



The Psychobiological of Pediatric Maltreated Related PTSD

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Neurobiology of Maltreatment & PTSD: understand both the adverse biological effects of maltreatment and the rationale for interventions

- Developmental achievements in childhood.
- Animal models of chronic stress and biological stress systems.
- Diagnosis posttraumatic stress disorder (PTSD) in maltreated children.
- The psychobiology of maltreatment (abuse & neglect) and maltreatment+PTSD in childhood.
- Review a series of studies which examined brain & cognitive development in maltreated children with PTSD.

Core Concepts of Development

Human Brains develop over time, neural circuits are wired in a bottom-up sequence, and the capacity for change decreases with age.

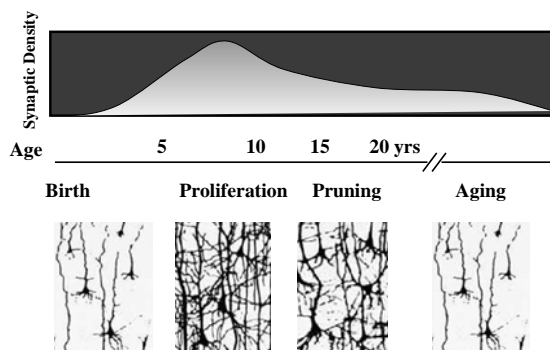
The interaction of genes and experience shapes the architecture of the developing brain, and the active agent is the “reciprocal” nature of children’s relationships with the important adults in their lives.

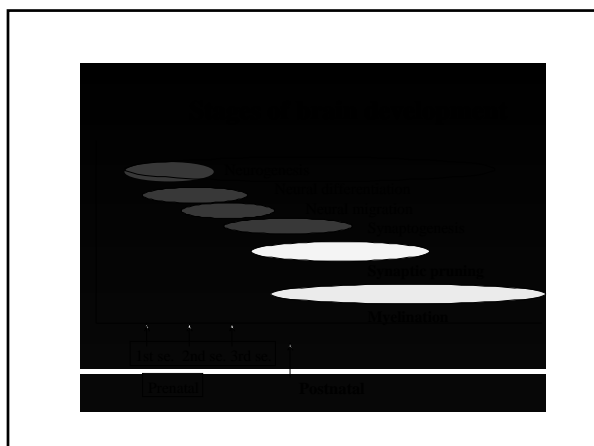
Core Concepts of Development-2

- Positive and tolerable stress are compatible with normal child development.
- Toxic stress can damage developing brain architecture and create dysregulation in the body's stress response systems that leads to adverse brain development and lifelong problems in learning, behavior, and both physical and mental health.

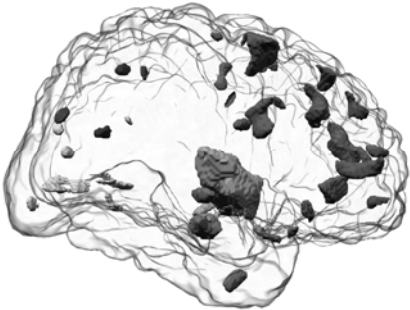
Developmental Stages & Achievements

Postnatal development of the human Brain



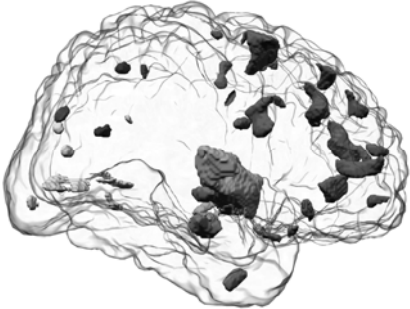


Child & Adolescent Brain is Still Developing



- Frontal Lobes
- Temporal Lobes
- Cerebellum

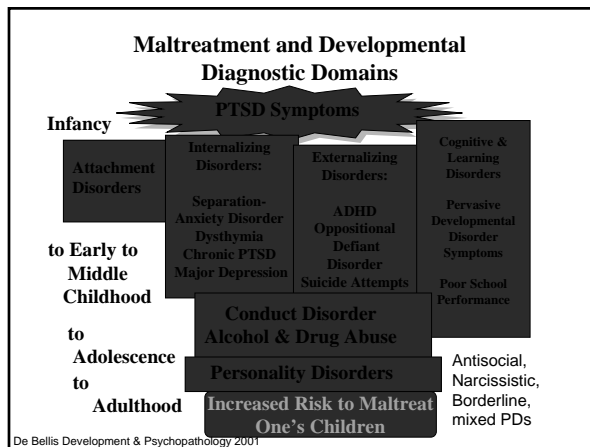
Child & Adolescent Brain is Still Developing



- Memory
- Problem Solving
- Mental Flexibility
- Planning
- Behavioral Regulation
- Emotional Regulation

Psychological Studies of Maltreated Children

- Attachment problems
- Emotional Regulation Problems
- Behavioral Regulation Problems
- Posttraumatic stress disorders
- ADHD
- Low IQ: Perez, C., & Widom, C. S., Childhood victimization and long-term intellectual and academic outcomes. *Child Abuse & Neglect*, 18(8), 617-633, 1994.
- Poor Academic Achievement Outcomes
- High Rates of alcohol and substance abuse
- High rates of conduct disorder, antisocial, borderline, and narcissistic, personality disorders
- High rates to abuse and neglect one's children (25-33%).



Child Maltreatment: Chronic Pediatric Stress

In USA: (<1 million per yr <1% false reports)
Neglect & Emotional Maltreatment - 60%
Physical Abuse - 25%
Sexual Abuse - 15%
In North Carolina-Neglect is 80%

Witnessing Domestic Violence
It is under-estimated that 6 to 12 million women are battered/year by their partners. Half of these are thought to be witnessed by children (Sassetti, 1993). Today estimated at 22 million.

