Effects of Verbal Abuse on Brain Structure

Fiber tracts (white matter) using diffusion tensor imaging.

Gray matter analyzed using voxel based morphometry.

Verbal Abuse: Voxel-based morphometry

Increased gray matter volume left superior temporal gyrus - auditory cortex


Peer Verbal Abuse

subjects

63 participants (23M/40F, 21.9±1.9 years) - no history of exposure to abuse, peer physical bullying, parental verbal abuse and no psychiatric disorders.

Recruited as healthy normal comparison subjects for other studies.

Participants differed in their degree of exposure to 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).

Corpus Callosum

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).

Witnessing Domestic Violence

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.
V1 (primary visual cortex)  
V2 (vis association cortex)  
MT/V5 (Middle temporal)  
Inferior occipital gyrus and sulcus  
Cuneus gyrus  
Middle occipital gyrus  
Superior occipital gyrus  
Lateral fusiform gyrus  
Lingual gyrus  
Occipital Pole

Cortical Thickness Analysis

Right Lingual Volume (VBM)

% Variance Explained

Dur IP Physical  
Dur IP Verbal  
Financial Suffix  
Parental Ed  
Parental Verb Aggr

Corporal Punishment

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

Harsh Corporal Punishment

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

Increased T2-RT (decreased blood flow) in right caudate

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.
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?

Figure 5. Heart rate and cortisol response of healthy young controls and subjects with history of harsh corporal punishment during the Trier Social Stress Test. Gray shaded areas indicate time of the acute stressor.

Harsh Corporal Punishment

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.

Summary

Childhood Abuse and Psychopathology

Ecophenotypes

Childhood maltreatment increases risk for psychopathology.

For some highly prevalent disorders (i.e., major depression, anxiety disorders including PTSD and substance abuse) there is a substantial subset of individuals with maltreatment histories and a substantial subset without.

Do those with maltreatment histories represent a clinically and biologically distinct subtype?

Personality Disorders
Dissociative Identity Disorder

Major Depression & Dysthymia
Post-Traumatic Stress Disorder
Anxiety Disorders (Panic & Phobias)
Substance Use Disorders

Schizophrenia
Bipolar Disorder
Ecophenotype (adj. ecophenotypic)

A phenotype (visible physical characteristics or behaviors) that is a result of environmental or ecological conditions rather than genetic expression (nurture instead of nature).

**Ecophenotypes**

**Major Depressions**

- Maltreatment Hx negative
- Maltreatment Hx positive

**Post-Traumatic Stress Disorder**

Childhood maltreatment is a major risk factor for the development of PTSD in adulthood.

Scott et al 2010 report adjusted odds ratios of 10.92 and 4.86 for 12-month and lifetime diagnoses of PTSD in adult subjects with vs. without Childhood Protective Service histories followed prospectively.

Post-Traumatic Stress Disorder

Individuals who experience both childhood adversity and adult traumatic events are more likely to develop lifetime PTSD than those who experience either type of adverse event alone.


Ecophenotypes

Developmental timing of abuse may be critical to the type of pathology later evidenced.

Individuals reporting childhood sexual abuse after age 12 had a 10-fold increase in relative risk of severe PTSD in adulthood compared to individuals reporting CSA before age 12.

Conversely, more severe depressive symptoms were present in individuals reporting CSA before age 12 then after age 12.


Anxiety Disorders

Childhood adversity accounted for 32.4% of the PARF for anxiety disorders.


Ecophenotypes

Specific phobias, social anxiety disorder (SAD), generalized anxiety disorder (GAD), as well as panic disorder with or without agoraphobia

Substance Use Disorders

Risk is related to the number of different types of maltreatment an individual experienced. Compared with individuals with 0 ACEs, adults with > 5 ACEs are 7- to 10-fold more likely to report illicit drug use problems, addiction to illicit drugs, and parenteral drug use.

The PARF for these outcomes were 56%, 64%, and 67%, respectively.

Major Depression

Course
Earlier Onset
Longer, more severe course

Clinical Features
more severe mood sx, neurovegetative & reverse neurovegetative sx, more frequent psychomotor retardation, psychotic features & suicidality

Differences

PTSD

Course
Earlier Onset
Longer, more severe course

Clinical Features
Greater symptom complexity, more comorbid mood disorders and greater symptoms of dissociation and alexithymia

Differences

Anxiety Disorders

Course
Earlier Onset
Longer, more severe course

Clinical Features
Greater symptom complexity, more comorbid mood disorders, more impairment in social function and lower quality of life

Differences

Substance Use Disorders

Course
Earlier Onset
Longer, more severe course

Clinical Features
Greater risk of comorbid personality disorders, more psychological distress, greater likelihood of recent incarceration

Differences

Major Depression

Associated medical disorders
Autoimmune
Metabolic
Cardiovascular (Mirgaine)
Inflammation

Response to treatment
more unfavorable (metaanalysis)¹

better response to nefazadone than CBASP, combination helpful²

Miller GE, Cole SW. Clustering of depression and inflammation in adolescents previously exposed to childhood adversity. Biological psychiatry. 2012;72(1):34-40


Nemeroff, CB et al., PNAS (USA), 2003;100(24):14293-6
Depression with Early Trauma/Loss

Response to treatment

- More unfavorable with greater use of substances during treatment, and more persistence of substance-related problems post-discharge.

