Current Directions in the Study of Risk And Adversity in Early Childhood

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Faculty Disclosure Information

- I have no relevant financial relationship with the manufacturers of any commercial products and/or providers of commercial services discussed in this CME activity.
- Neither I nor any member of my immediate family has a financial relationship or interest with any proprietary entity producing health care goods or services related to the content of this CME activity.
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Outline of talk

- Models of risk
- Understanding adverse environments
- Experience getting under the skin
- Importance of child caregiver relationships

Models of Risk

Lack of specificity in risks and outcomes
Cumulative risk
Diathesis-stress
Differential susceptibility

Lack of specificity between risk factors and outcomes

Multifinality of risks

- A single risk factor increases risks for multiple outcomes
- Maternal depression:
  - Insecure attachment
  - Emotion regulation difficulties
  - Language and cognitive problems
  - Social interactive problems
  - Behavior problems

Equifinality of risks

- A variety of risk factors may increase risk for a single outcome.
- Risk for aggression:
  - Maternal depression
  - Insecure attachment
  - Difficult temperament
  - Parental conflict

Cumulative risk models

Adverse Childhood Experiences

Household dysfunction:

Substance abuse	27%
Parental separation/divorce	23%
Mental illness	17%
Battered mother	13%
Criminal behavior	6%

Abuse:

Psychological	11%
Physical	28%
Sexual	21%

Neglect:

Emotional	15%
Physical	10%

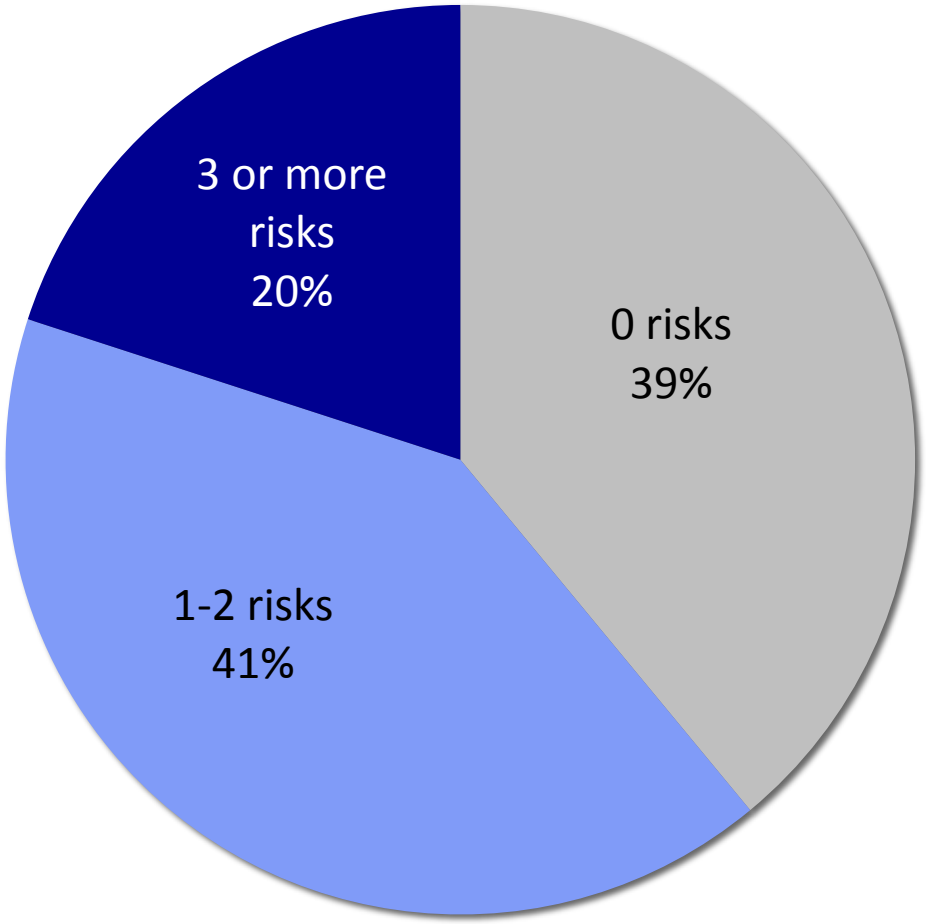
Adverse Childhood Experiences Study (ACE)

ACE Score	Prevalence
0	33%
1	26%
2	16%
3	10%
4 or more	16%

ACE Results

- Persons with ACE of 4 compared 0:
  - 7.4 fold increase for alcoholism
  - 10.3 fold increase for drug abuse
  - 4.6 fold increase for depression
  - 12 fold increase in suicide attempts
  - 2.2 fold increase in ischemic heart disease
  - 1.9 fold increase cancer

Percentage of young children in the U.S. challenged by major risk factors



Percentage of Children

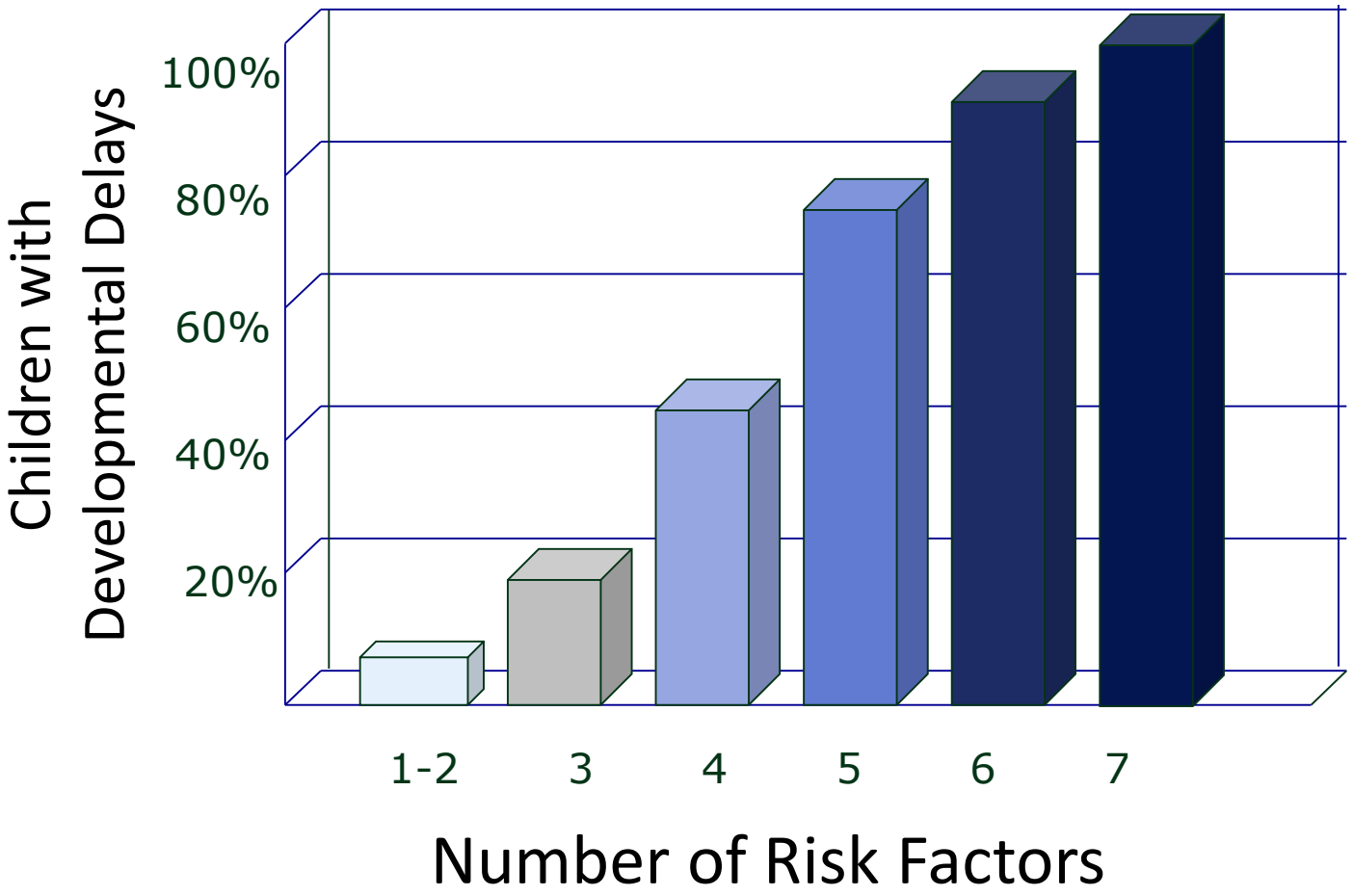
National Center for Children in Poverty
www.nccp.org

Preschool Maltreated Sample

Caregiver Mental Health Problem	30%
Minority Status	58%
Low Caregiver Education	29%
Single Caregiver	48%
Biomedical Risk Condition	22%
Poverty	46%
Teen-aged Caregiver	19%
Domestic Violence	40%
4 or More Children in Home	14%
Caregiver Substance Abuse	39%

Barth et al. (2008)

Significant Adversity Threatens Development in the First Three Years



Barth et al. (2008)

Summary of Cumulative Stress

- Individual risk factors contribute non-specifically to adverse outcomes.
- Rarely occur in isolation.
- Sum of number of risk factors powerfully predictive.

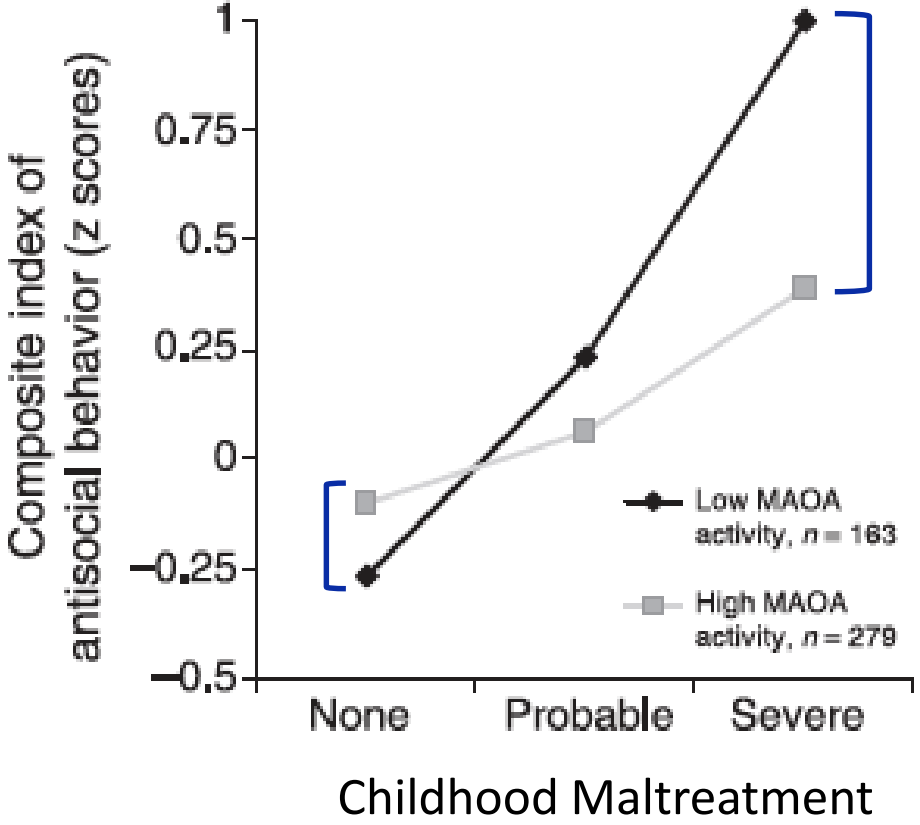
Diathesis Stress

vs.

