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Life Course Intervention Research Network (LCIRB)
& The Forum for Children's Well-Being



UNIVERSITY *of*
DENVER

Developmental Origins of Children's Mental Health Disorders: Roles of Childhood Adversity and Brain Development

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Overview

- Childhood Adversity and Mental Health Disorders
- Neurobiological Mechanisms from the Life Course Perspective
 - Prenatal period and infancy
 - Childhood and adolescence
 - Long-term impacts on adulthood
- Adaptation and Vulnerability

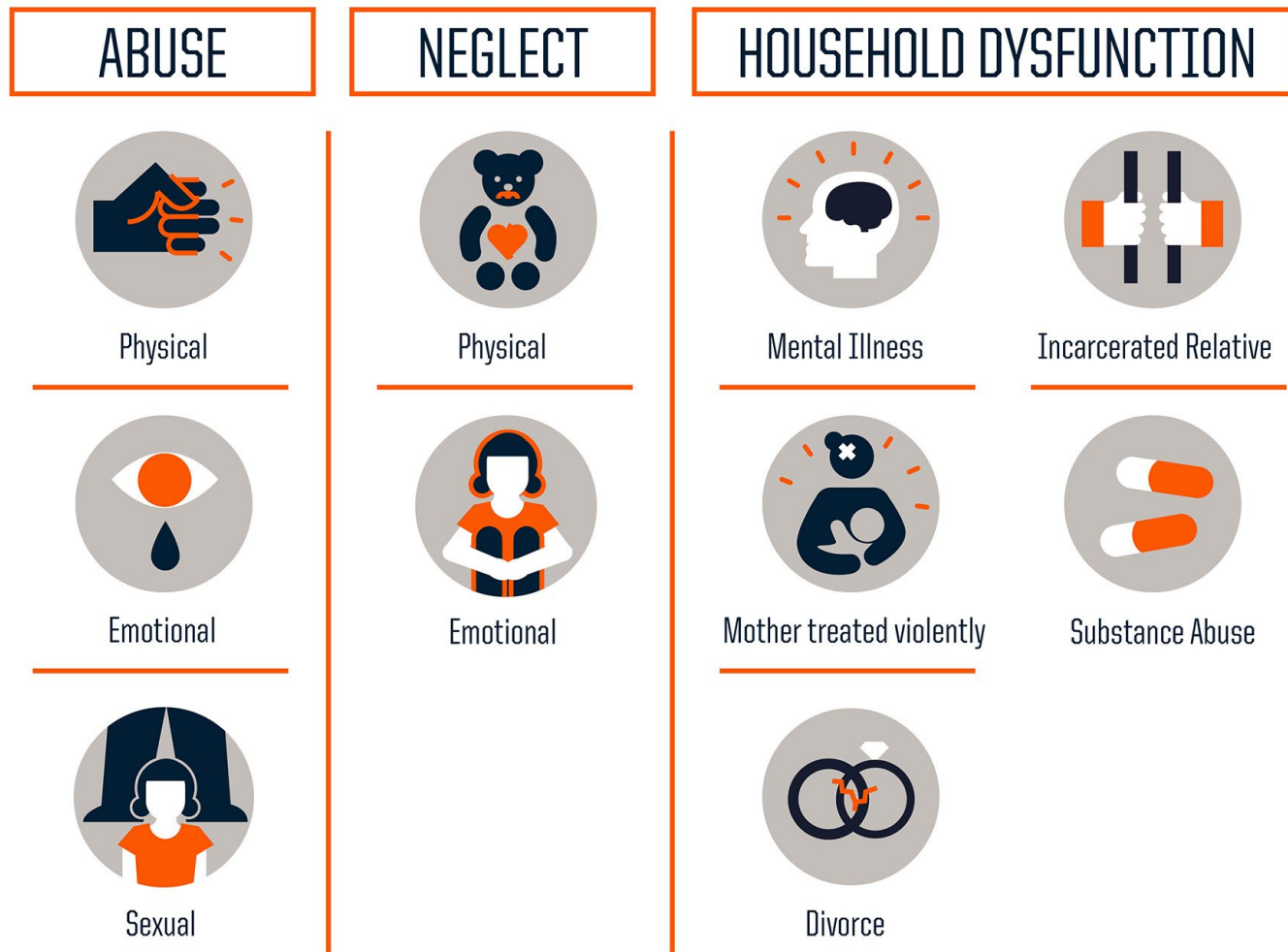
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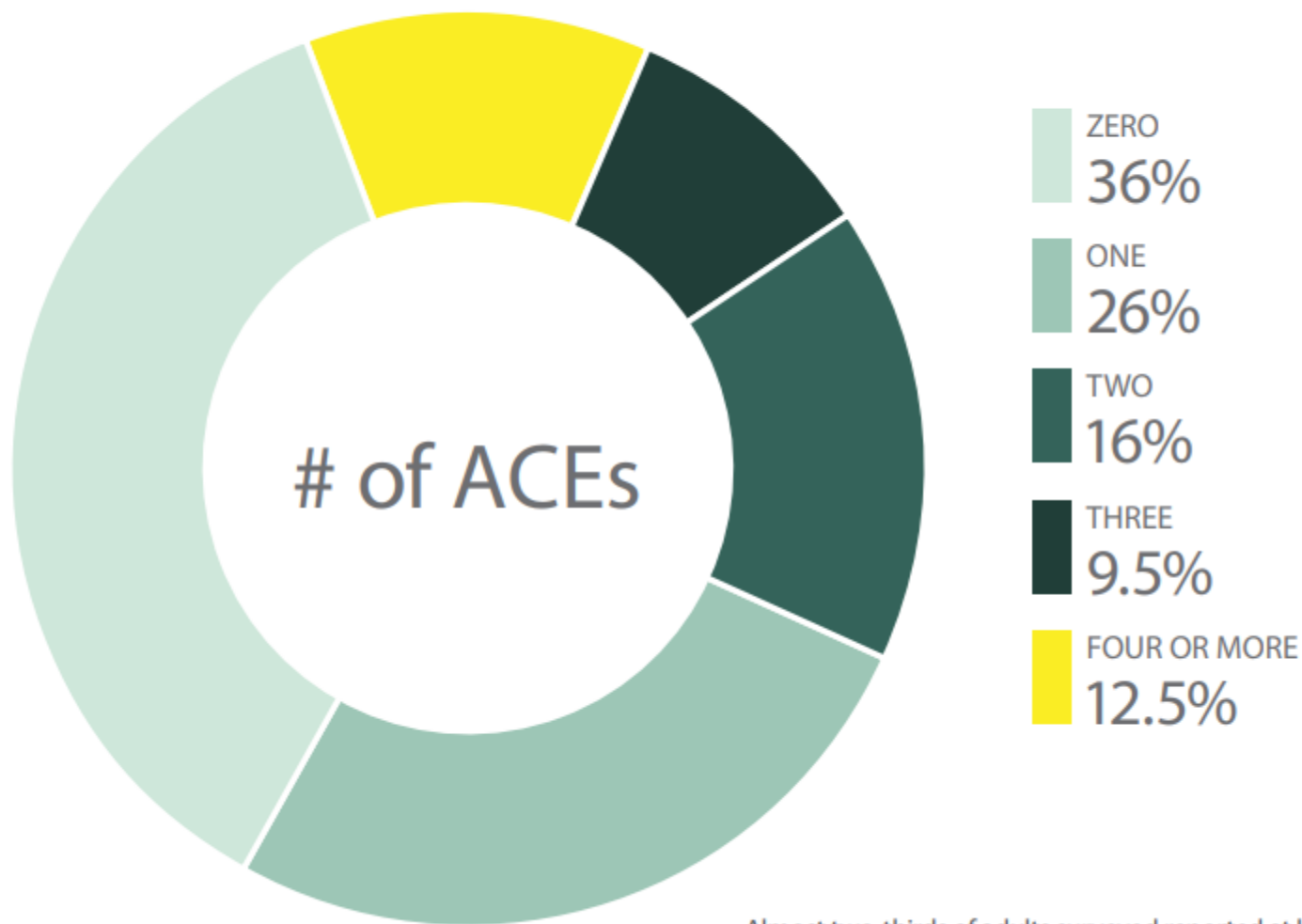
Childhood Adversity

