subjects exposed to physical maltreatment \((p<0.02)\).
- Subjects exposed to emotional maltreatment had higher ratings of anxiety than controls \((p<0.001)\) or subjects exposed to physical maltreatment \((p<0.004)\).

Controlling for age, gender, family history of drug abuse, family history of alcohol abuse.
Controlling for age, gender, family history of drug abuse, family history of alcohol abuse.

To explore the potential relationship between early abuse and limbic system dysfunction, we devised a self-report questionnaire, the Limbic System Checklist-33 (LSCL-33), which ascertains the frequency with which patients experienced 33 symptom often encountered during seizures in patients with temporal lobe epilepsy (psychomotor or limbic seizures).

**Childhood Abuse and Limbic Irritability**

To explore the potential relationship between early abuse and limbic system dysfunction, we devised a self-report questionnaire, the Limbic System Checklist-33 (LSCL-33), which ascertains the frequency with which patients experienced 33 symptom often encountered during seizures in patients with temporal lobe epilepsy (psychomotor or limbic seizures).

**Limbic System Checklist (LSCL-33)**

In the following questions, you will be asked how often you experience certain symptoms. To help you in selecting the best answer, the following guidelines are provided: If you have never experienced a certain symptom, or are not sure if you have experienced it, check NEVER. If you have experienced a symptom, but only a very few times in your entire life (say 1 to 3 times), check RARELY. If you have experienced a symptom more than a few times, but not regularly, or with disturbing frequency, check SOMETIMES. If you have experienced the symptom with some regularity, consistency, or disturbing frequency check OFTEN.

A. How often have you experienced the sudden, abrupt and unexplained onset of:

1. Headache
2. Numbness or tingling
3. Dizziness
4. Sensation of something crawling under your skin
5. Flushing or hot sensation
6. Feeling that your heart had stopped or is pounding or racing
7. A rising or sinking feeling in your stomach - like you were in an elevator
8. Sudden urge to throw up - like your intestines were tied in knots, or you were punched in stomach

B. How often have you experienced - for no particular reason:

9. Flashing lights - either white or colored
10. Seeing patterns or geometric shapes
11. Seeing fully formed images - such as a person in a doorway, a demon, a God-like image
12. Hearing a ringing or a buzzing sound
13. Hearing a voice calling your name
14. Hearing a voice repeating a sentence or phrase
15. Having a sense of your heart race in your throat
16. Smelling an odor such as ammonia, burning rubber, decaying waste, or garbage
17. Smelling an overly pungent or sickeningly sweet smell

E. How frequently have you had the visual illusion that:

31. An object or person suddenly became distorted or transformed
32. An object or person suddenly looked smaller, farther away, or out of reach
33. An object or person suddenly looked larger, closer, or towered over you
## Limbic System Checklist (LSCL-33)

**C. How frequently have you had unexplained or uncontrolled episodes in which you experienced or engaged in:**

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. Complex automatic behavior - such as purposeless running in circles, closing window, or picking at your clothes</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>19. Turning off into space</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>20. Staring off into space, looking over your shoulder, scanning your surroundings</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>21. Stuttering, slurred speech, brief loss of ability to speak</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>22. Twitching or jerking of the arms or legs</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>23. Transient weakness in the arms or legs, possibly resulting in falling to one side</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

### Automatisms

### Dissociative Disturbances

## Limbic System Checklist (LSCL-33)

**D. How often have you experienced:**

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
</tr>
</thead>
<tbody>
<tr>
<td>24. Memory flashbacks (for example feeling exactly as you did as a child during an upsetting event)</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>25. The sensation that events, conversations, or a place was strangely familiar, as if you had experienced or dreamed the situation before</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>26. The sensation that a familiar person or place has become unfamiliar, changed, different or almost as if you had never experienced it before</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>27. The feeling that an unseen presence is watching over you or observing you from nearby</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>28. The sudden feeling that you have become possessed, or that you have multiple personalities</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>29. The sensation that your mind has left your body, or that you are watching yourself as a detached observer</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>30. The sudden feeling that you are no longer real, or not the same person</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

The ability of the instrument to detect ictal symptoms suggestive of TLE was ascertained by comparing a group of normal adult control subjects (n=10) without psychiatric or neurological abnormalities (or childhood abuse histories) to patients with well documented TLE responsive to anticonvulsants (n=8). Normal controls invariably had total scores <10, while patients with documented TLE had scores >23 (range 23-60).

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**Childhood Abuse and Limbic Irritability**

![LSCL-33 Graph](image)

- **McLean -- Adult Outpatient Clinic**
  - 38% (n=109) No Abuse
  - 49% (n=77) Physical Abuse
  - 113% (n=41) Combined Abuse