Differential Susceptibility

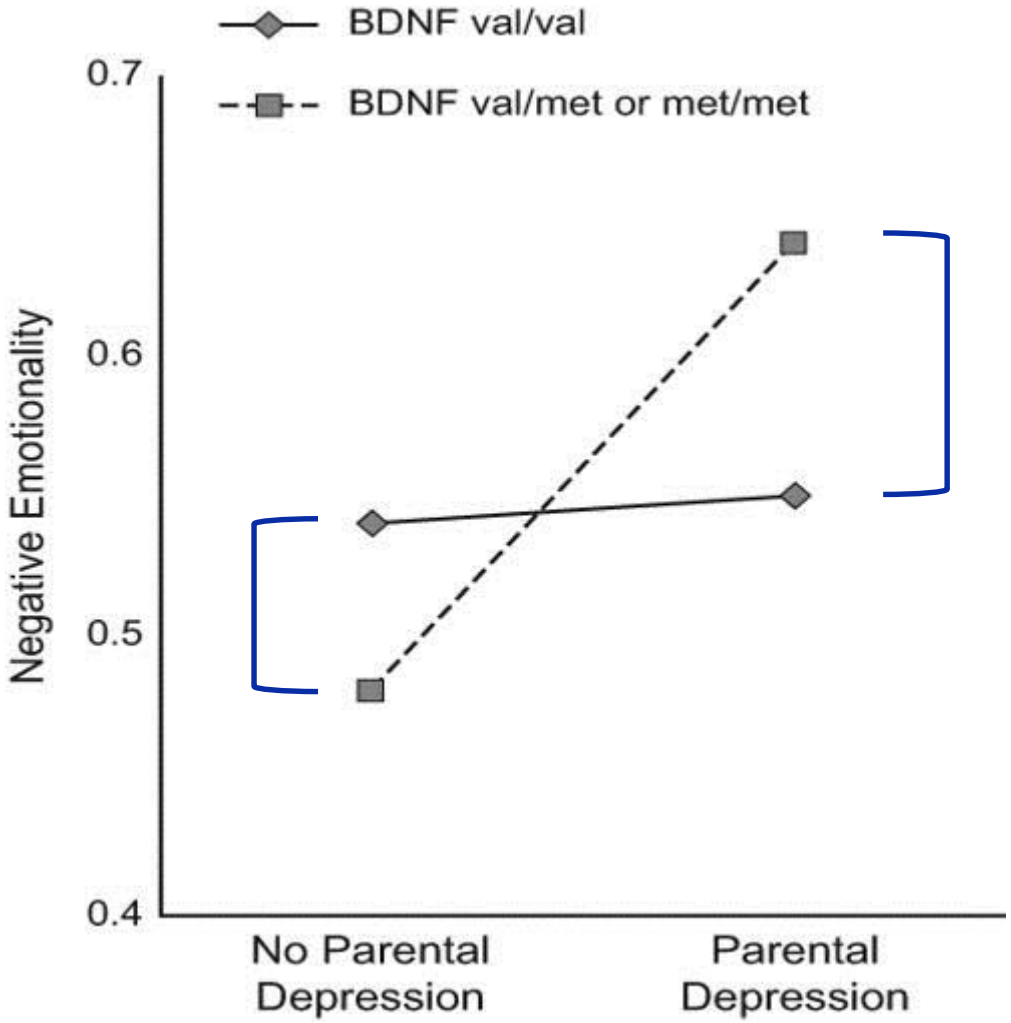
Diathesis stress

Inherited vulnerability plus stressful experience leads to poor outcome = G X E



Caspi et al., 2002

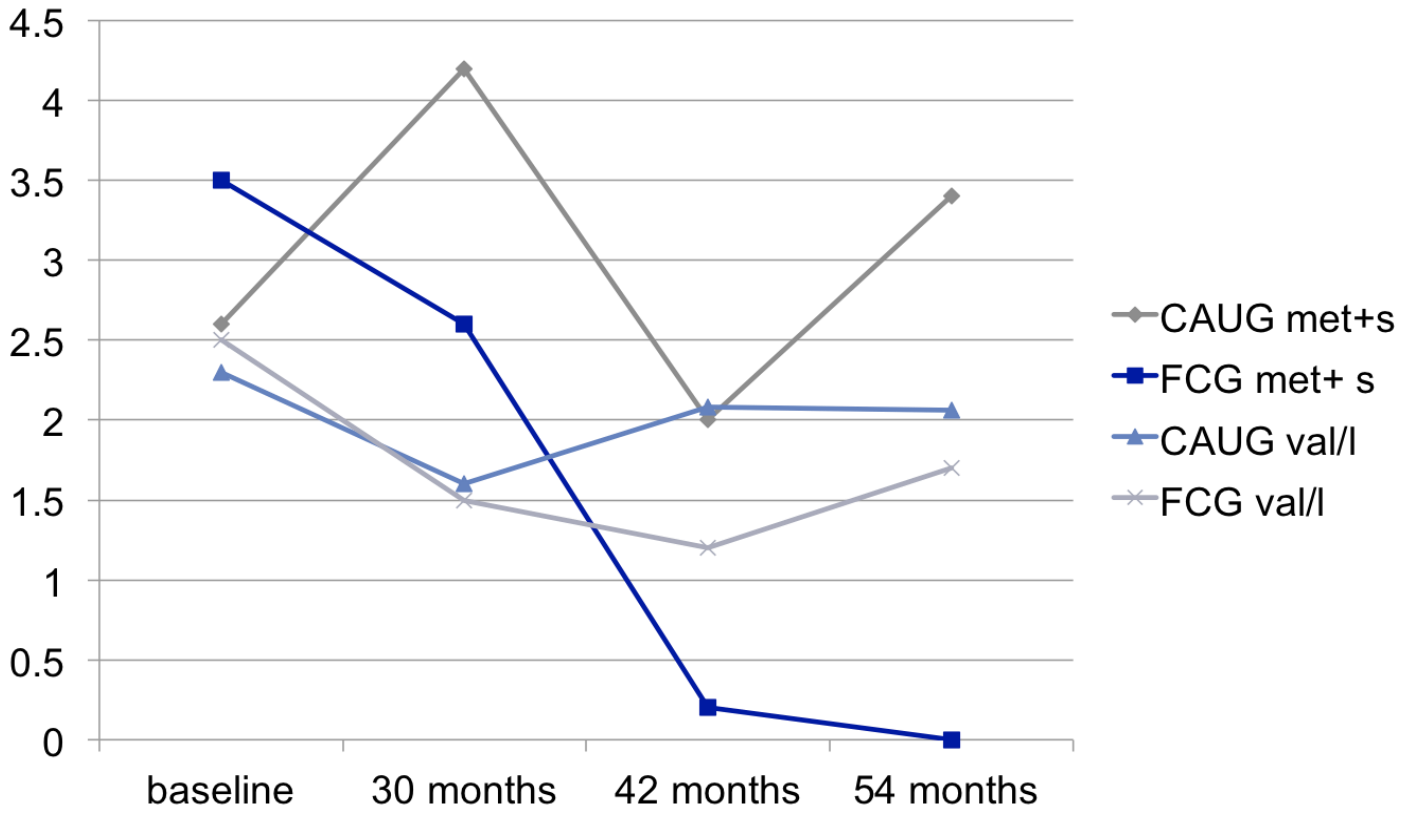
Differential susceptibility: BDNF, parental depression and child negative emotionality



Hayden, et al. (2011)

Differential susceptibility in 4 ½ year old children

s/s +met/* genotypes and indiscriminate behavior



Drury et al., 2012

Effects of adverse environments

Toxic stress

Inadequate input

Excessive unwanted input

Toxic stress

Levels of stressful experiences

Positive Stress

- A personal challenge that has a satisfying outcome
- **Result**: Sense of mastery and control
  - HEALTHY BRAIN ARCHITECTURE
  - good self esteem, judgment and impulse control

Tolerable Stress

- Adverse life events buffered by supportive relationships
- **Result**: Coping and recovery
  - HEALTHY BRAIN ARCHITECTURE
  - good self esteem, judgment and impulse control

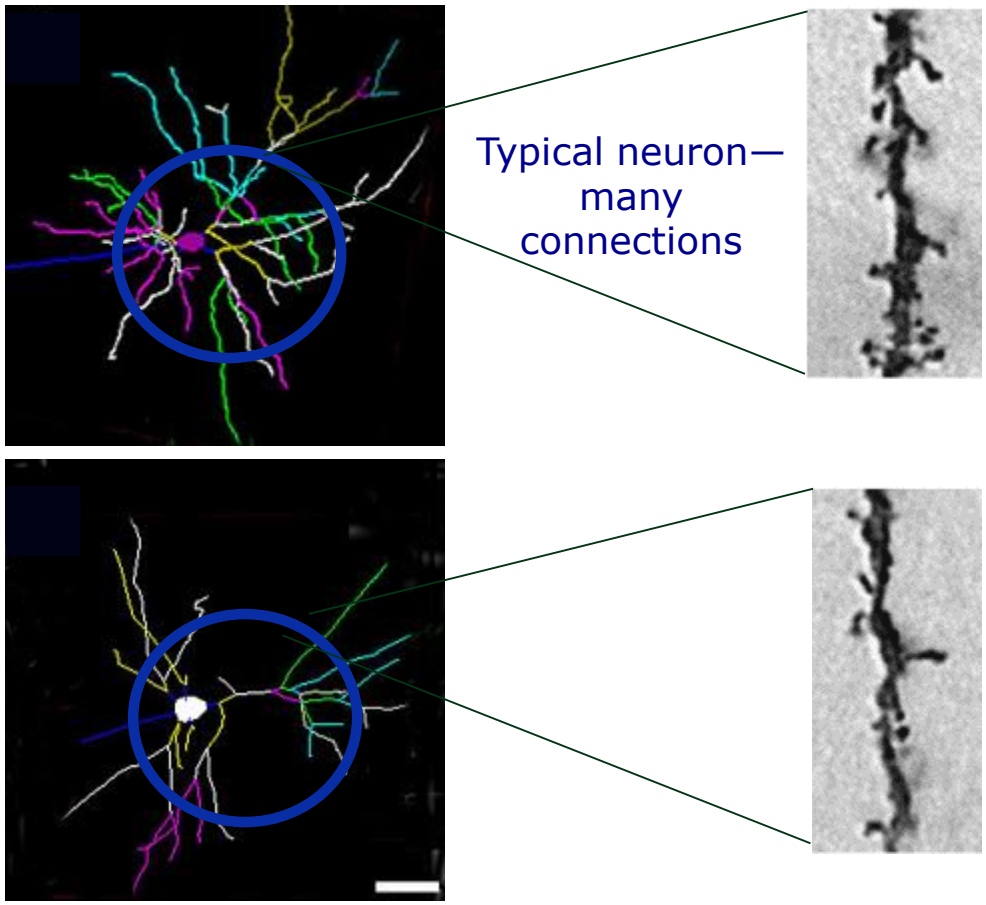
Toxic Stress

- *Unbuffered adverse events of greater duration and magnitude*
- ***Result**: Poor coping and compromised recovery*
- ***Result**: Increased life-long risk for physical and mental disorders*
  - *COMPROMISED BRAIN DEVELOPMENT*
  - *Dysregulated physiological systems*

Toxic Stress Changes Brain Architecture

Normal

Toxic stress



Prefrontal Cortex and Hippocampus

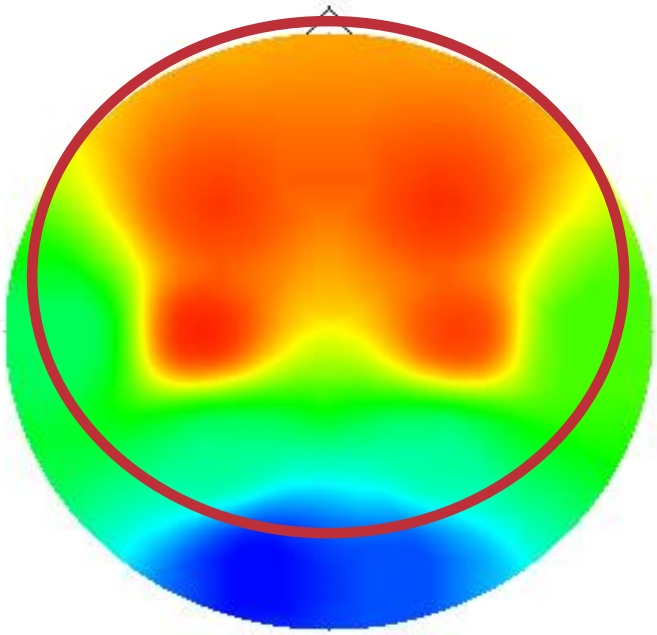
Examples of Toxic Stress for Children

- Chaos in home
  - Poor self regulatory behavior
  - Obesity, elevated blood pressure and cardiovascular reactivity
- Witnessing verbal and physical violence
  - Increased risk for lasting physical and mental health problems
- Abuse
  - Increased risks for lasting physical and mental health problems
  - Shorter lifespan
- Neglect
  - cortisol dysregulation
- Problematic parenting
  - Internalizing and externalizing behavior problems

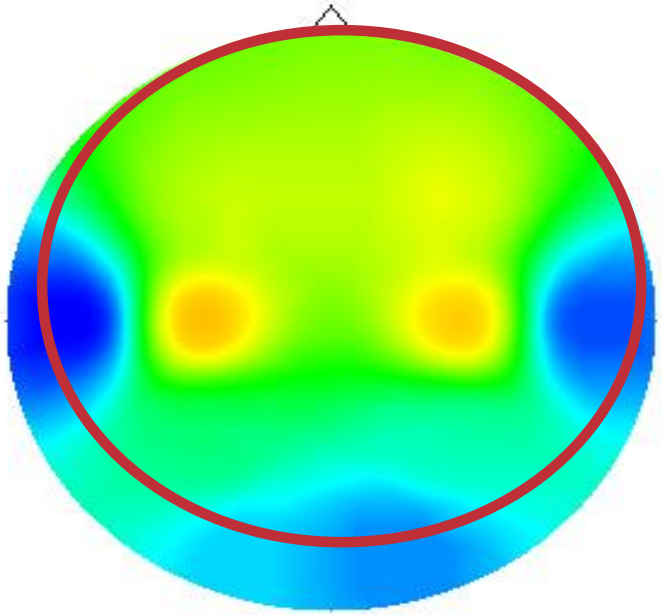
Inadequate input
(neglect/deprivation)
vs.