- Adverse childhood experiences (ACEs)
 - Maltreatment or neglect
- Poverty

Adverse childhood experiences (ACEs)



HOW COMMON ARE ACEs?



Almost two-thirds of adults surveyed reported at least one Adverse Childhood Experience – and the majority of respondents who reported at least one ACE reported more than one.

ACEs can have lasting effects on...



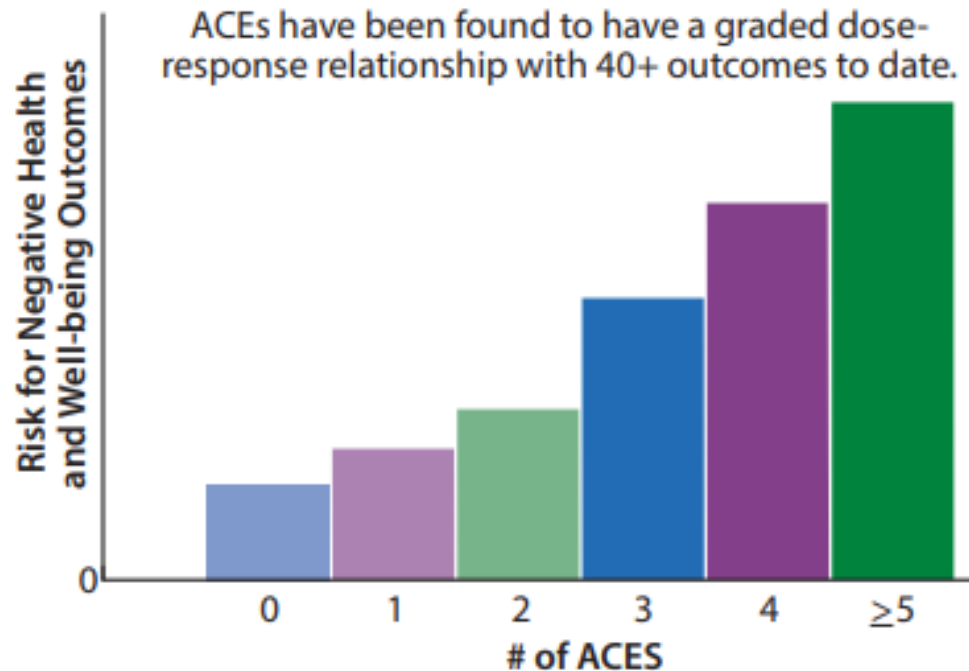
Health (obesity, diabetes, depression, suicide attempts, STDs, heart disease, cancer, stroke, COPD, broken bones)



Behaviors (smoking, alcoholism, drug use)



Life Potential (graduation rates, academic achievement, lost time from work)

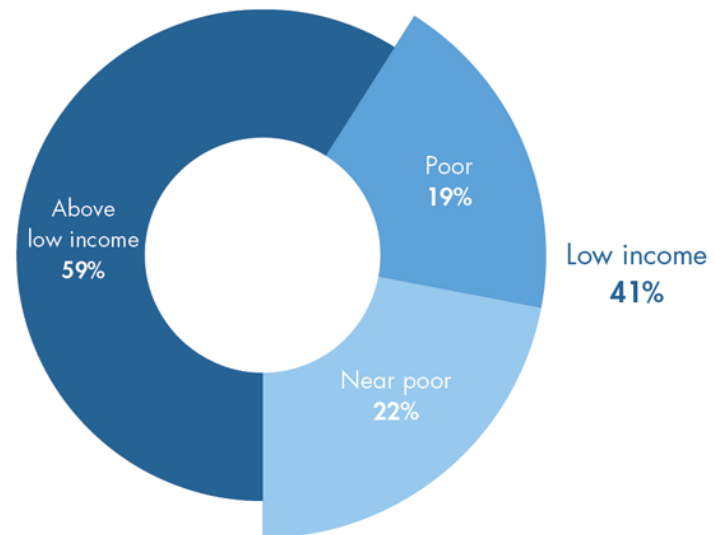


*This pattern holds for the 40+ outcomes, but the exact risk values vary depending on the outcome.

What is Poverty?