Abuse is a Chronic Stressor

- Sexual Abuse occurs repeatedly, typically for years prior to disclosure.
- Physical Abuse occurs repeatedly, typically for years prior to disclosure.
- Association with Parental Poverty, Parental Mental Health and Parental Substance Abuse problems.
- Association with High Rates of Domestic Violence.
- Association with poor parenting skills and Neglect and Emotional Abuse.

Neglect as a Stressor

- Failure to Provide Age Expected Emotional and Social Stimulation: Humans are a Social Species
- High Rates of Substance Abuse-Domestic Violence
- Poverty associated high rates of community violence
- Failure to Supervise: Higher Rates of Accidents
- Failure to Provide: Lead to social isolation, teasing, being bullied (e.g. child who goes to school w dirty clothes).
- Failure to Provide Developmentally Appropriate Discipline- Teach Self Discipline or Self Regulation
- Failure to Teach Appropriate Coping and Problem Solving Life Skills

Experiences of Maltreated Youth

Bad things that happen:

- Physical harm
- Domestic violence
- Community violence
- Exposure to adult alcohol and drug use
- Exploitation (sexual or otherwise)

Neglect and Life Experiences...

Good things that don't happen:

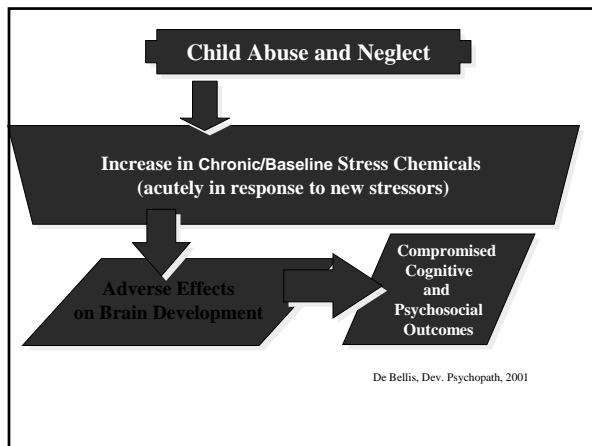
- Basic needs not met
- Adults can't demonstrate trust
- Life not structured or predictable:
 - School, homework
 - Sports teams
- Not Learning from role models how to develop internal and behavioral self-controls (Self Discipline or Self regulation)

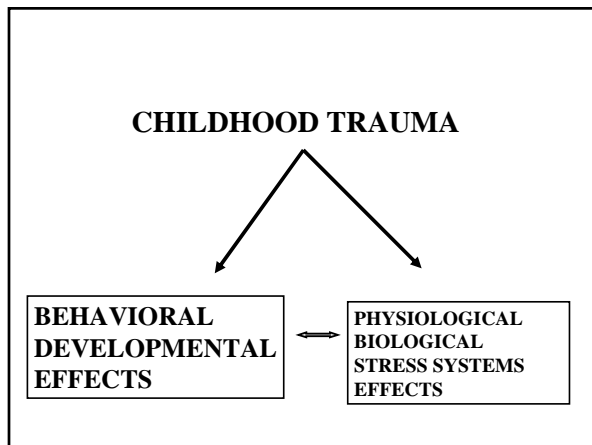
Risk of PTSD from Childhood Trauma

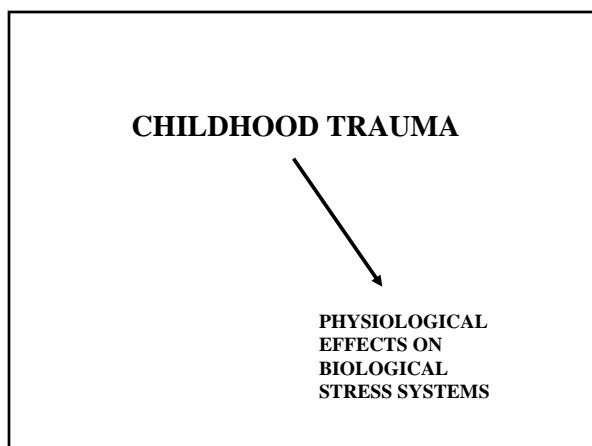
Sexual Abuse	42-48%
Physical Abuse	11-50%
Witnessing Mother's Sexual Assault	100%
Witnessing/Experiencing Community Violence	27-60%
Warfare	47%
Natural and Man-Made Disasters	6-50%
Medical Illnesses:	
Severe Burns	30%
Bone Marrow Transplantation	50%

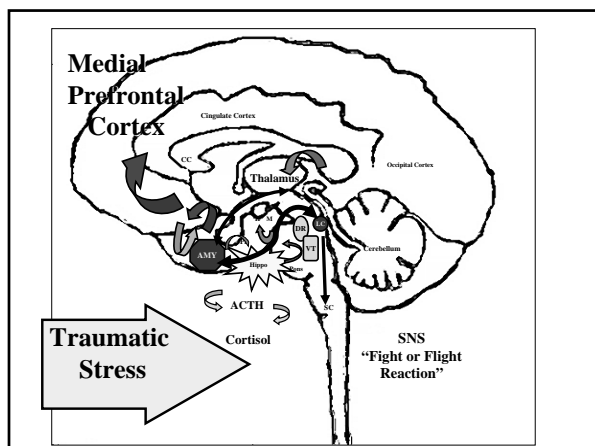
DSM-IV Posttraumatic Stress Disorder

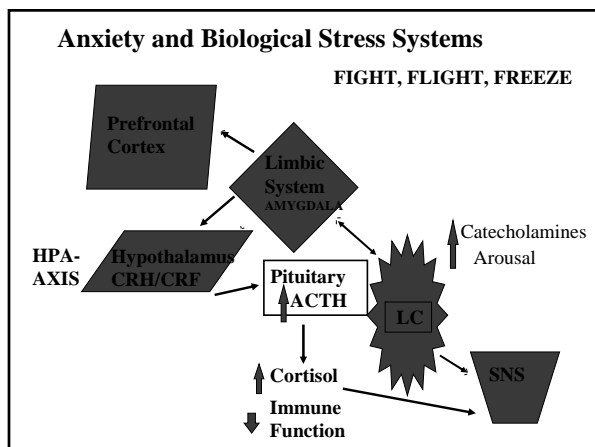
- Type A: Exposure and intense fear/numbness/regression in response to a traumatic event(s) that involved actual or threatened injury to self or others
- Cluster B: Intrusive re-experiencing of the trauma
- Cluster C: Persistent avoidance of trauma stimuli and numbing of responsiveness
- Cluster D: Persistent symptoms of increased physiological arousal
- Duration of symptoms > 1 month
- Clinically significant distress
- MANY TRAUMATIZED CHILDREN HAVE PTSD or ANXIETY/MOOD SYMPTOMS (not the disorder)