Excessive unwanted input
(abuse/exposure to violence)

Extreme Neglect Reduces Brain Power



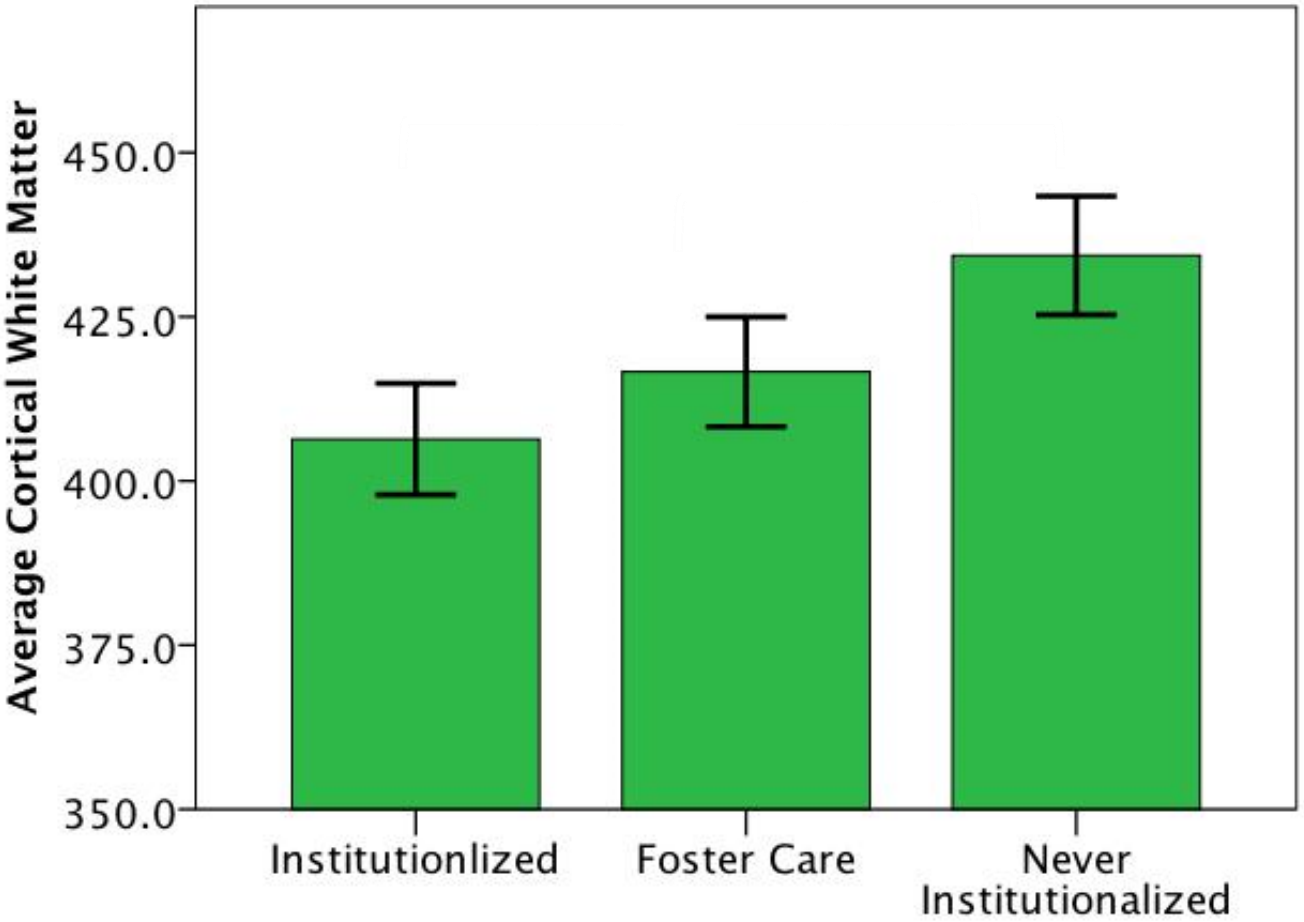
Positive
Relationships



Extreme
Neglect

Marshall, Fox & BEIP (2004)

Total Cortical White Matter



CAUG B= -24.1, t= -2.17, p= .03

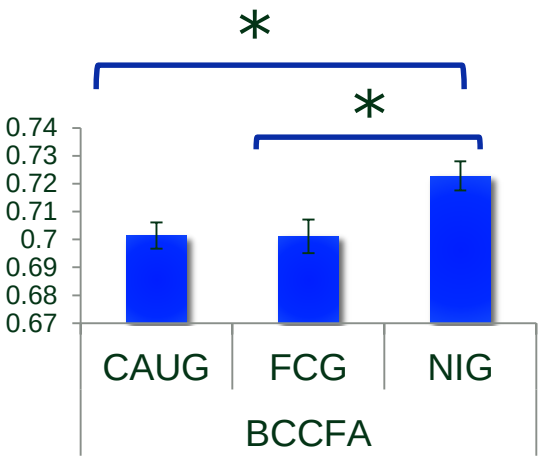
FCG B= -18.1, t= -1.5, p= .12

Regression controlling for age and gender

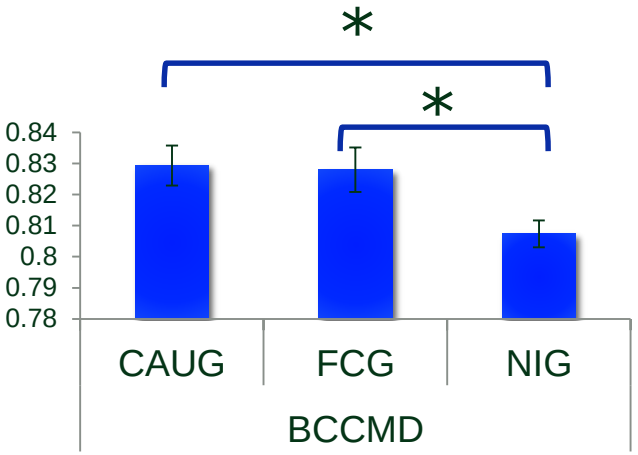
Sheridan et al 2012

Body of Corpus Callosum

EIG differed from NIG



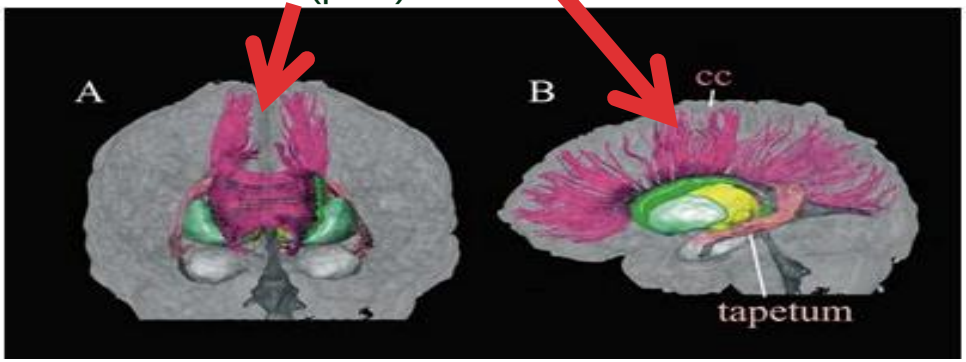
FA: p = .01



MD: p = .005
(also RD)

EIG differed from NIG

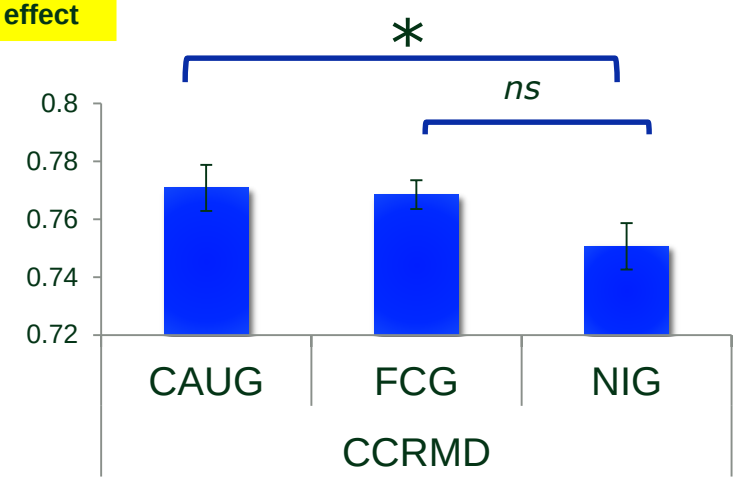
Body CC
(pink)



Tracts involved in limbic circuitry

Cingulum (cingulate gyrus; right)

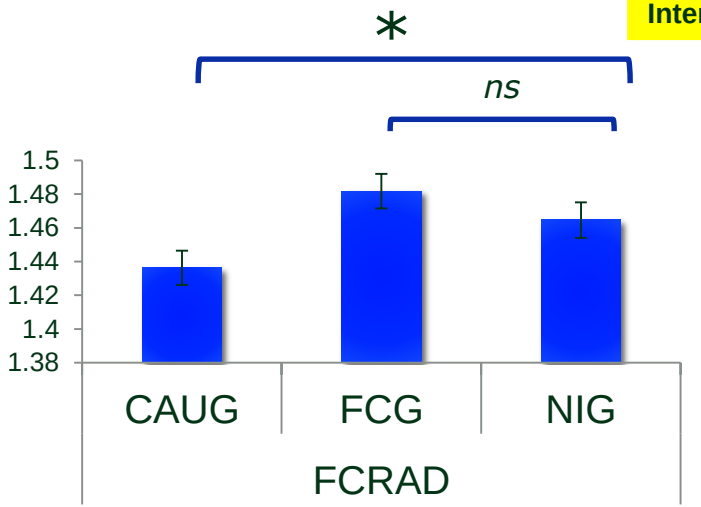
Intervention effect



MD: p = .049 (also RD)

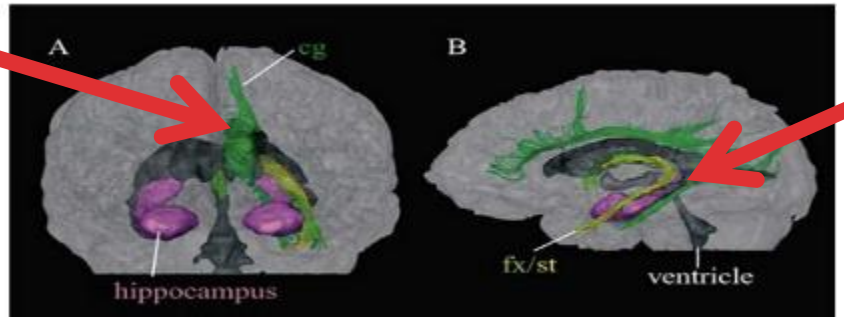
Fornix Crus (right)

Intervention effect



AD: p = .046

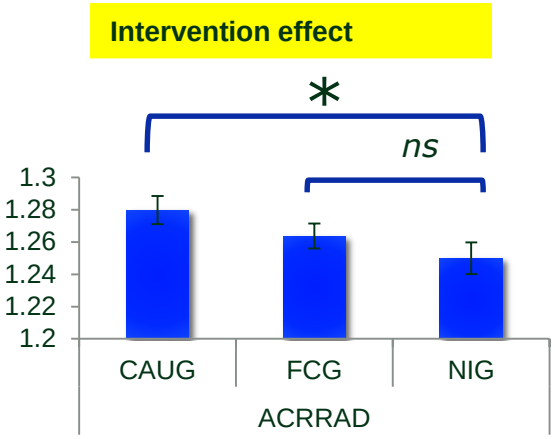
Cingulum (green)