- Based on income
 - income-to-needs ratio < 1
 - Federal Poverty Level (FPL) Family of four - \$25,750 (2019)
- Socioeconomic status (SES)
 - income, education, and occupation

Figure 1: Children by family income, 2016



Percentages may not add up to 100 due to rounding.

National Center for Children in Poverty

Children are most likely to experience poverty.

Figure 3: Family income by age, 2016

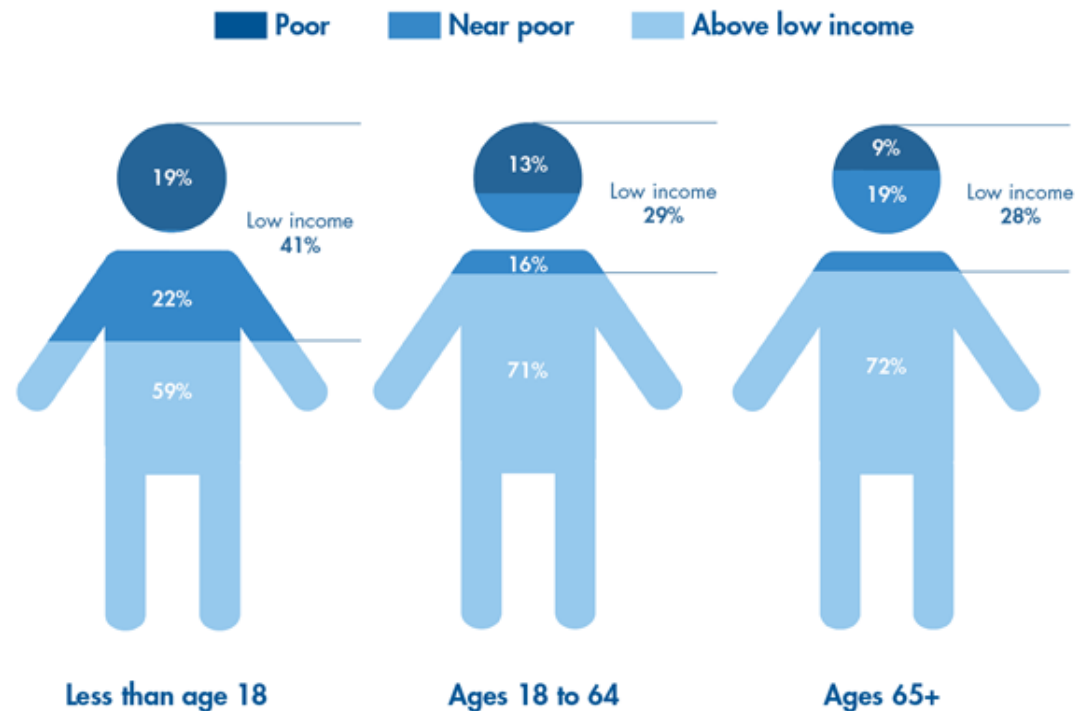
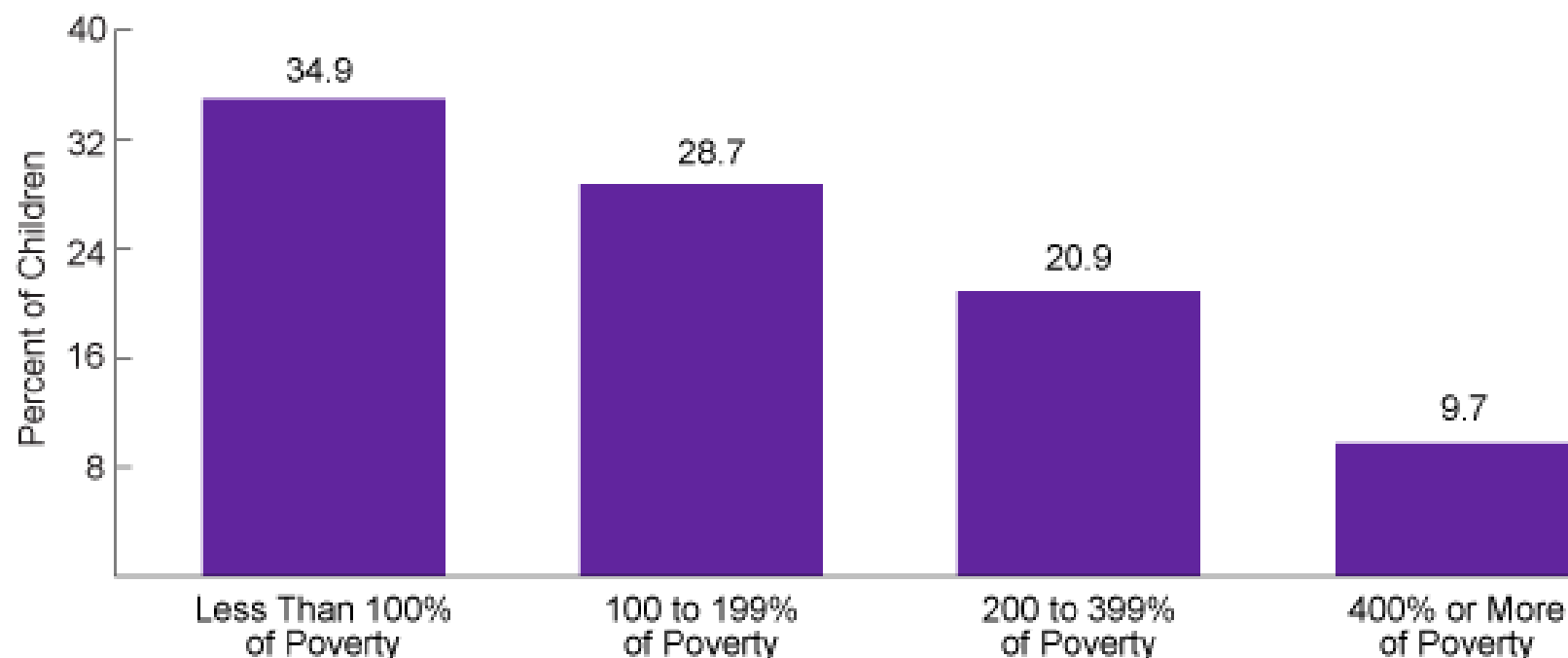