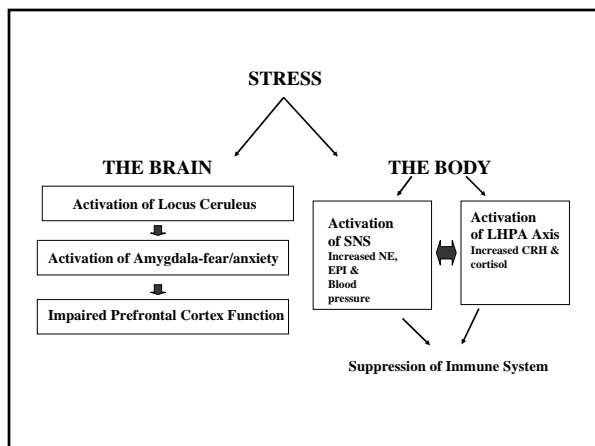








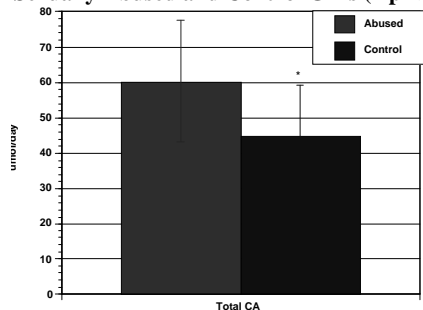




Studies on Catecholamines in Abused Children

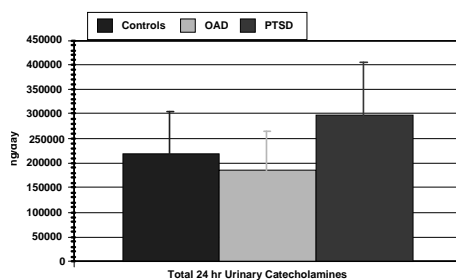
- Queiroz et al., Biochemical correlate of depression in children. *Arg Neuro-Psiquiat* 49: 418-425, 1991.
- De Bellis et al. Urinary catecholamine excretion in sexually abused girls. *J Am Acad of Child and Adol Psych* 33: 320-327, 1994.
- Perry. Neurobiological sequelae of childhood trauma: PTSD in children. In *Catecholamine Function in Posttraumatic Stress Disorder: Emerging Concepts*. MM Murburg (Ed) pp. 233-255, 1994.
- Galvin et al., Serum dopamine beta hydroxylase and maltreatment in psychiatrically hospitalized boys. *Child Abuse Neglect* 19:821-832, 1995.
- De Bellis et al., Developmental Traumatology: Part I Biological Stress Systems. *Biological Psychiatry* 45: 1259-1270, 1999.

Total 24 hr Urinary Catecholamine Excretion (Mean \pm SD) in Sexually Abused and Control Girls (* $p < .05$)



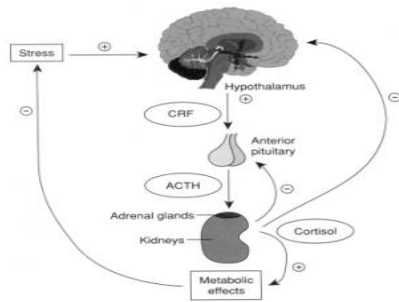
De Bellis MD, Lefter L, Trickett PK, & Putnam FW: J. Am. Acad. Child Adolesc. Psychiatry, 33:320-327, 1994.

24 hr Urinary Catecholamine Excretion in Maltreated Prepubertal Children with PTSD (n=18), Non Abused Anxious Children (n=10), and Controls (n=24) PTSD>OAD and Controls; $p < .05$



De Bellis et al., Biological Psychiatry 1999

The HPA Axis



<http://www.montana.edu/wwwai/imsd/alcohol/Vanessa/vwhpa.htm>

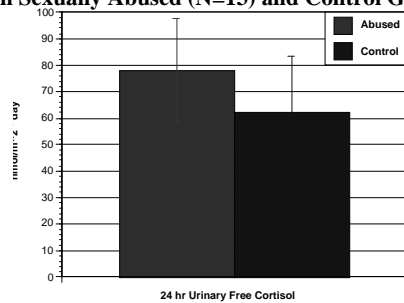
What turns on the HPA Axis?

- Physical injury
- Uncontrollable and unpredictable environment
- I.E. STRESS and DISTRESS

Studies on HPA Axis in Maltreated Children

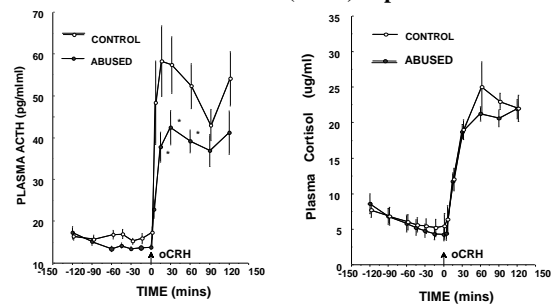
- De Bellis et al., Hypothalamic-pituitary-adrenal axis dysregulation in sexually abused girls. JCEM 78:249-255, 1994.
- Hart et al., Altered neuroendocrine activity in maltreated children related to symptoms of depression. Development and Psychopathology 8:201-214, 1996.
- Kaufman et al., The corticotropin-releasing hormone challenge in depressed abused, depressed nonabused, and normal control children. Biological Psychiatry 42:669-679, 1997.
- De Bellis et al., Developmental Traumatology: Part I Biological Stress Systems. Biological Psychiatry 45: 1259-1270, 1999.
- Elevated salivary cortisol in Romanian children (Gunner et al., 2001).
- Carrión et al., Diurnal Salivary Cortisol in Pediatric Posttraumatic Stress Disorder. Biological Psychiatry 51: 575-582, 2002.