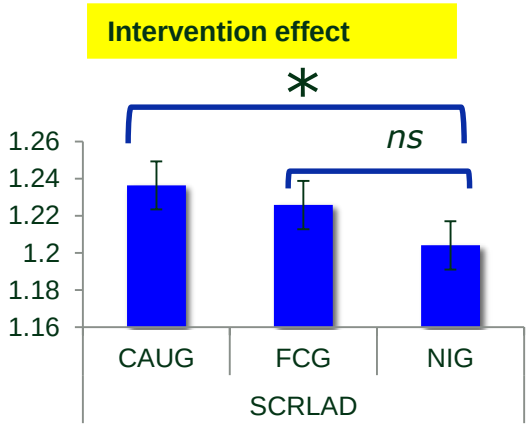
Fornix (green)

Tracts involved in fronto striatal circuitry

Anterior (right) and Superior (left) Corona Radiata

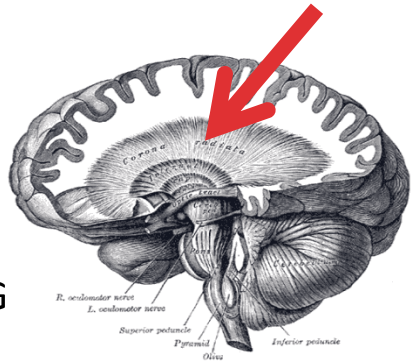


AD right: p = .018

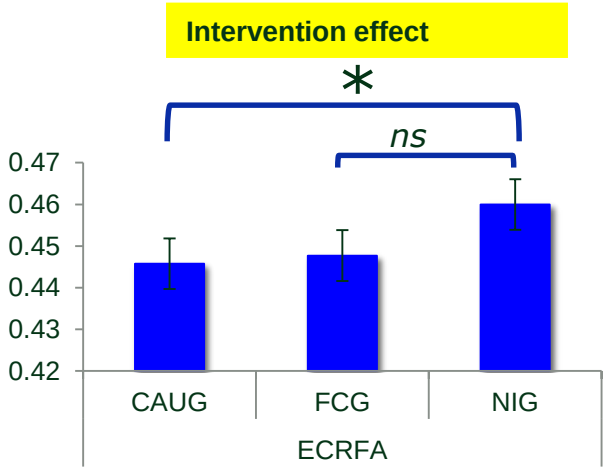


AD left: p = .019 (also MD, but EIG > NIG

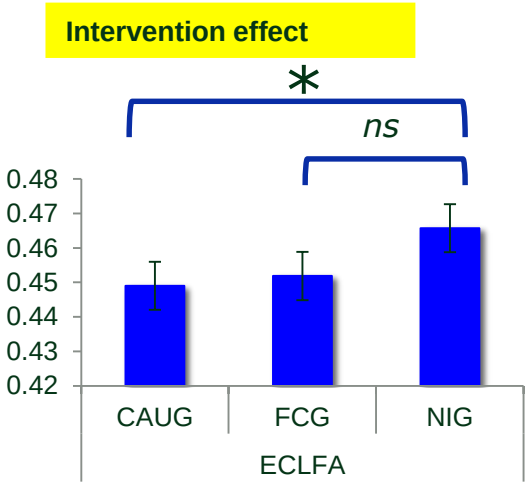
Corona Radiata



External Capsule (Right and Left)



FA right: p = .028



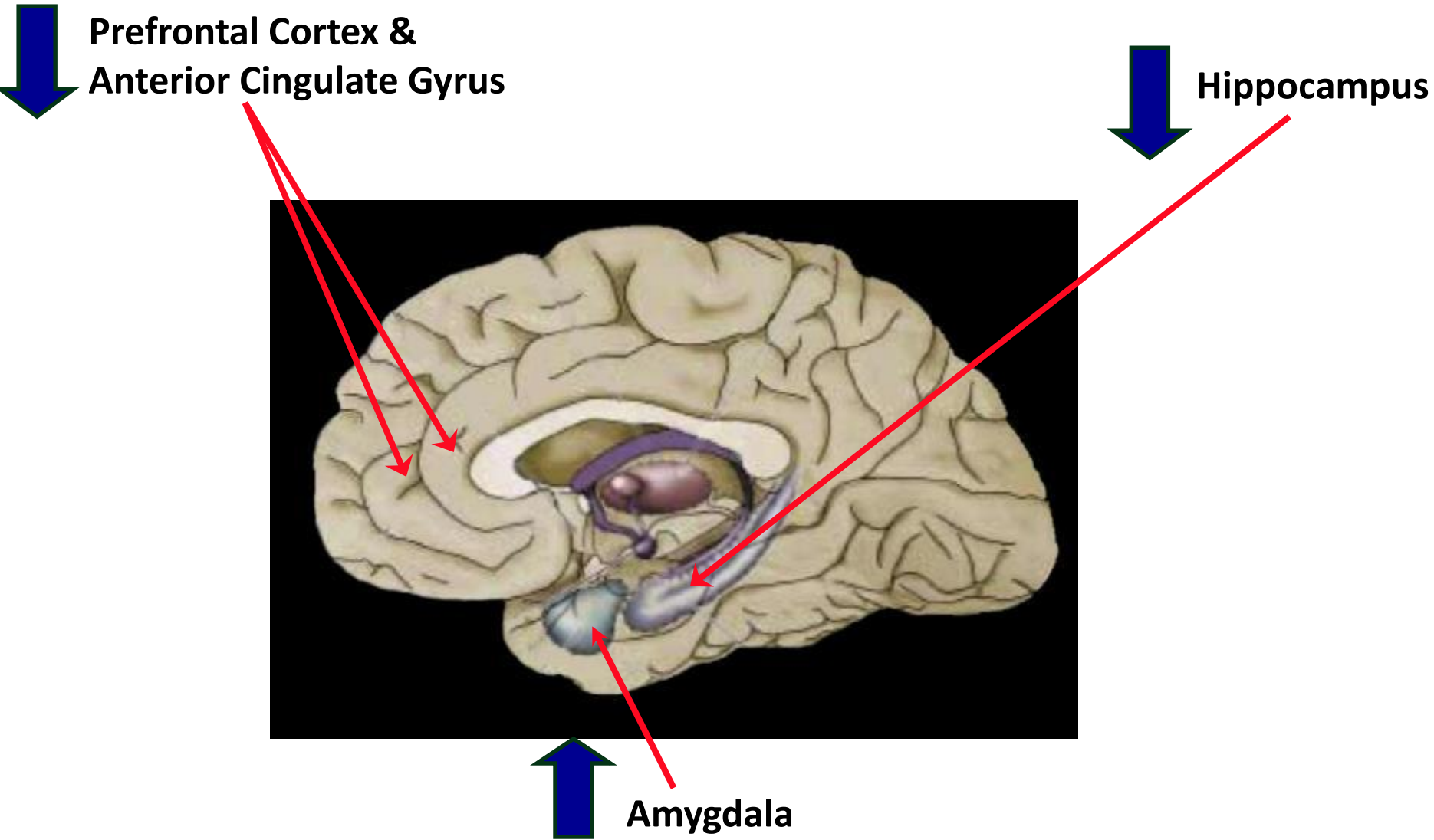
FA left: p = .025 (also RD and MD, but EIG > NIG)

External capsule

PTSD

- Exposure to trauma
- Re-experiencing
- Avoidance
- Alterations in mood or cognition
- Hyperarousal
- Impairment
- One month duration

Functional neuroanatomy of chronic anxiety, fear and PTSD



Summary of environmental adversity

- Toxic stress
  - child's coping mechanisms overwhelmed
  - compromises health and mental health
- Inadequate input, neglect and deprivation
  - abnormal brain structure
  - abnormal brain functioning
- Excessive unwanted input, emotional abuse & exposure to violence
  - leads to harm if chronically overactivates fear circuitry

Experience Getting Under the Skin

Sensitive periods

Epigenetics

Sensitive periods in brain and behavioral development

Research with Rhesus Macques

Judy Cameron and colleagues

Heritability estimates

(with 126 Rhesus monkey infants)

- Play room test (exploration vs. inhibition)
  - Latency to leave mom, h^2=1.0
  - Time away from mom, h^2=1.0
- Remote-Controlled Car test (approach to novel object)
  - Vocalizations, h^2=1.0
- Human Intruder test (approach to stranger)
  - Movement (profile), h^2=0.54
  - Movement (stare), h^2=0.75
  - Teethgrinding (stare), h^2=0.89
- Novel Fruit test (approach to novel rewarding stimulus)
  - Latency to inspect, h^2=1.0
  - Latency to touch, h^2=0.74

Summary of results

- 3 month separated
  - minimal effects
- 1 month separated
  - depressed initially
  - followed by clingy behavior, persists into adolescence
- 1 week separated
  - aloof
  - asocial

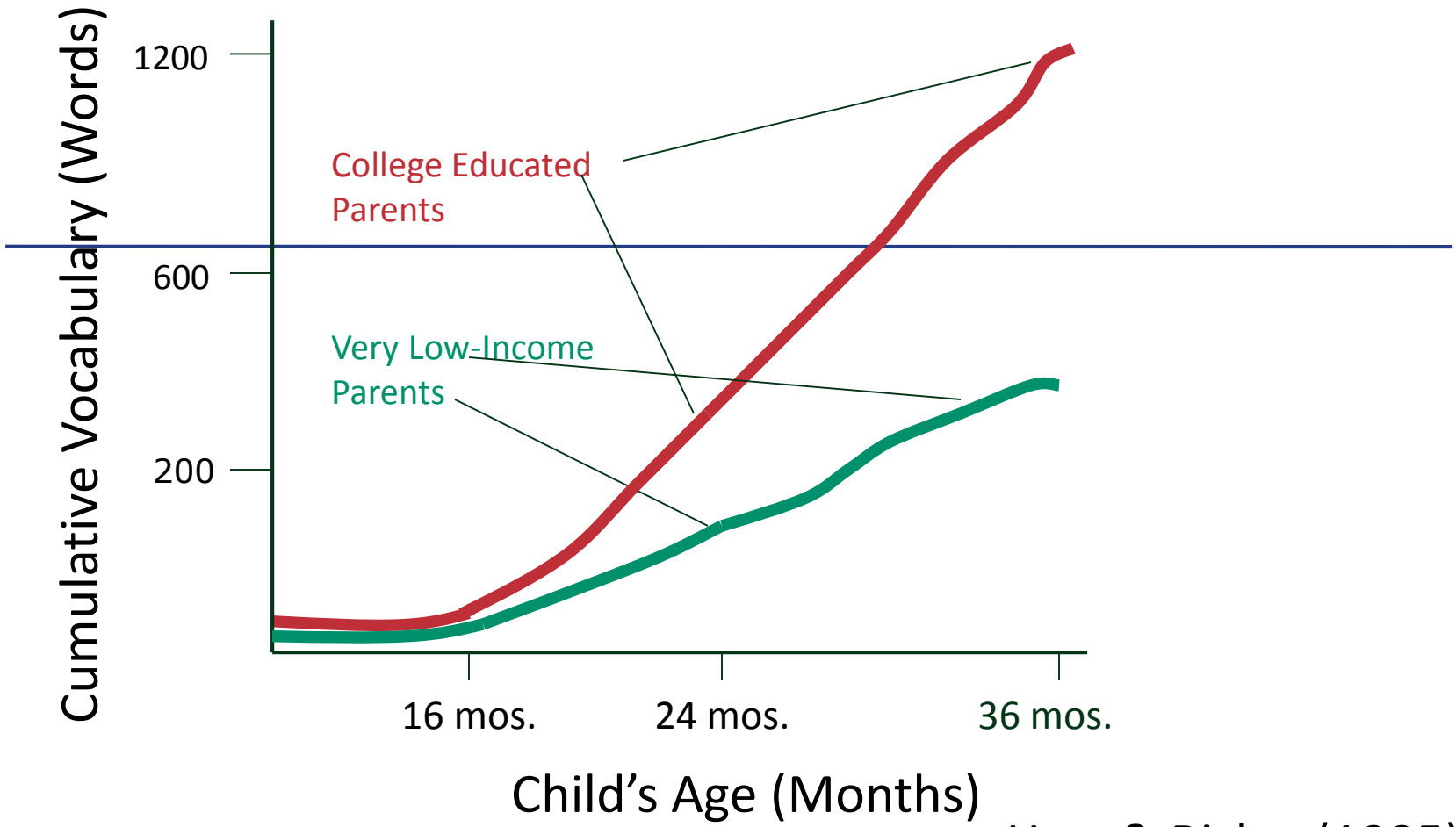
Super Mom Results

- Pairing with an experienced mother is more effective when initiated earlier.
- Critical period of 7 days after which remediation no longer possible.