*HISTORY*
CHILDHOOD ABUSE AND NEUROLOGICAL DYSFUNCTION

**DEMOGRAPHICS**

<table>
<thead>
<tr>
<th>ABUSE HISTORY</th>
<th>N</th>
<th>% female</th>
<th>AGE</th>
<th>VIQ</th>
<th>PIQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-abused group</td>
<td>27</td>
<td>26%</td>
<td>13.5</td>
<td>102</td>
<td>104</td>
</tr>
<tr>
<td>Any abuse</td>
<td>77</td>
<td>60%</td>
<td>12.8</td>
<td>100</td>
<td>104</td>
</tr>
<tr>
<td>Psychological</td>
<td>22</td>
<td>41%</td>
<td>12.9</td>
<td>100</td>
<td>109</td>
</tr>
<tr>
<td>Phys./Sexual (all)</td>
<td>55</td>
<td>67%</td>
<td>12.8</td>
<td>99</td>
<td>102</td>
</tr>
<tr>
<td>Phys./Sexual (severe)</td>
<td>38</td>
<td>68%</td>
<td>13.0</td>
<td>97</td>
<td>102</td>
</tr>
</tbody>
</table>

*Abused and non-abused patients differed most clearly in the prevalence of left-sided frontal or temporal abnormalities (p = 0.036). They did not differ in either the prevalence of right-sided abnormalities (p > 0.8), or bilateral abnormalities (p > 0.5).*
Early Abuse and EEG Abnormalities in Children

- Early abuse, particularly psychological abuse, was associated with an increased incidence of left-sided abnormalities on neuropsychiatric testing.

- EEG abnormalities were associated with a greater likelihood of self-destructive behavior and suicidal thinking.

![Graph showing left-right localization of neuropsychological abnormalities](image)

EEG Abnormalities and Suicidality

Previous studies have also identified a strong association between suicidal behavior, EEG abnormalities and seizure disorders.

- Perhaps the earliest study of the physiological determinants of suicide reported a marked positive association between paroxysmal EEG disturbances, suicidal ideation, attempts, and assaultive-destructive behavior (Struve et al. 1972).

- The risk of completed suicide is 4-5 times greater in patients with epilepsy than among patients with other medical disorders of comparable severity. This risk may be 25-fold greater in patients with TLE (Barraclough 1981; Matthew & Barabas, 1981).


EEG Abnormalities and Suicidality

As many as one third of all epileptic patients attempt suicide at some point in their life (Delay et al 1957; Jensen, 1975).


Borderline Personality Disorder and EEG Abnormalities

Snyder and Pitts [1984]
- Borderline patients 38% abnormal EEGs
- Dysthymic patients 13% abnormal EEGs

Cowdry et al [1985]
- Borderline patients, 41% definite sharp wave abnormalities
- Unipolar depression, 5% definite sharp waves (p < 0.005).

Cerebellar vermis
a.k.a.
arborvitae
“the tree of life”

Infants maintained in partial isolation manifest violence and aggression as adults.

• William Mason (1968), working with Harlow, found that a lack of somatosensory stimulation (especially vestibular proprioception) was the ingredient responsible for disturbed behavior in sensory-isolated monkeys.

• James Prescott (1971) proposed that early vestibular stimulation was important in the development of appropriate emotional behavior.

Harlow’s Surrogate Mother Studies

Heath found spiking and spindling in limbic and fastigial sites from Harlow’s monkeys.

From Heath, Diseases of the Nervous System, 33(3) 157–163, 1972

Key Lessons About Abuse

Neurobiological effects depend on timing of exposure (sensitive periods)

Effects on sensory systems and pathways influenced by type of exposure

Neurobiological and clinical consequences may be delayed (silent periods)
Summary

Childhood adversity
• number
• type

Brain development

Genetics
Age

PTSD
Depression
Medical Disorders
Addiction
Dissociation
Other psych disorders
Cognition

Summary

Gray Matter Regions
• Hippocampus
• Prefrontal Cortex
• Medial
• Dorsolateral
• Orbital
• Visual and Auditory Cortex
• Precuneus (Posterior Parietal Cortex)

Summary

White Matter Fiber Pathways
• Corpus Callosum
• Arcuate Fasciculus
• Cingulum Bundle
• Fornix
• Inferior Longitudinal Fasciculus
• Cortical Pain Pathways

Relative Importance: Current Depression Ratings
Using method of Lindeman, Merenda & Gold

n=1662
Relative Importance: Current Anxiety Ratings
Using method of Lindeman, Merenda & Gold

Relative Importance: Current Dissociation Scores
Using method of Lindeman, Merenda & Gold

Summary

Sexual Abuse
Witnessing Domestic Violence

Medial Prefrontal Cortex

Precuneus

Physical Maltreatment

Autobiographical memory
Self versus non-self representation
Self-referential judgements
First- versus third-person perspective
Perceived agency
Mind reading/social cognition.
### Summary

Decreased hemispheric Integration

### Implications for Treatment

#### Amygdala
- Hypersensitive
- Hypo-responsive

**Limbic Irritability**

- Anticonvulsants

**Hypothalamus**

- Locus ceruleus
- Pituitary
- Autonomic Nervous System
- Norepinephrine
- Beta blockers
- Alpha2 agonists

**Cortisol**

#### Implications for Treatment

- Abnormal EEGs
- 72% children severe physical and sexual abuse (Ito et al., 1994)
- 72% incest survivors (Davies, 1979)
- 36% seizure disorders (Harlow's monkeys, Heath, 1972)

### Implications for Treatment

- Eye Movements
- Vestibular and Proprioceptive Stimulation
- Biofeedback
Integration

Richard P. Kluft, M.D.
Catherine G. Fine, Ph.D.

Left versus Right Visual Field Stimulation


The End

Thank you!