Figure 2. Children Aged 0–17 Years Experiencing Two or More ACEs, by Poverty Status,* 2011–2012

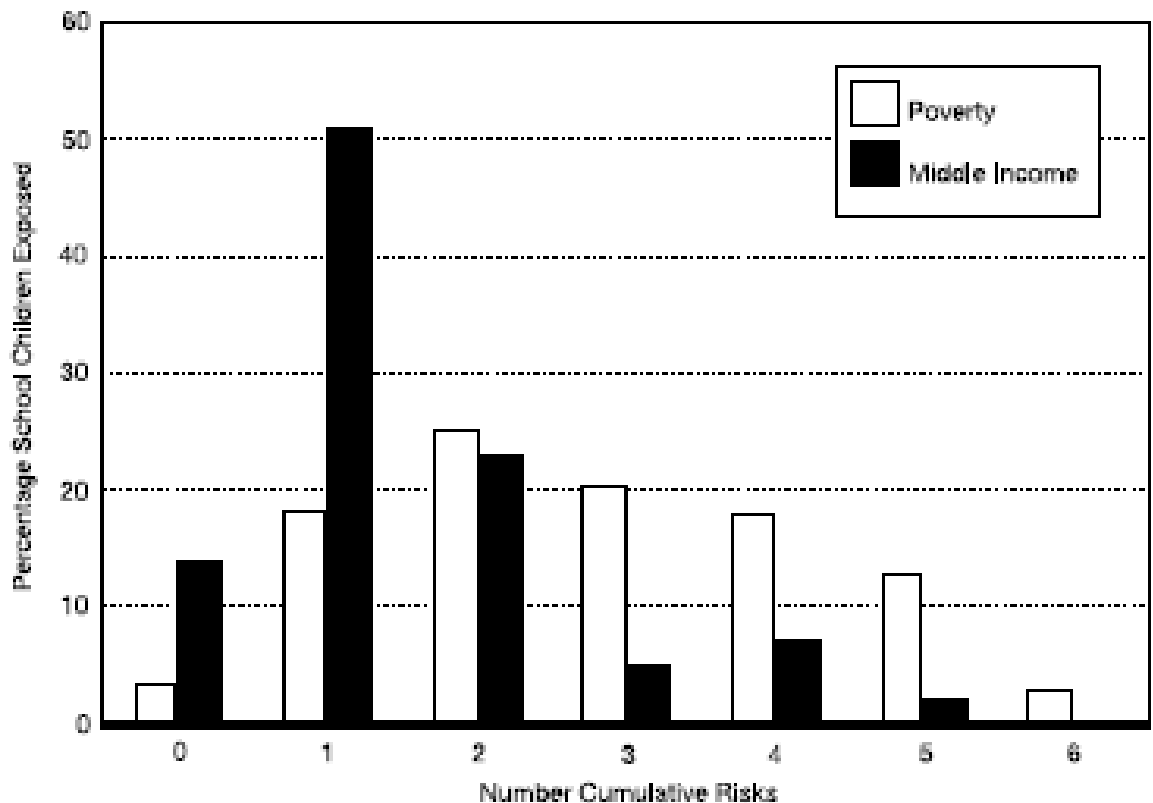


**Based on the U.S. Department of Health and Human Services poverty guidelines, poverty was \$23,050 for a family of four in 2012.*

Source: Health Resources and Services Administration, Maternal and Child Health Bureau; and Centers for Disease Control and Prevention, National Center for Health Statistics, National Survey of Children's Health. Analyzed by the Health Resources and Services Administration's Maternal and Child Health Bureau.

Exposure to High, Chronic Multiple Risks

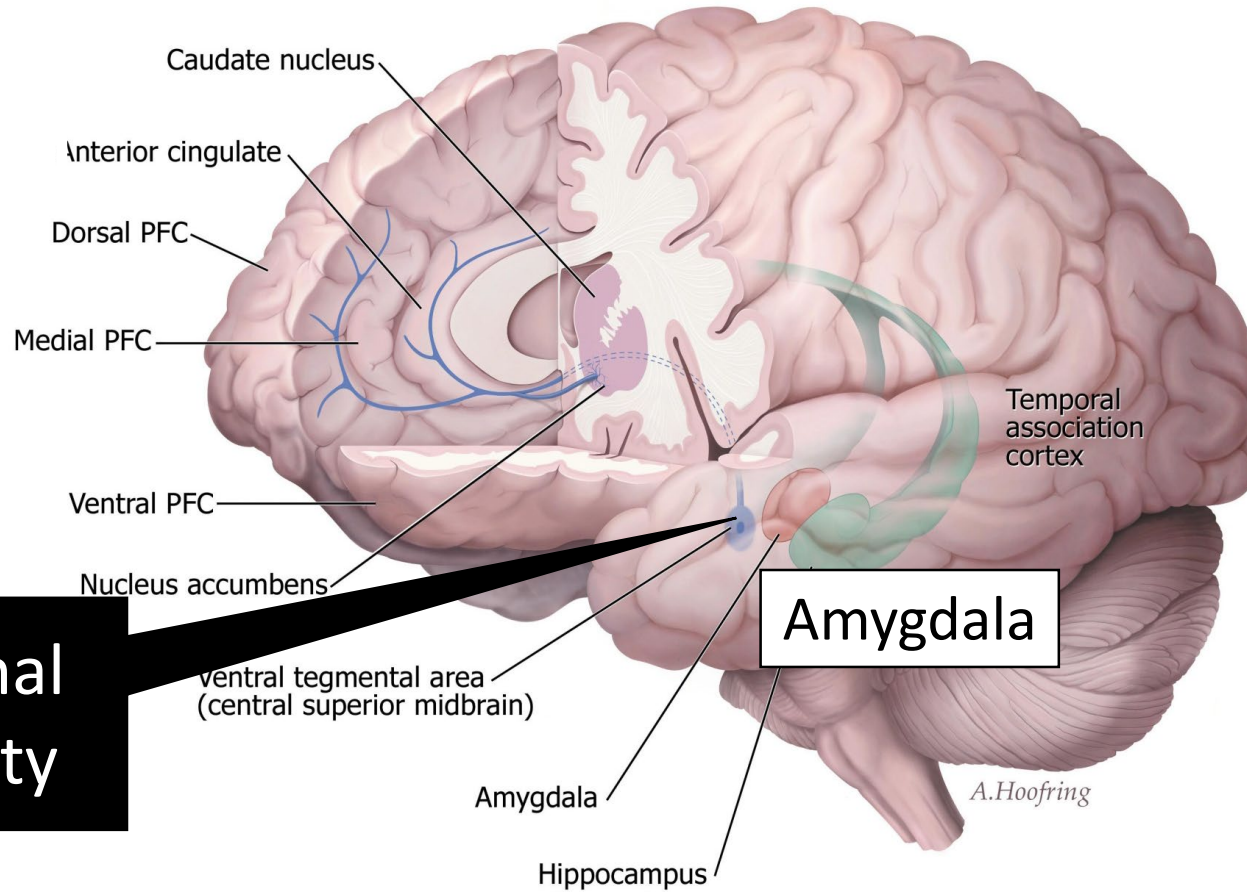
- Exposure to violence
- Family turmoil
- Child separation from family
- Noise
- Housing problems
- Crowding