Feral children and language development

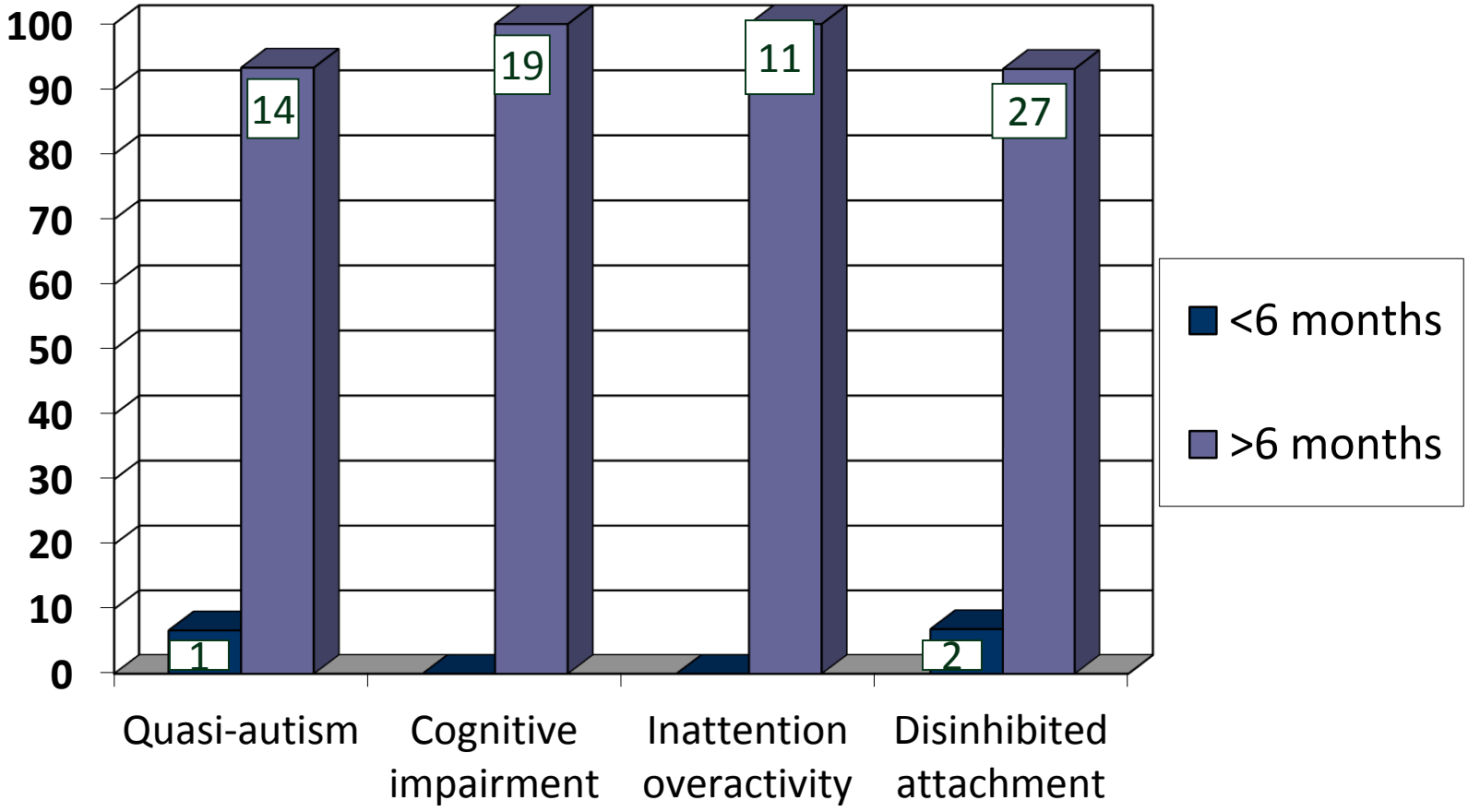
- Shamdeo, the wolf boy
- Found in forest in 1972 playing with wolf cubs
- Walked on all fours, craved blood, ate dirt, hunted chickens, loved the dark, and preferred company of dogs and jackals to people.

30,000,000 word gap



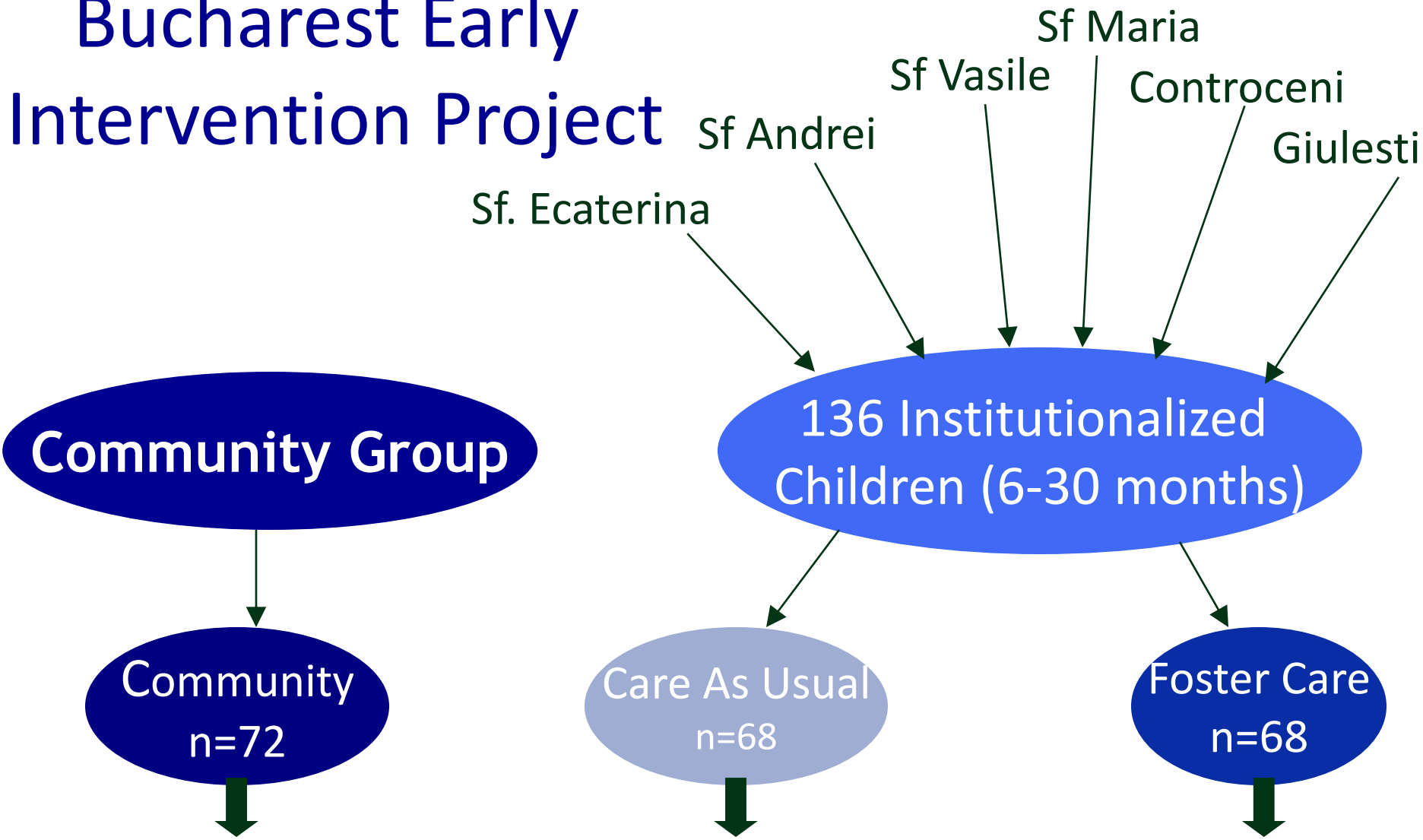
Hart & Risley (1995)