**24 hr UFC (Mean \pm SD)
in Sexually Abused (N=13) and Control Girls**



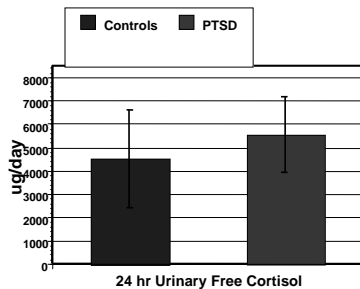
De Bellis, MD, Chrousos, GP, Dorn, LD, Burke, L, Helmers, K, Kling, MA, Trickett, PK, & Putnam, FW: JCEM, 78:249-255 1994.

**Mean \pm SEM Plasma ACTH and Cortisol Responses to
ovine CRH Stimulation in Sexually Abused (N=13)
and Control Girls (N=13) * $p < .05$**



De Bellis MD, et al., JCEM, 78:249-255 1994.

**24 hr Urinary Free Cortisol Excretion in
Maltreated Children with PTSD (n=18) and Controls (n=24)
PTSD > Controls; $p < .05$**



De Bellis et al., Biological Psychiatry 1999

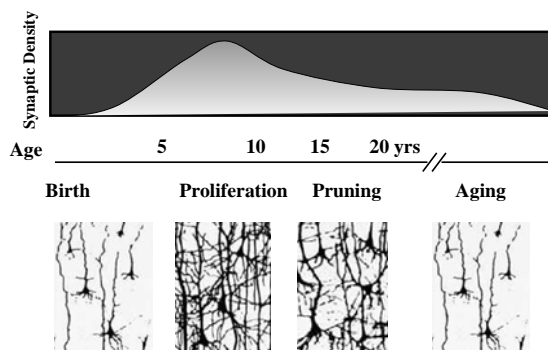
Long Term Effects of High Catecholamines and Cortisol

- High Blood Pressure
- Heart Disease
- Problems with immunity-cancers, autoimmune diseases
- Self-medication of high arousal levels with alcohol and drugs or food (obesity)
- Mental illness

Biological Stress Systems and Adverse Brain Development Mechanisms:

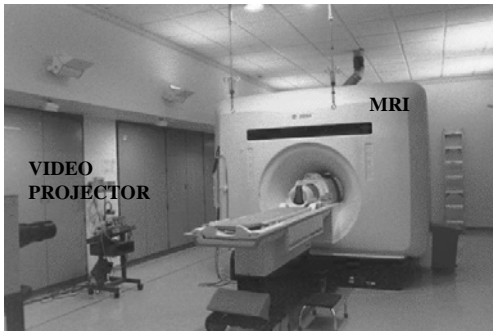
- Catecholamine or Glucorticord-Induced Accelerated Loss of Neurons (Sapolsky et al., 1990; Simantov et al., 1996; Smythies 1997) "premature aging"
- Glucorticord-Induced Delays in Myelination (Dunlop et al., 1997).
- Glucorticord- Inhibition of Neurogenesis (Gould, McEwen, Tanapat, Galea, & Fuchs, 1997a; Gould, Tanapat, & Cameron, 1997b; Tanapat, Galea, & Gould, 1998) decreased BDNF.
- Catecholamine-Induced Abnormalities in Developmentally Appropriate Pruning (Lauder 1988; Todd 1992).

Postnatal development of the human Brain



Effects on Brain Development





The Clinical Profiles of Maltreated Children with PTSD and Non-Abused Healthy Control Children

Sex (F/M)	30/31	60/62	ns

De Bellis et al., Biological Psychiatry 1999, 2002

Causes of PTSD in Pittsburgh Sample of Maltreated Children with PTSD

- 42/61 Sexual Abuse
- 19/61 Witnessing Domestic Violence
- 5/61 Physical Abuse
- 7/61 Witnessing Domestic Violence & Sexual Abuse

De Bellis et al., Biological Psychiatry 1999, 2002

Co-Morbidity in Pittsburgh Sample of Maltreated Children with PTSD

Mean 3.0 ± 1.2 Axis I Disorders

- 41/61 Dysthymia
- 31/61 Major Depression
- 26/61 Oppositional Defiant Disorder
- 21/61 Attention Deficit Hyperactivity Disorder
- 6/61 Separation Anxiety Disorder

De Bellis et al., Biological Psychiatry 1999, 2002

STUDIES OF PEDIATRIC MALTREATMENT RELATED PTSD: Brain Findings



MRI Measures in Maltreated Children with Chronic PTSD(N=61) Compared to Controls (N=122)

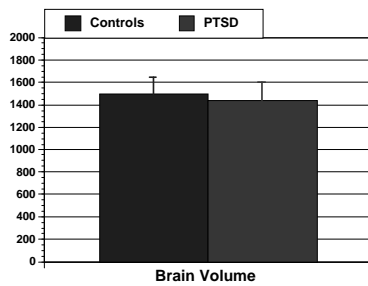
Males

+

+

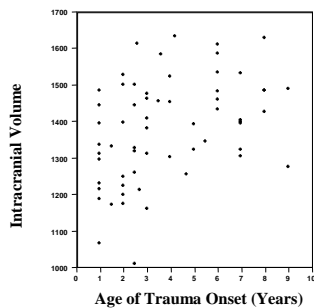
De Bellis et al., Biological Psychiatry 1999, 2002

MRI Brain Volumes in Maltreated Children with PTSD Compared to Matched Controls (F=4.5; p<.05)