Differences

- Substance Use Disorders
- Substance Use Disorders MAL

Genetics

- 5HTTLPR GxE more strongly linked to maltreatment (P = .00007) than other stressful life events (P = 0.03)\(^1\)
- Other polymorphisms - (COMT, BDNF)

Genetics

- Epigenetic modification of the neuron-specific glucocorticoid receptor promoter (Nr3C1) in hippocampal cells (maltreated suicides)\(^1\)

Genetics

- Mild forms of MDD show little evidence of heritability (h\(^2\) = 0.0-0.07)\(^1\)

Genetics

- Polymorphism of FKBP5 (regulates cortisol-binding affinity)

Genetics

- TT genotype of rs9470080 - lowest risk for PTSD
- TT genotype of rs9470080 - highest risk for PTSD

\(^1\)Karg K Arch General Psychiatry. 2011;68(5):444-54

\(^1\)McGowan PO. Nat Neurosci. 2009;12(3):342-8

Neurobiology of MDD

*Key findings in MDD include:*

- Reduced hippocampal volume
- Reduced prefrontal blood flow or metabolic activity (L)
- Increased amygdala response to sad faces
- Abnormal HPA response to dexamethasone, CRF

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<tr>
<th>Neurobiology</th>
<th>Differences</th>
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<tr>
<td>MDD</td>
<td>MDD-MAL</td>
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<td>Reduced hippocampal volume may be specific to MDD-MAL</td>
<td>Amygdala activation to sad faces may be specific to MDD-MAL</td>
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Vythilingam M. Am J Psychiatry, 2002;159(12):2072-80
Grant MM. J Psychiatric Research, 2011;45(7):886-95

Ecophenotypes

In short, what the field has regarded as a key neurobiological finding in MDD may have relatively little to do with the disorder. Rather, these neurobiological differences are more likely a consequence of early stress exposure, and may serve as risk factors for depression and other forms of psychopathology.

Maltreatment

- Impulse control disorders
- Drug and Alcohol Abuse
- Antisocial Personality DO
- Generalized Anxiety & Phobias
- Major Depression
- Bipolar DO (early onset)
- Post-traumatic Stress
- Borderline Personality DO
- Dissociative Identity DO
- Psychotic Disorders

Psychopathology

- Impulse control disorders
- Drug and Alcohol Abuse
- Antisocial Personality DO
- Generalized Anxiety & Phobias
- Major Depression
- Bipolar DO (early onset)
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- Psychotic Disorders

Reduced Hippocampal Volume
Neurobiology of Anxiety Disorders with Intense Fear and Panic (Panic DO, PTSD, Phobias, Social Anxiety DO)

Amygdala hyperreactivity, which may stem from underactivity of the prefrontal cortex and insufficient inhibition of the amygdala.

Overactivation of the insula, a paralimbic region associated with disgust and somatic reactions, has also been frequently observed.

Childhood Maltreatment and Stress Response


Ecophenotypes

The hypothesis that neurobiological alterations, such as reduced hippocampal volume, are the result of childhood maltreatment and only a risk factor for psychopathology, may explain the following.

1. Why so many different psychiatric disorders have very similar neurobiological findings.

2. Inconsistencies between studies in presence or absence of these findings within a given sample of subjects selected by disorder without regard to exposure history.

Ecophenotypes

Subtyping by maltreatment history may be essential in an effort to identify the neurobiological and genetic underpinnings of these disorders.

Ecophenotypes

Subtyping by ecophenotypes may lend clarity to the understanding and treatment of these disorders.

Studies of subtyped individuals should result in more targeted treatment guidelines, therapeutic algorithms and better outcomes.

Key Lessons About the Neurobiology of Abuse

Both gray matter and white matter (fiber tracts) appear to be affected

Brain regions differ in susceptibility - key targets appear to be cortico-limbic

Also sensory systems and pathways that convey the adverse sensory input appear to be affected
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

- **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

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)

- **Anticonvulsants**

- **Limbic Irritability**
  - Amygdala
  - Hypothalamus
  - Locus ceruleus

- **Beta blockers**
  - Alpha2 agonists

- **Vestibular and Proprioceptive Stimulation**

- **Eye movements**

- **Cerebellar Vermis**

- **Limbic Irritability**

- **Vestibular and Proprioceptive Stimulation**

- **Biofeedback**
Decreased hemispheric Integration

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

Affective Regulation

Trauma Exposed
Controls

Right Anterior Insula

Unexposed
Maltreated
Somatization

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<tr>
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<th>Right Precuneus</th>
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<td>Self-referential thinking</td>
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<td>Maltreated</td>
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The End

Thank you!