Persistence to age 15 years of deprivation specific patterns of impairment



Rutter et al., 2010

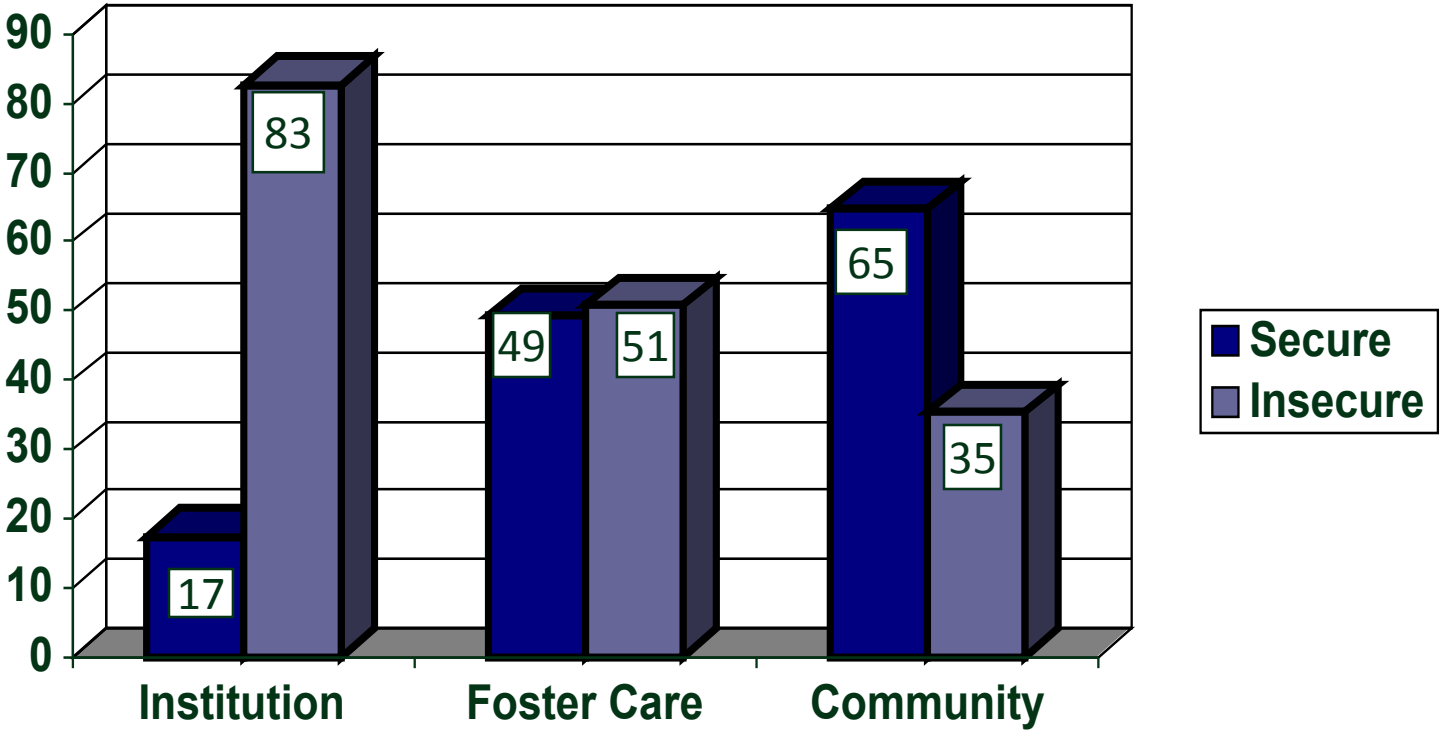
Bucharest Early Intervention Project



Assessments at 30, 42, 54 months

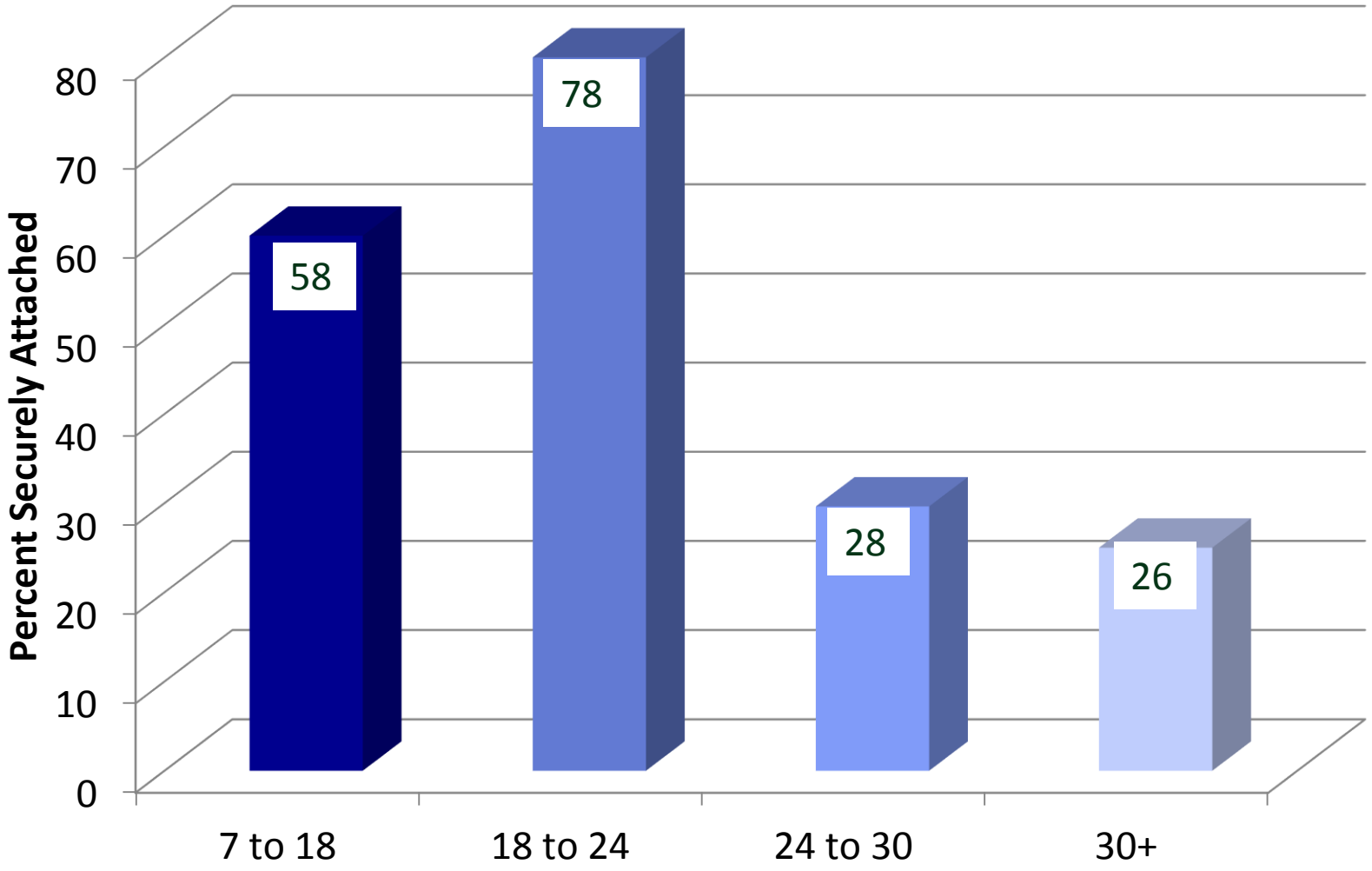
Follow-ups at 8 and 12 years

Secure vs. insecure: 42 months



Smyke et al., 2010

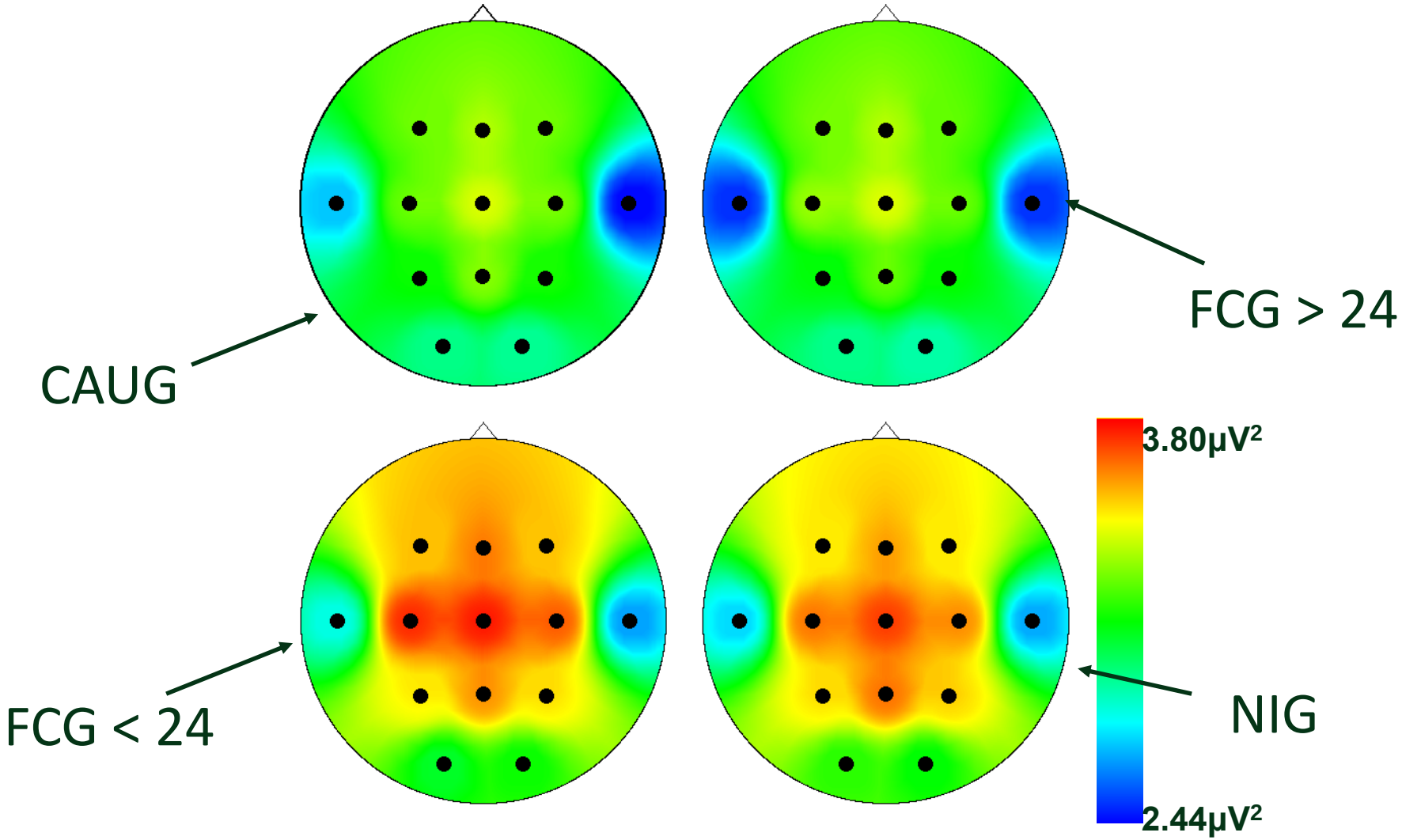
Attachment security and age at entry



Smyke et al., 2010

C A

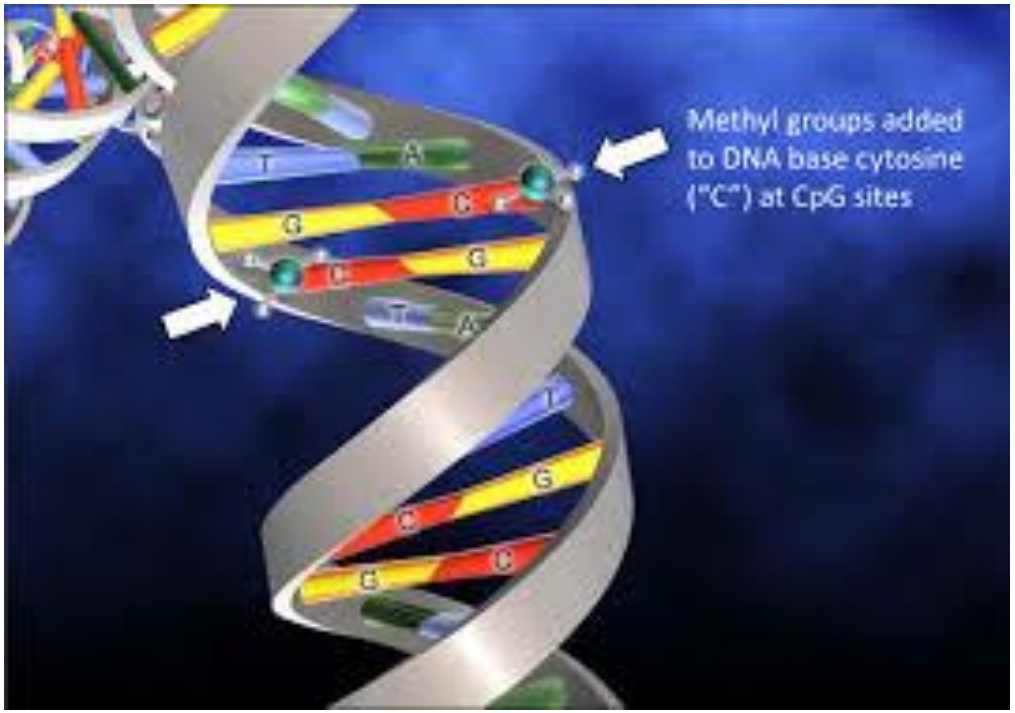
Distribution of alpha power across the scalp by timing and group

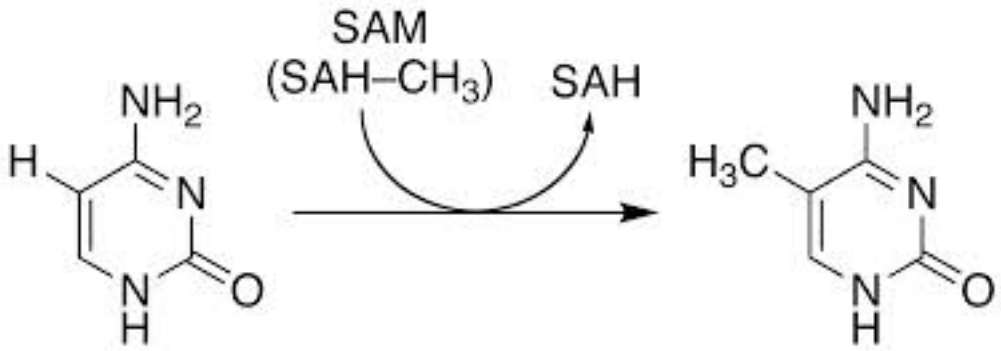


Epigenetics: non-inherited changes in DNA

DNA methylation
Telomere modification

Methylation and gene expression





Michael Meany and Licking and Grooming Rats

Low licking/grooming (LLG) mothers

High licking/grooming (HLG) mothers

<u>Offspring</u>
High corticosterone
High anxiety
Low licking as mothers

<u>Offspring</u>
Low corticosterone
Low anxiety
High lickers as mother

Francis et al., 1999

Cross fostering rats

LLG mothers foster

Non-anxious offspring

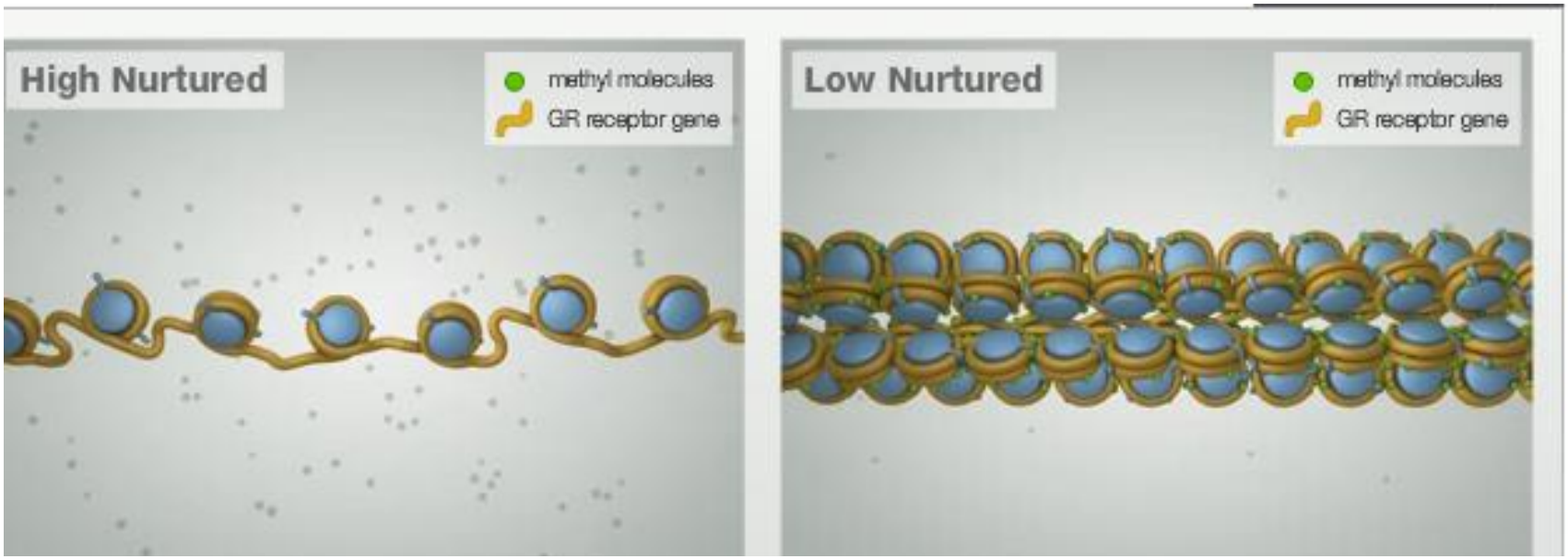
Offspring
High corticosterone
High anxiety
Low licking as mothers