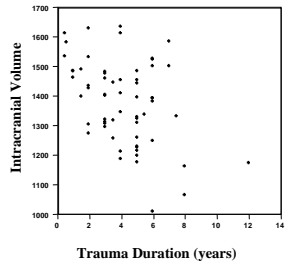
De Bellis et al., Biological Psychiatry 1999

Relationship Between Age of Onset of Abuse and Intracranial Volume (r=.43, df=59, p=.0006) in Maltreated Children with PTSD



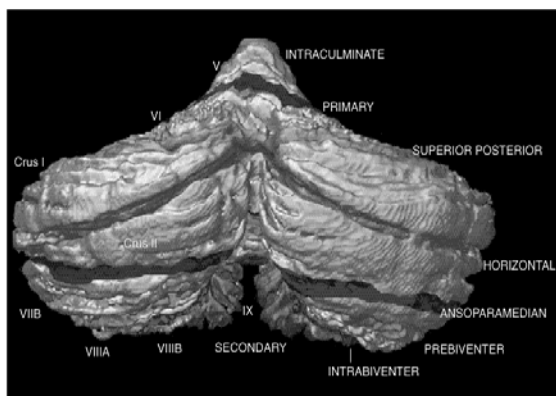
De Bellis et al., Biological Psychiatry 1999, 2002

Relationship Between Years of Abuse and Intracranial Volume ($r = -.36$, $df=59$, $p=.004$) in Maltreated Children with PTSD



De Bellis et al., Biological Psychiatry 1999, 2002

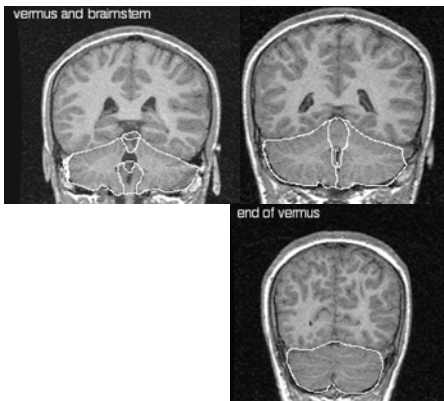




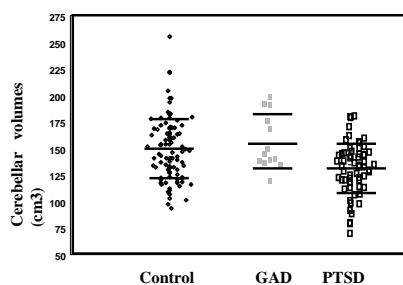
c

Cerebellum

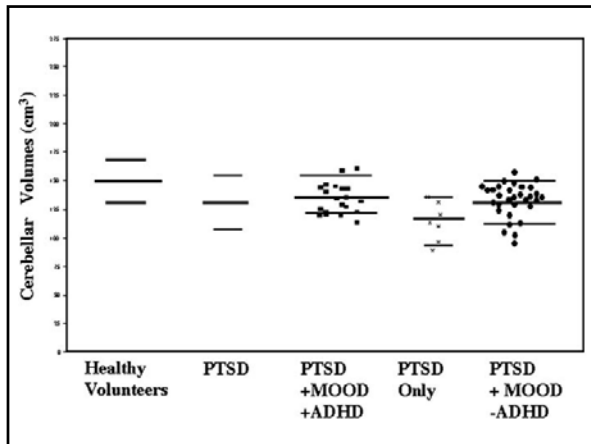
- Historically, the brain region primarily involved in the coordination of motor movements.
- Subserve higher cognitive functions as well as language development and emotional regulation.
- Grows dramatically during childhood and adolescence, age 17yrs (Giedd et al., 2002).
- Most sexually dimorphic, latest maturing, and some areas are the least heritable (relatively high correlations for both MZ and DZ twin pairs) (Giedd et al., 2002).

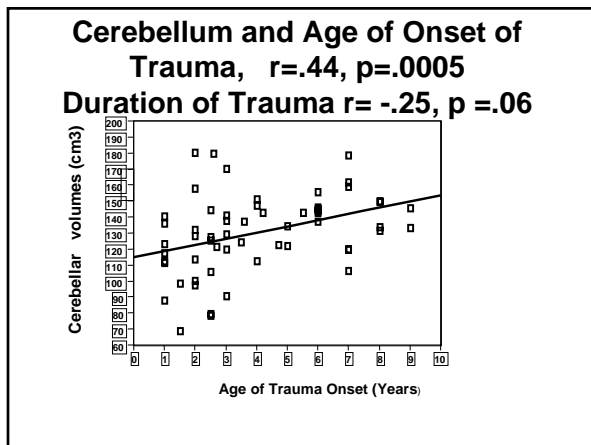


Cerebellar Volumes of Maltreated Children & Adolescents with PTSD, non-traumatized Children & Adolescents with GAD and Non-Maltreated Healthy Control Subjects
($F_{1,165} = 6.32, p = .002$)



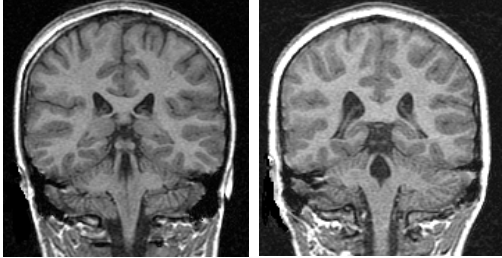
De Bellis et al., Biological Psychiatry, 2006





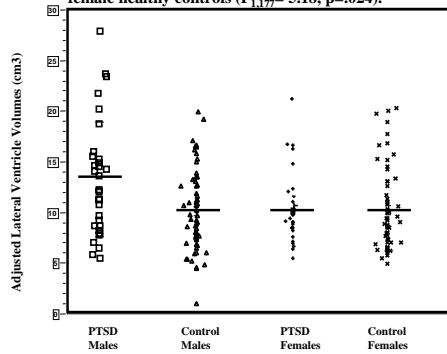
**STUDIES OF PEDIATRIC
 MALTREATMENT
 RELATED PTSD:
 Gender Differences**

Lateral Ventricles Measures in an 11 Year Old Maltreated Male with Chronic PTSD, Compared with a Healthy, Non-Maltreated Matched Control



De Bellis et al., Biological Psychiatry, 1999.