- Why does childhood adversity lead to negative mental health outcomes?
 - Stress Pathway in the brain

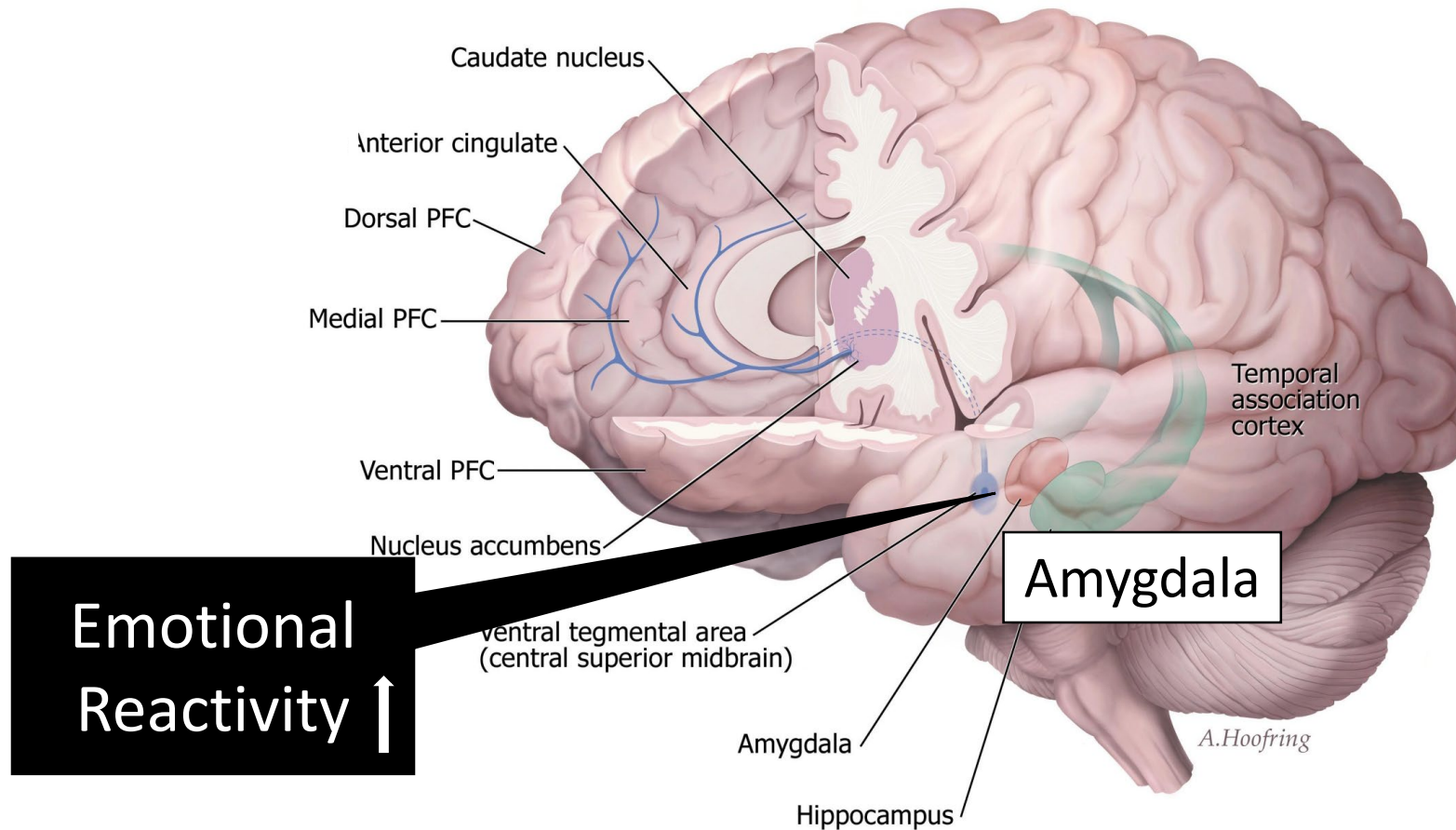


Amygdala





Chronic Stress and Brain

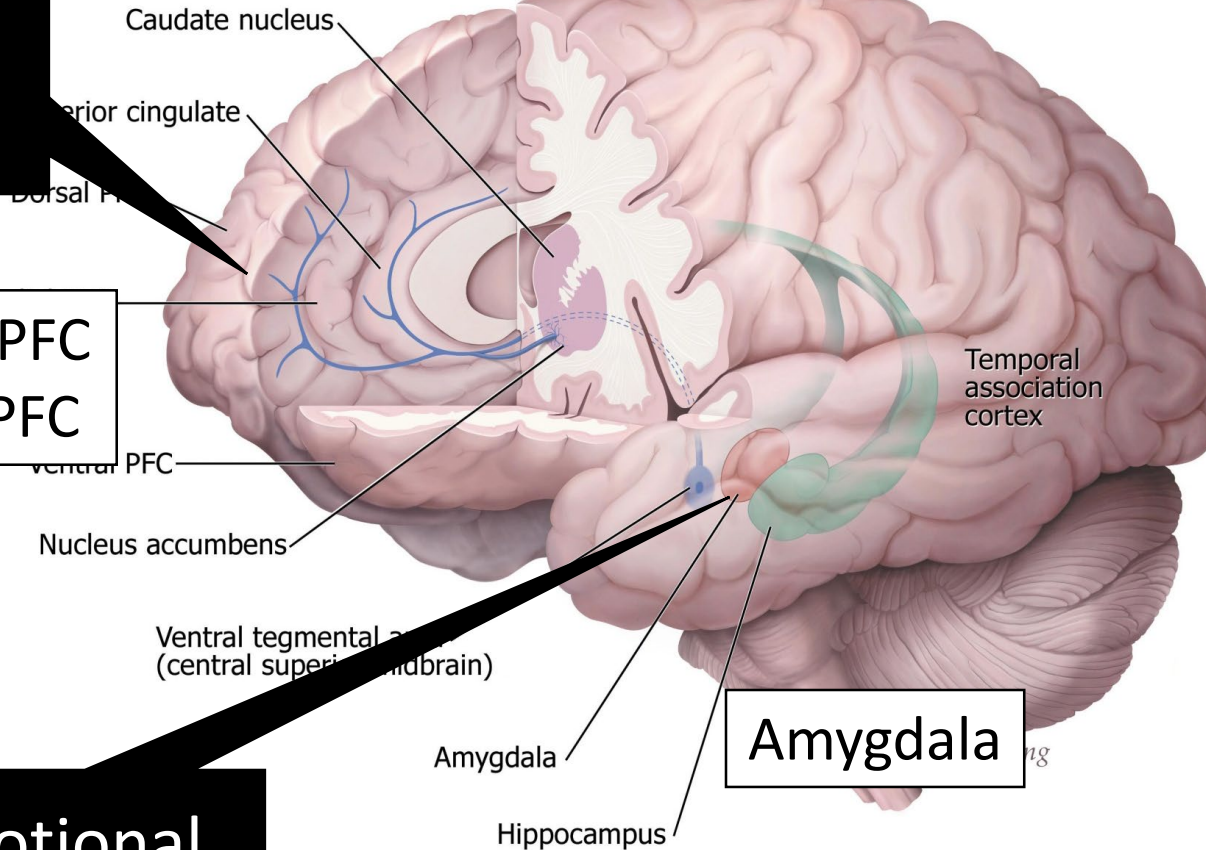


Neural Substrate of Emotional Regulation

Emotion
Regulation

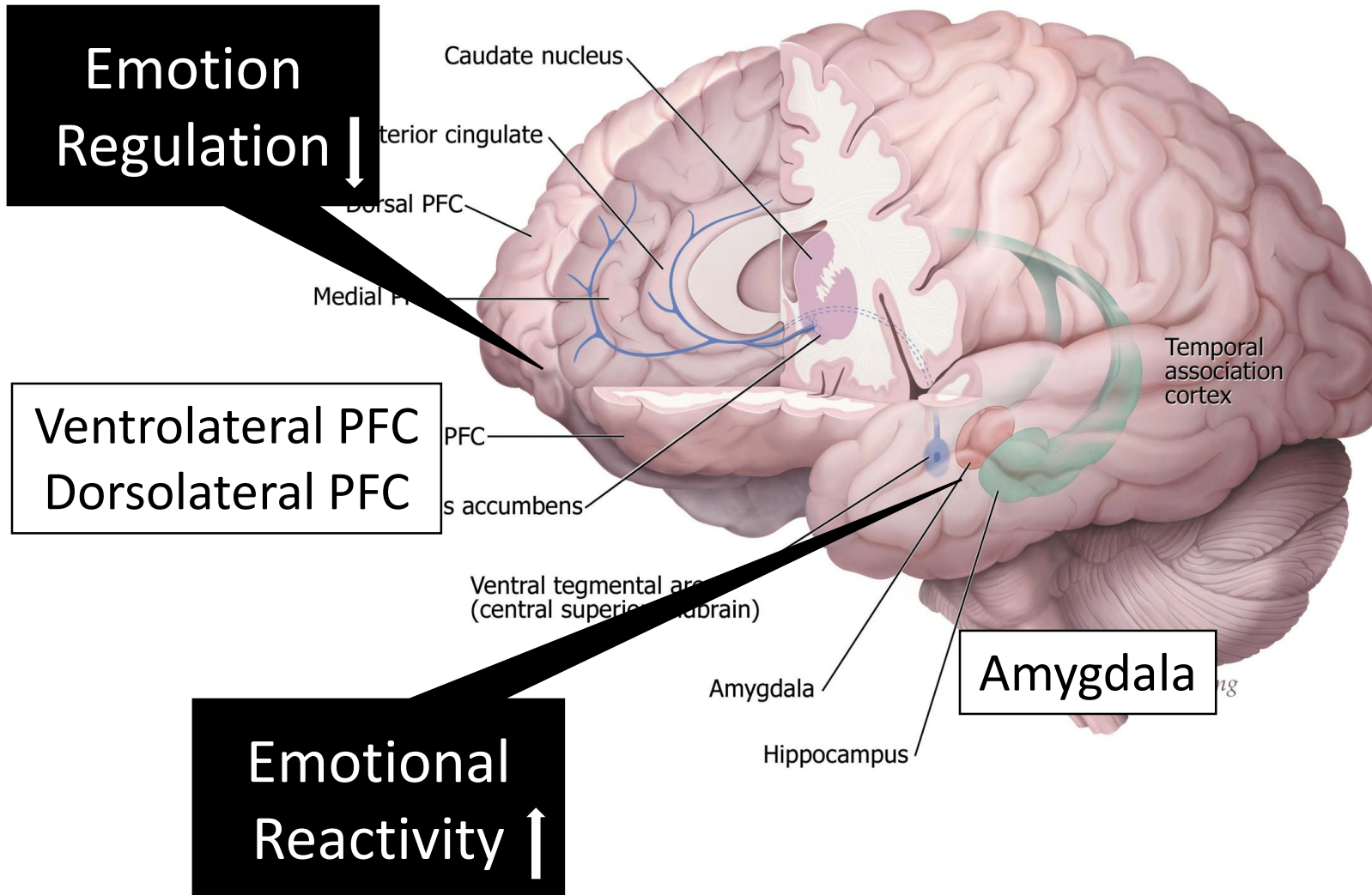
Ventrolateral PFC
Dorsolateral PFC

Emotional
Reactivity