HLG mothers foster

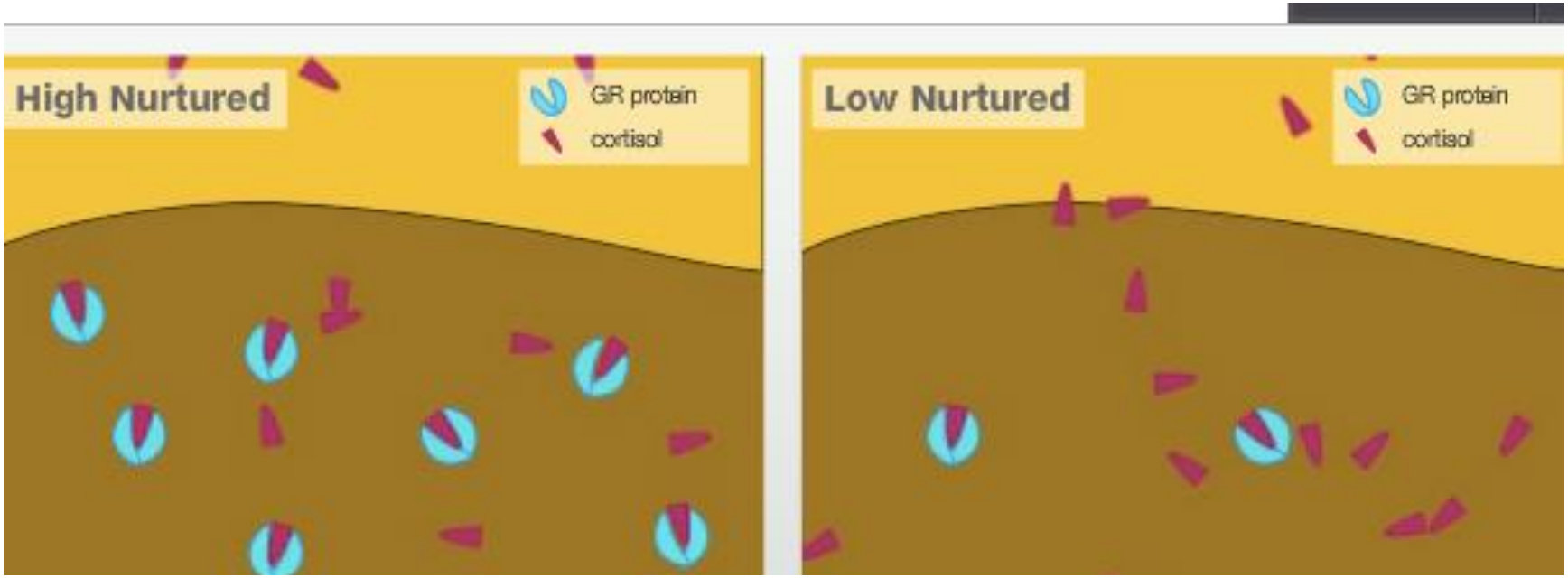
Anxious offspring

Offspring
Low corticosterone
Low anxiety
High licking as mothers

High nurturing (HLG) releases methyl groups increasing GR (NR3C1) expression

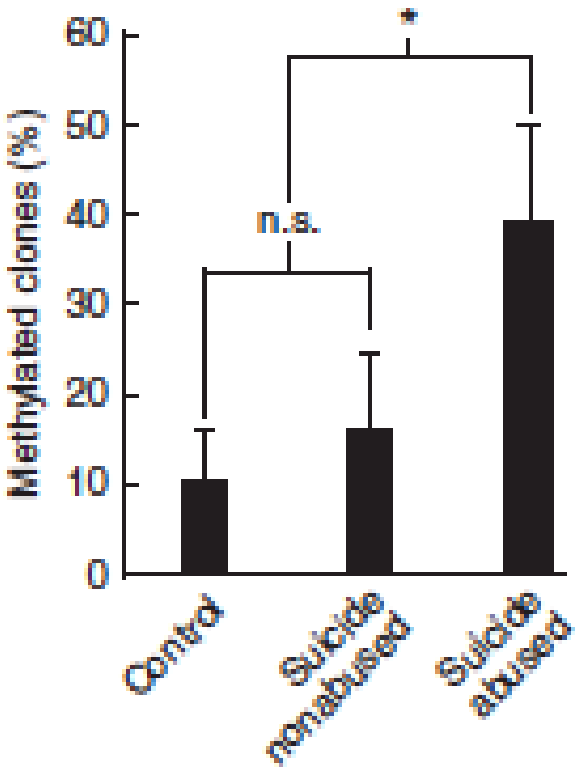


GR protein binds cortisol— significantly more in HLG rats



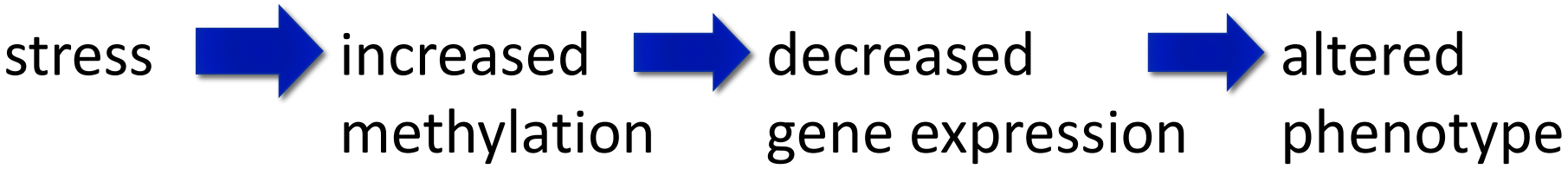
Inside the hippocampus

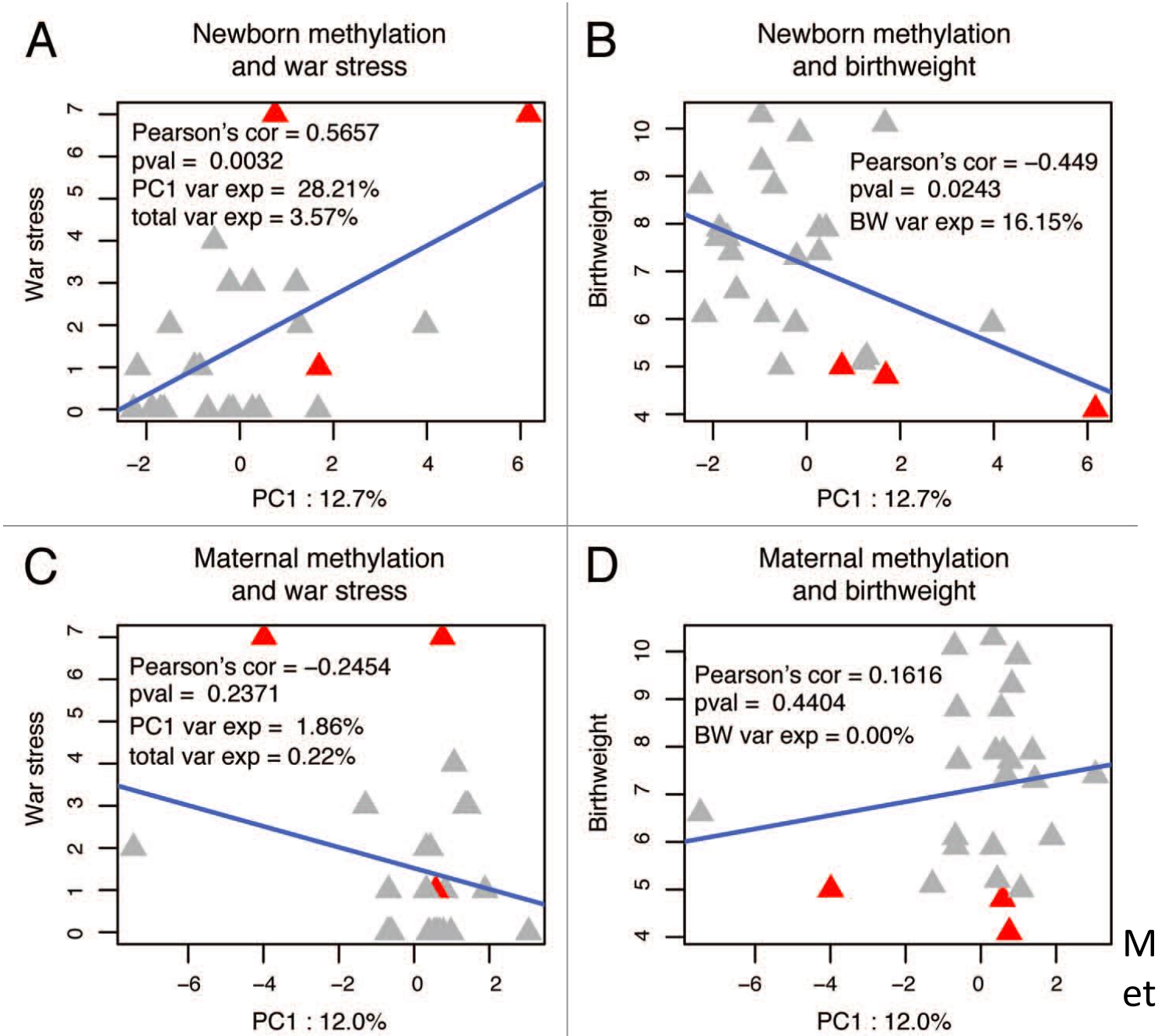
Methylation of the NR3C1 promoter in the hippocampus