Total lateral ventricle volumes and means (cm³) of maltreated male and female children and adolescents with PTSD and non-maltreated male and female healthy controls ($F_{1,177} = 5.18, p = .024$).

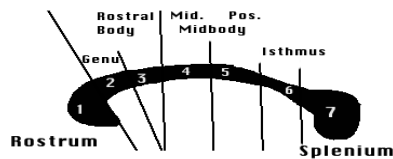


De Bellis et al., Neuroscience & Biobehavioral Reviews, 2002

Corpus Callosum

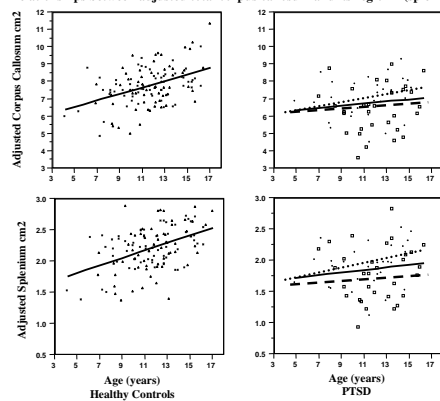


Midsagittal Divisions of the Corpus Callosum for Quantitative MRI Measurements



- Region 1-orbital prefrontal & inferior premotor
- Region 2-prefrontal cortex
- Region 3-premotor
- Region 4-motor
- Region 5-post. parietal
- Region 6-sup. temporal
- Region 7-occipital, inferior temporal

Relationships between adjusted total corpus callosum and its region 7 (splenium) with age.



De Bellis et al. *Neuroscience & Biobehavioral Reviews*, 2002

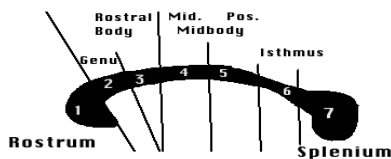
Male Neuro-Vulnerability

- Maltreated males with PTSD did show a trend towards more PTSD cluster C symptoms than maltreated females with PTSD.
- Cluster C symptoms represent both avoidant and dissociative behaviors and can be thought of as ways to control painful and distressing reexperiencing of symptoms.
- Cluster C can lead to diminished interest in others, feelings of detachment, a restricted range of affect, and dissociation.
- Emotional numbing and diminished interest in others, particularly during development, may result in lack of empathy increased risk for antisocial behaviors.
- Sociobiological basis -detachment behaviors during adverse circumstances (i.e. killing game, warfare) would be more beneficial to male than to female primitive humans.
- Interestingly, follow-up of males subjects from the original study (1999) revealed that eight of 25 males and only one of the 19 females with PTSD studied and none of the controls developed conduct disorder or were arrested on more than one occasion within 3 years of initial brain scan.

Is Adverse Brain Development due to Maltreatment or PTSD secondary to Maltreatment?

New Studies Started at Duke in 2003

Midsagittal Divisions of the Corpus Callosum for Quantitative MRI Measurements



- Region 1-orbital prefrontal & inferior premotor
- Region 2-prefrontal cortex
- Region 3-premotor
- Region 4-motor
- Region 5-post. parietal
- Region 6-sup. temporal
- Region 7-occipital, inferior temporal

Clinical Methods:

- Medically Healthy
- Maltreatment defined by Child Protective Services for study entry.
- Currently be living in a Stable Home Environment.
- One Non-Abusing Parent or Caregiver who can Cooperate With the Protocol.
- Archival Records
- No Significant Prenatal Alcohol or Drug Exposure; birth weight 5lbs or greater
- No Prenatal or Birth complications.
- K-SADS-PL for DSM-III-R & DSM-IV Diagnosis of PTSD and other Disorders

Clinical Interview Day

- | | Child | Parent |
|---|---|------------------------------|
| • 9-12 | Cognitive testing | Mental Health Interview (FH) |
| • 12-12:30 | Child and parent have lunch together | |
| • 12:30-2 | Neuropsychological testing | Paper & pencil questions |
| • 2-4 | Mental Health Interview | Cognitive testing |
| • 4-5 | Wrap up & discuss Part II (MRI brain scan) Activities | |
| • Another Day Have MRI Brain Scan for anatomy, DTI, fMRI, MRS at Duke Radiology | | |

Neuropsychological Component

- Assess Neuropsychological Domains:
 - Intellectual Functioning
 - Academic Achievement
 - Fine-Motor Functions
 - Attention
 - Language
 - Visuospatial Skills
 - Memory and Learning
 - Executive Functions

What are the Benefits for Parents and Kids?

- Free and comprehensive psychiatric and psychological evaluation
- Recommendations to help with school problems/psychotherapy
- Parents and children will receive \$50-\$160 compensation for their participation

What are the Benefits for Counselors/Clinicians?

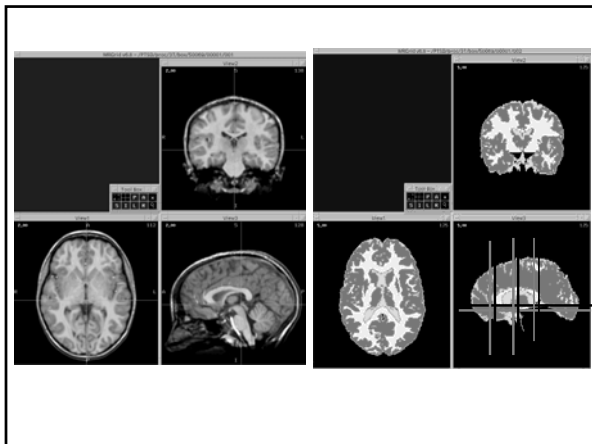
- Comprehensive diagnostic and neuropsychological evaluation that most clients would not receive as part of standard care (*with consent of parent/guardian and adolescent*)
- Recommendations to aid in treatment and gain access to services