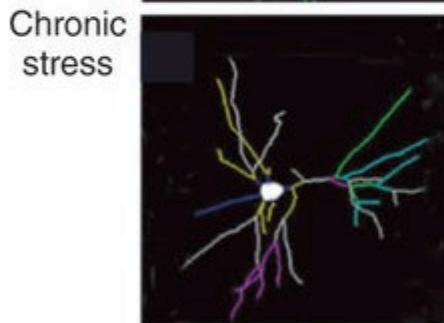
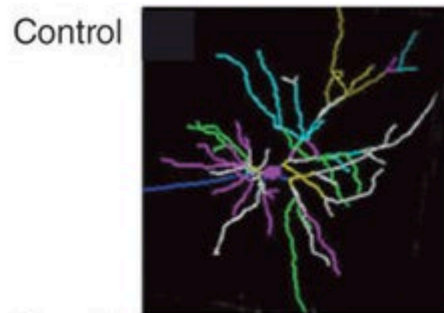


Chronic Stress and Brain

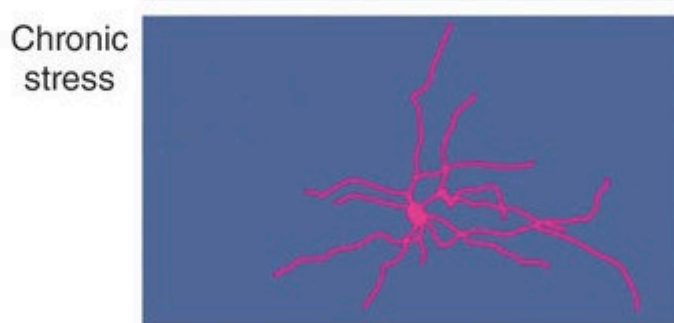


Repeated exposure to stress and Amygdala and PFC

- Repeated exposure to stress
 - Synapse loss, Changes in dendritic branching



Prefrontal cortex
and hippocampus



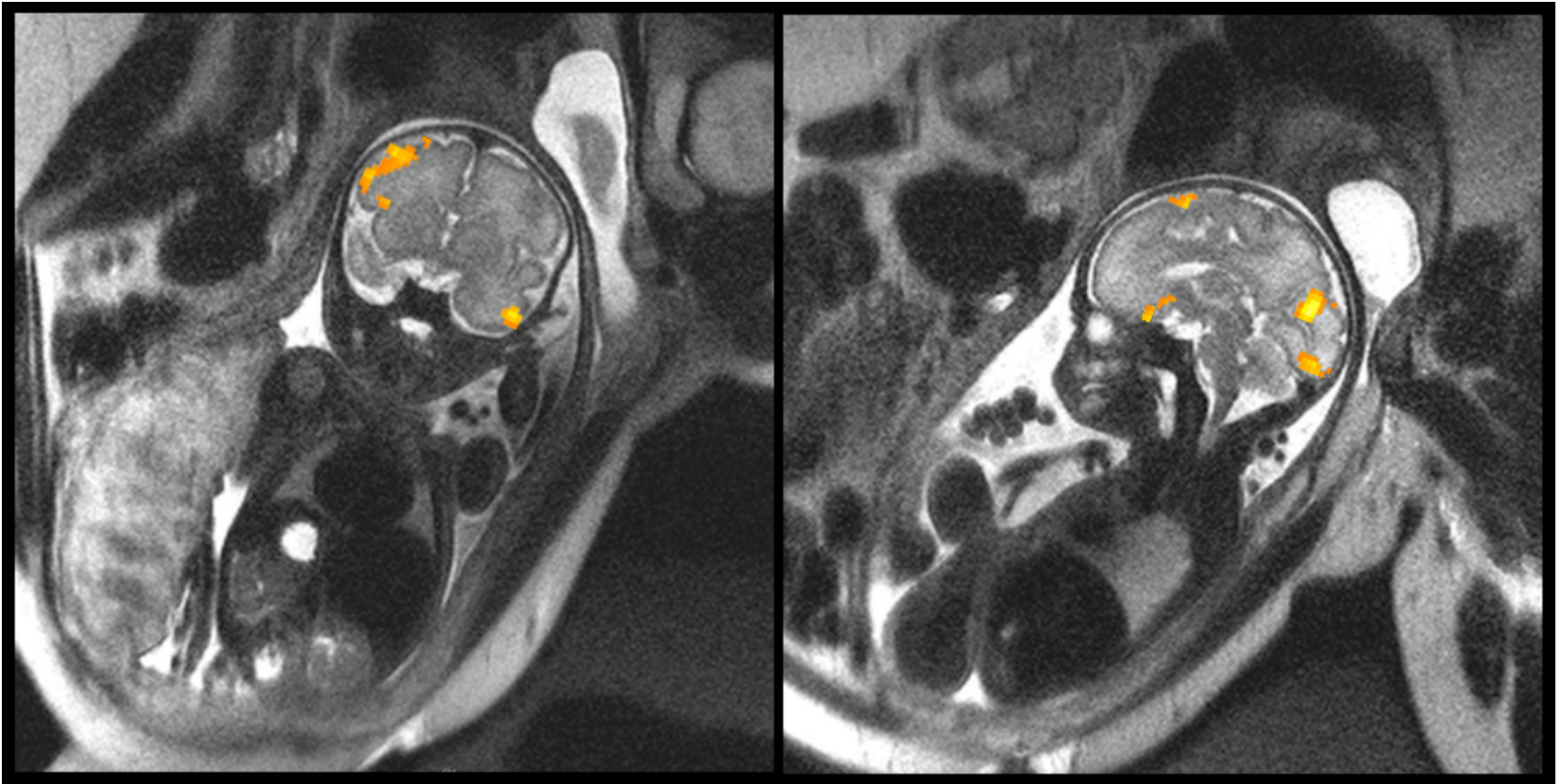
Amygdala and
orbitofrontal cortex

Amygdala-PFC as neural risk markers

- Impaired morphology and functional connectivity in the amygdala and prefrontal cortex (PFC)
 - Early neural markers for emotion dysregulation (Tottenham & Sheridan, 2010; Hanson et al 2015, Connolly et al 2013, Qin et al, 2014)
 - Commonly observed in psychiatric disorders across lifespan (Klumpp et al 2014, Kim et al 2012, Shin et al 2006, Hamilton et al 2008)