McGowan et al., 2009

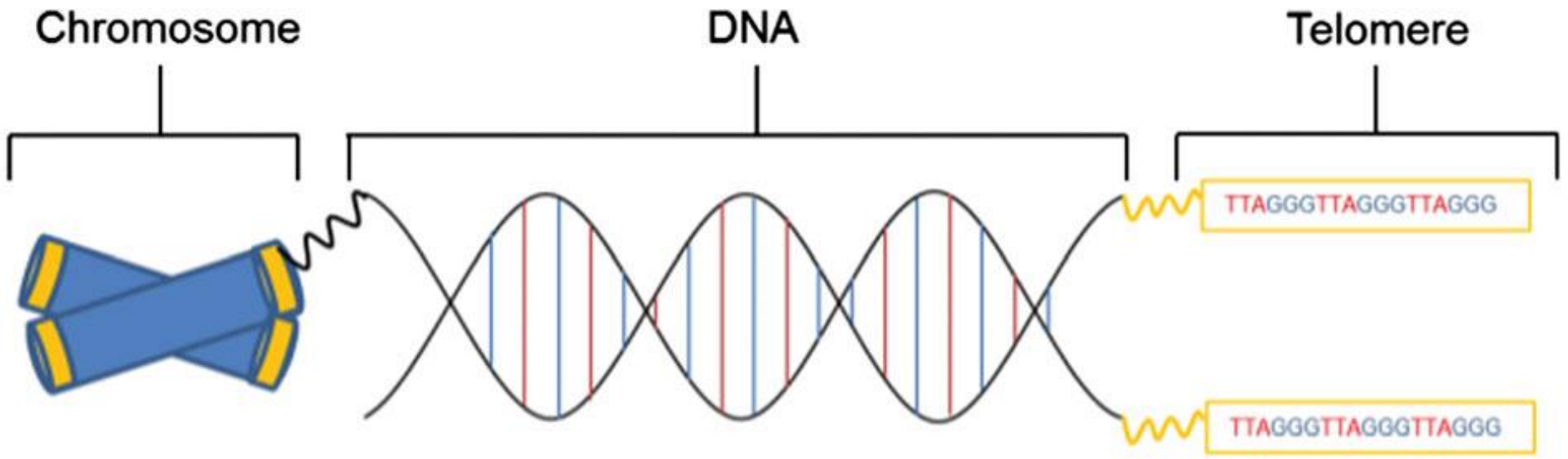
Model


stress
increased methylation
decreased gene expression
altered phenotype



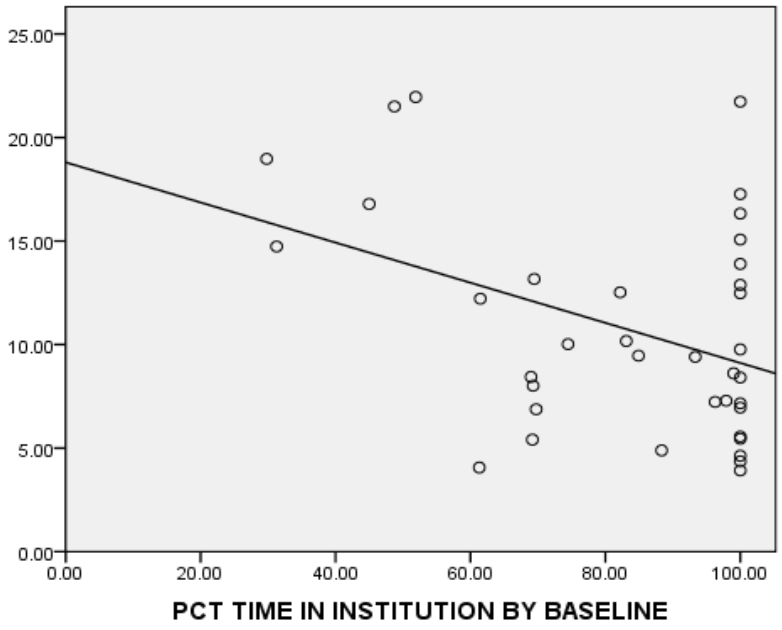
Mulligan et al., 2012

Telomeres

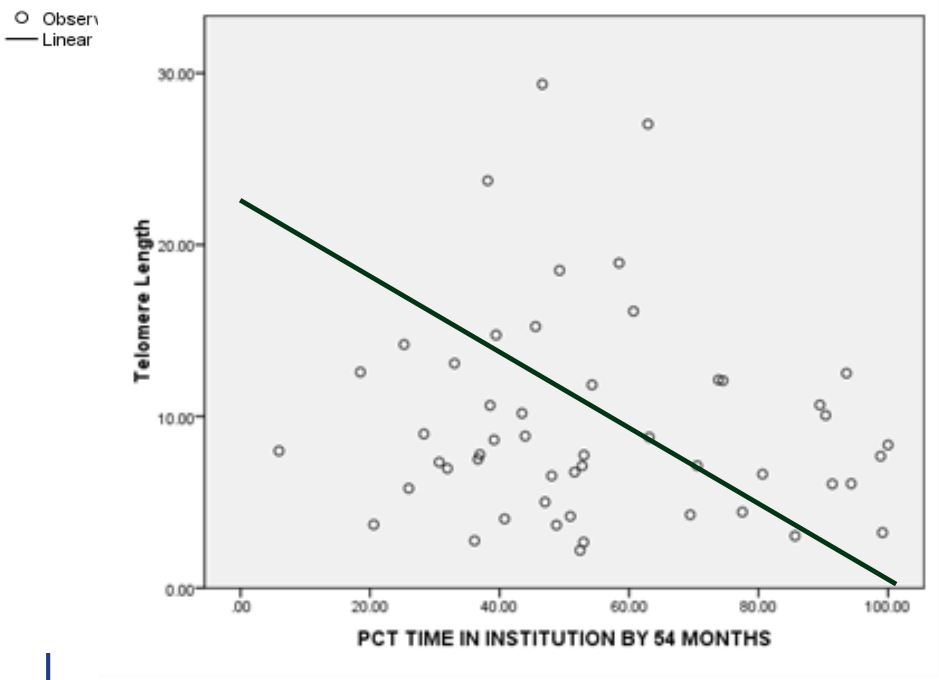

Chromosome
DNA
Telomere
TTAGGGTTAGGGTTAGGG
TTAGGGTTAGGGTTAGGG

Telomere length and percent of life in Romanian institutions

Girls at baseline (22months)

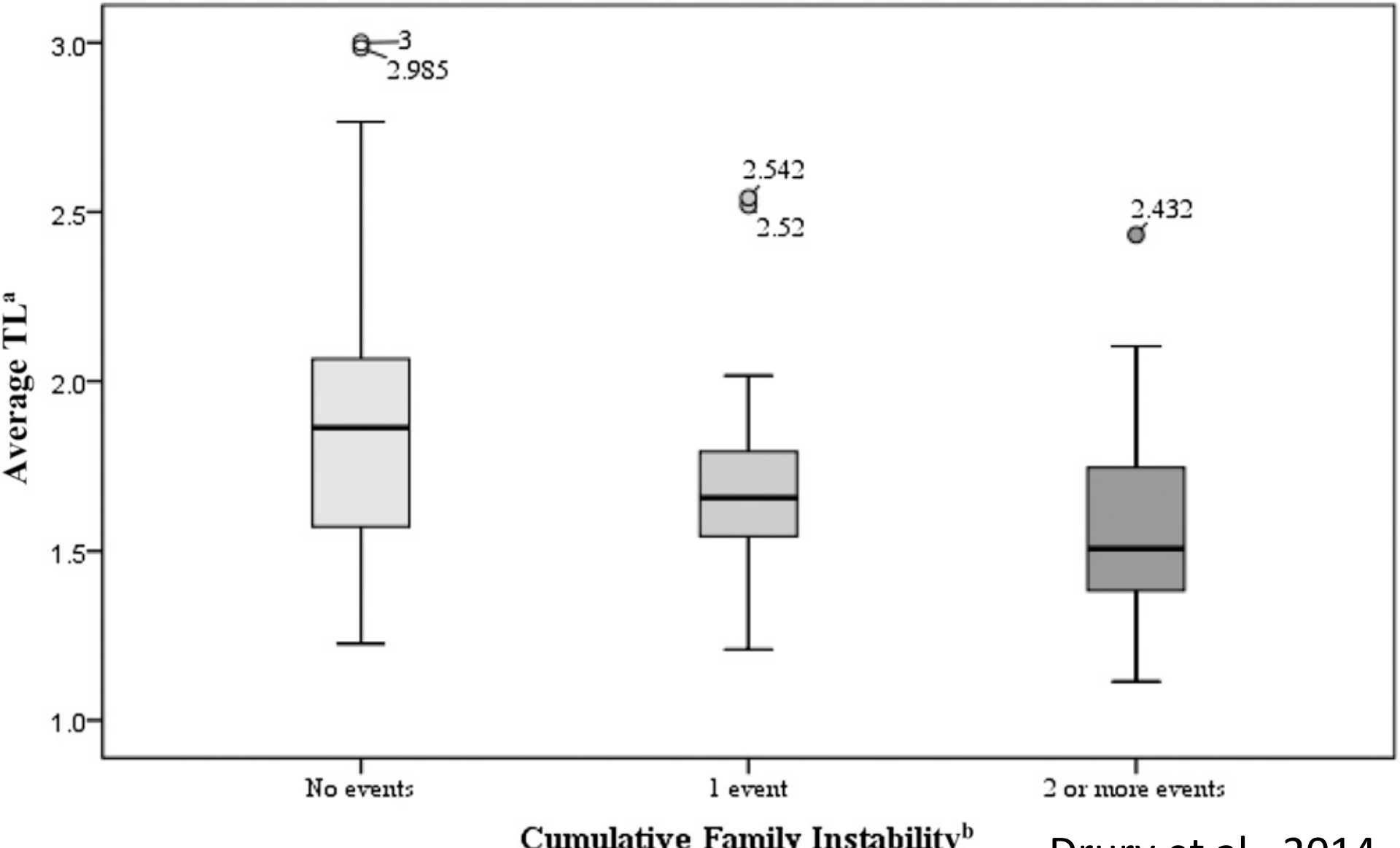


Boys through 54 months



Drury et al., 2012

Child telomere length and family instability



Drury et al., 2014

Summary of epigenetic mechanisms

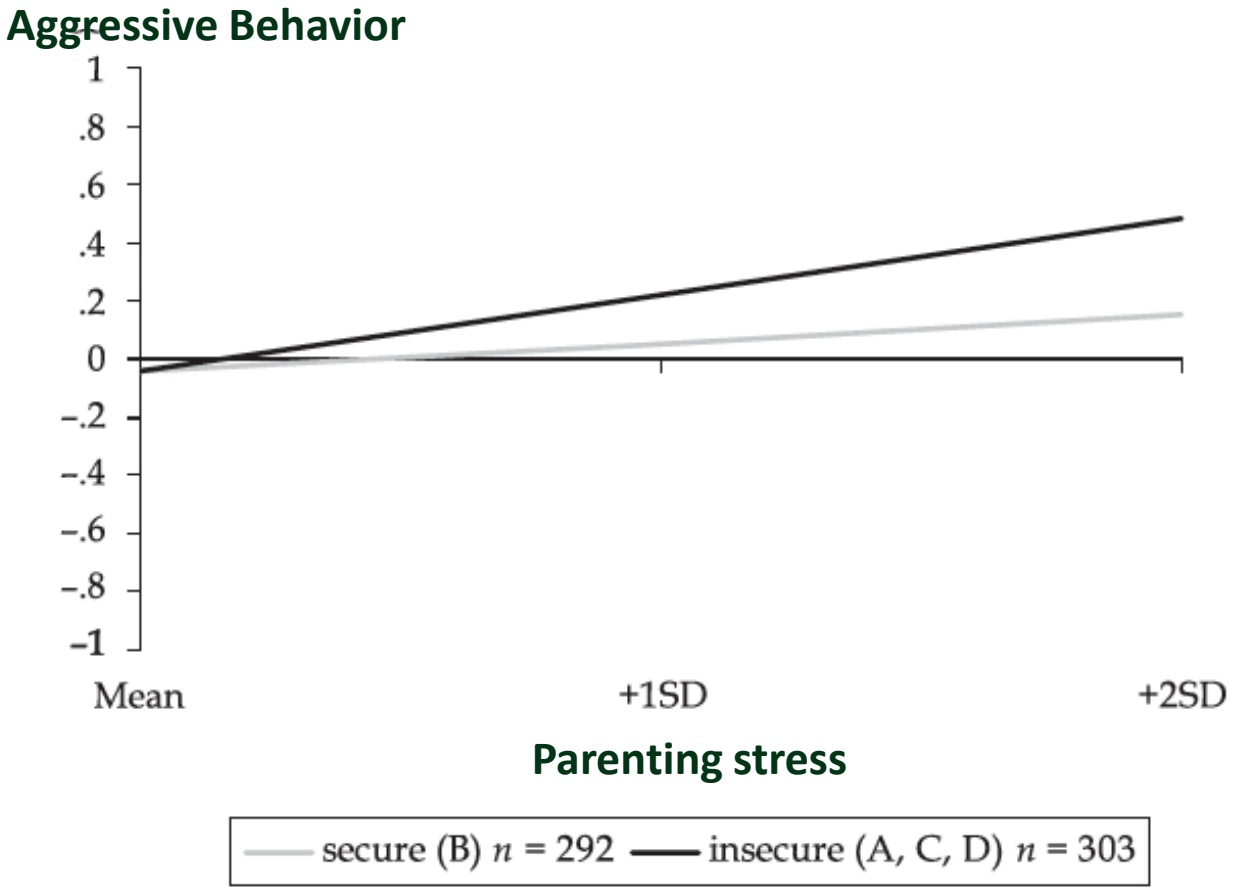
- Methylation affects gene expression leading to heritable changes (not involving DNA sequencing).
  - How experiences shape offspring
- Telomere lengthening
  - reflects cellular aging

Importance of the Infant Caregiver Relationship

Importance of child caregiver relationships

- Human infants *require* caregivers' *protection and support* to ensure survival for years after birth.
- Relationships with caregivers essential in helping children *regulate responses to stressors and adversity*.
- THE most important context for child development is child's *relationship(s) with caregiver(s)*.

Protection within risk Tharner et al 2012



Children with histories of severe deprivation

Security of attachment
at 42 mos.

Caregiving quality
30 months

Psychiatric symptoms, disorders
and impairment at 54 mos.

McGoron et al., 2012

What promotes health and well-being in young children?


Thankyou!
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