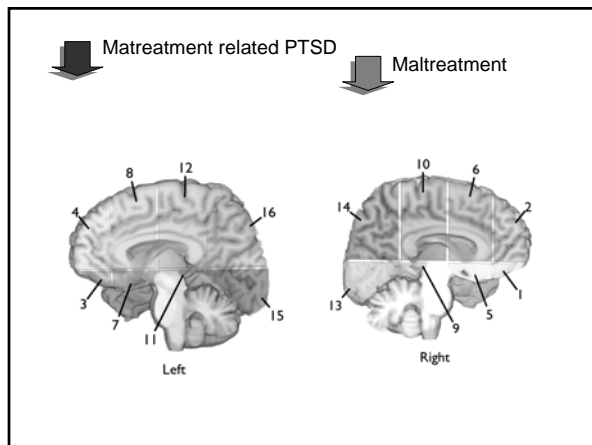
Mal Children w/o PTSD and Mal w/ PTSD Compared to non-Maltreated Controls

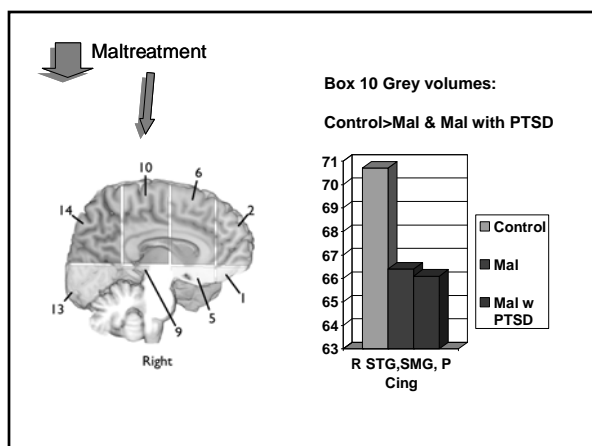
	Controls	Mal w/o PTSD	Mal w/ PTSD	p
N	105	46	50	
Gender (F/M)	61/44	26/20	30/20	NS
Age	11.4 (3.5)	8.4(2.7)	10.7(3.1)	C, PTSD>Mal
Race (C/AA/Other)	57/36/12	21/18/7	21/23/6	NS
SES	44.9(13.1)	39.5(15.5)	35.5(13.5)	C>PTSD
IQ	107.7(13.5)	94.1(13.4)	91.5(12.4)	C>PTSD, Mal
Sexual Abuse	---	20%	54%	PTSD>Mal
Other Abuse & Neglect	& Family Violence	78%	72%	NS
CBCL Tot T	41.0(9.2)	54.8(14.4)	61.8(10.5)	C>Mal>PTSD

Methods

- Automated, image-atlas-based methods developed by Dr. Koen Van Leemput at the Katholieke Universiteit Leuven (KUL) in pediatric neuroimaging for analysis of gray and white matter.
- Parcellation methods of cerebral regions are done semi-manually using anatomically-guided procedures.
- GLMs controlled for age, SES, gender, & interactions (pairwise comparisons used the LS mean differences Tukey HSD, a very conservative approach)





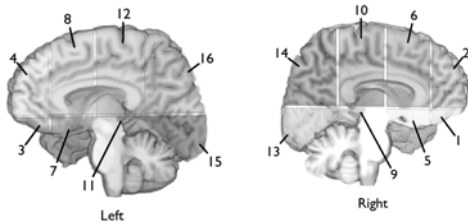


Brain Effects of Maltreatment (Box 10):
Decreased Grey Matter in Right Sided STG, AG, supramarginal gyrus, posterior cingulate.

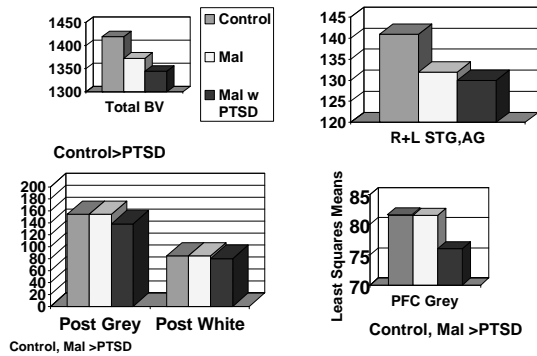
- Face Perception
- Affective Processes
- Phonological processing
- Sensory Integration
- Attention
- Parts of the Posterior Default Network (“autobiographical self”, “stimulus independent thought”)

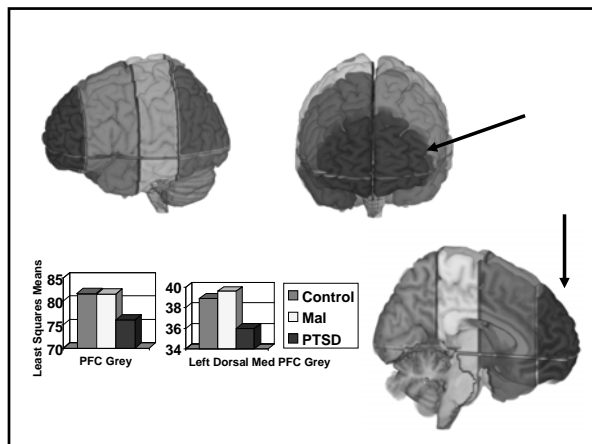


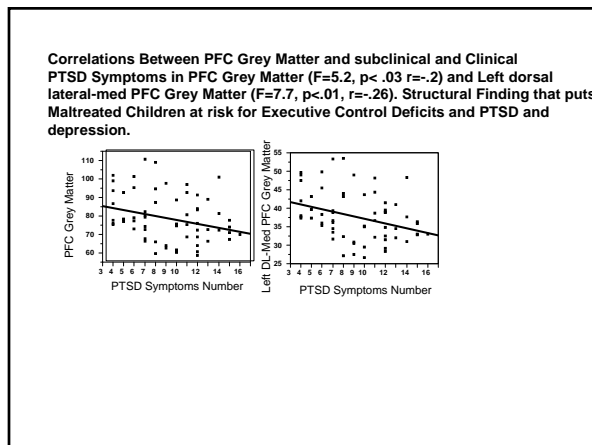
Maltreatment-Related PTSD



Brain Volumes in Maltreatment-Related PTSD



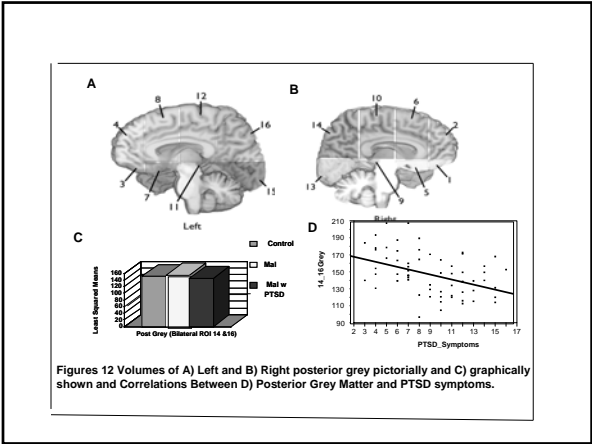


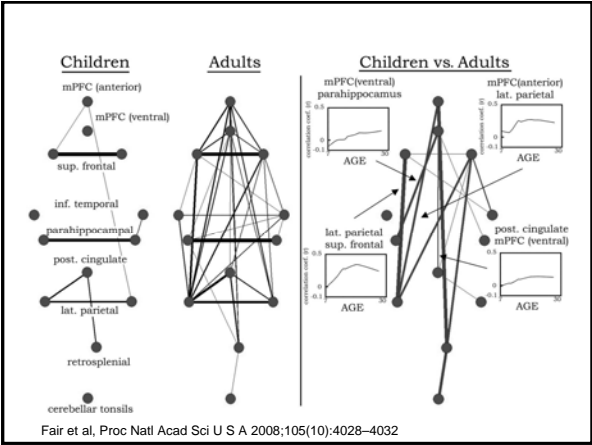


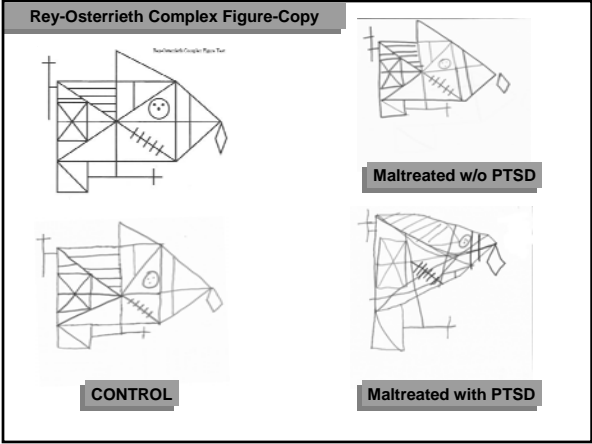
Brain Effects of PTSD from Maltreatment: Decreased Gray and White Left and Right Posterior Cortex
(e.g., AG, cuneus, precuneus, lateral occipital gyrus, superior parietal lobule, posterior cingulate)

- Visual Spatial Processing
- Reading
- Receptive language
- Attention
- Posterior Default Network (“autobiographical self”, “stimulus independent thought”, “social interactions”)

Risk for Major Depression, Anxiety, PTSD, PPD, Schizophrenia, Alzheimer’s, Addictions (e.g., PCC)





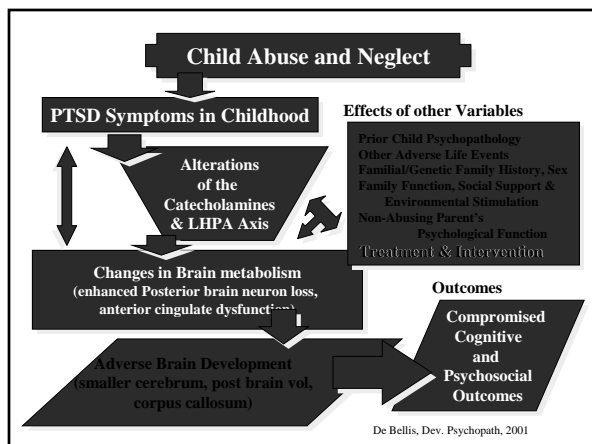


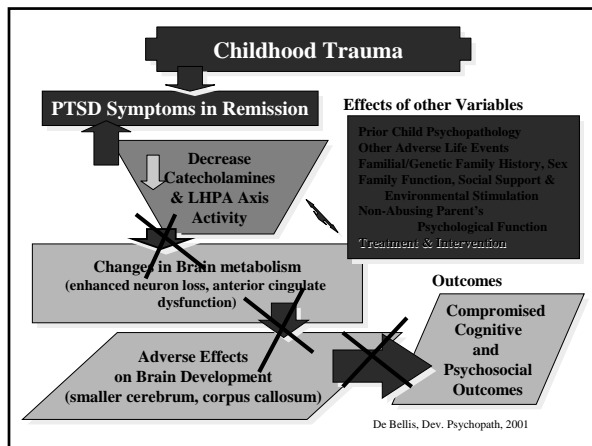
NO HIPPOCAMPAL FINDINGS IN PEDIATRIC PTSD

CHILDHOOD TRAUMA & ADVERSE BRAIN DEVELOPMENT

**MALTREATMENT
EFFECTS:**
Lower IQ
Smaller area 10
(Right Sup Temp
Gyrus, AG, Post
Cing)

**PTSD
EFFECTS**
Smaller PFC
Smaller Posterior
Areas
Smaller Cerebral
Volumes
Smaller PFC
Developmental
Trauma Disorder





Thank You

Questions?