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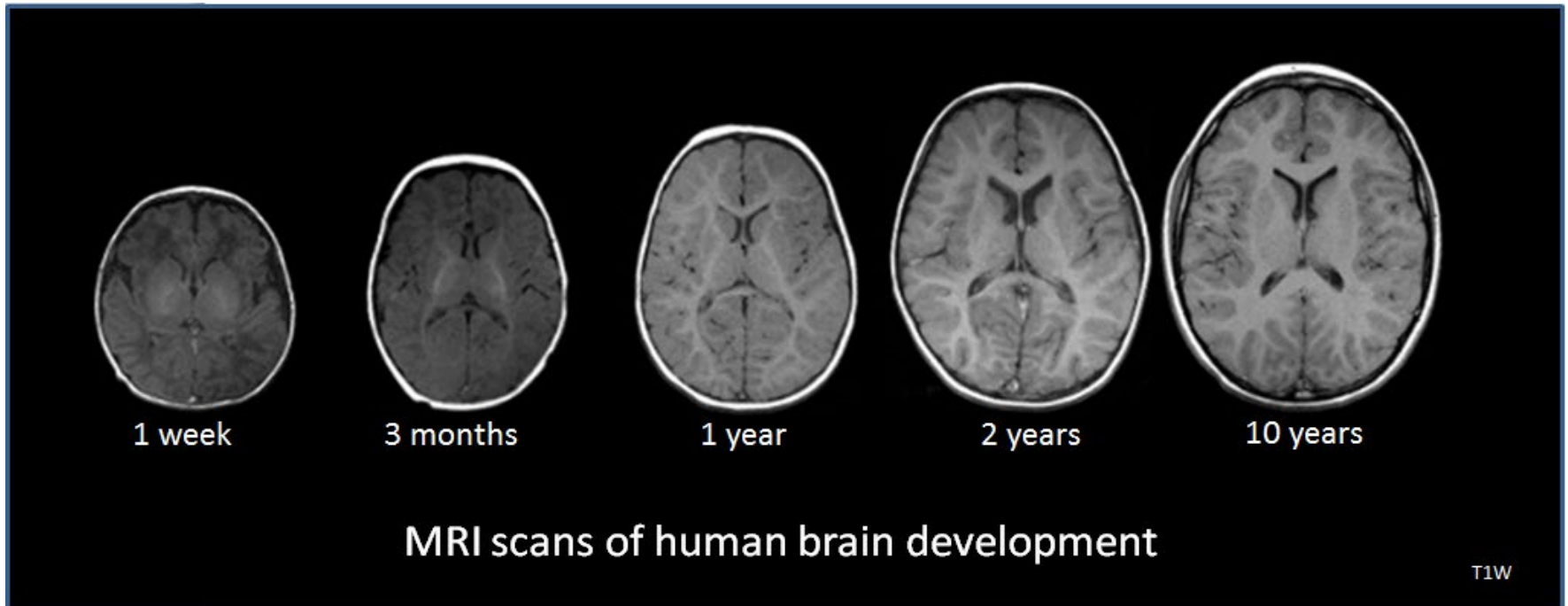


<http://www.sciencemag.org/news/2017/01/pioneering-study-images-activity-fetal-brains>

Prenatal Adversity and Brain Development

- During the third trimester the brain is forming 40,000 synapses per minutes
- What is programming? The action of a factor during a sensitive developmental period that affects the organization and maturity of specific organs
- Those biological systems that have rapid developmental changes are especially vulnerable to adversity

- During the first year, there is 100% brain volume increase.



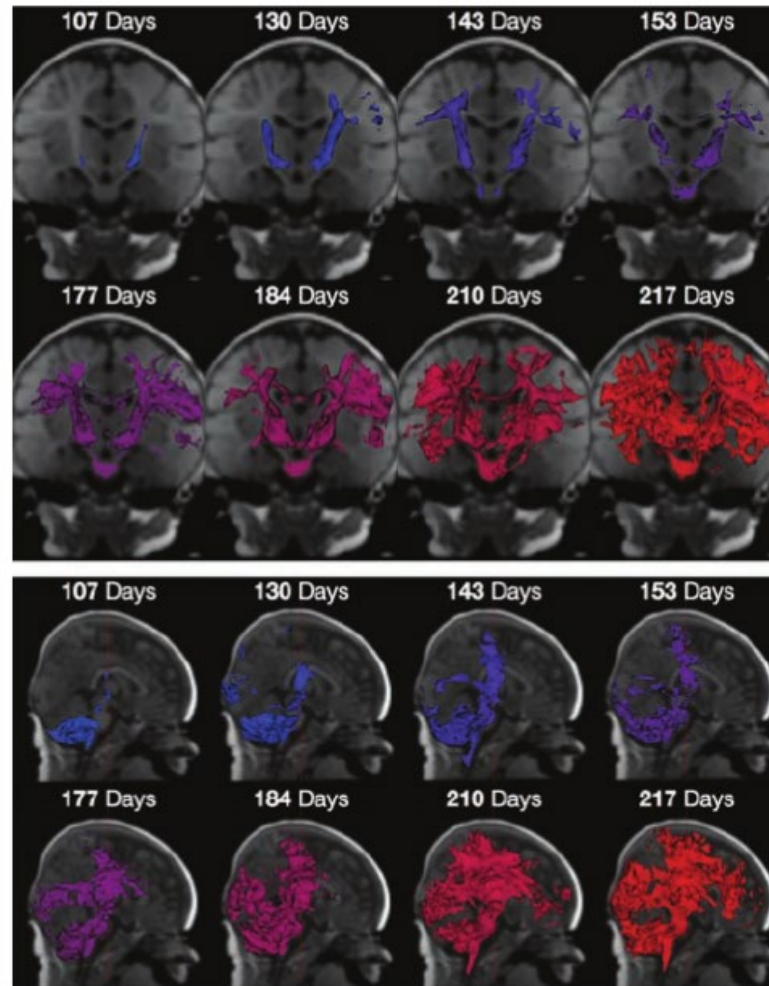
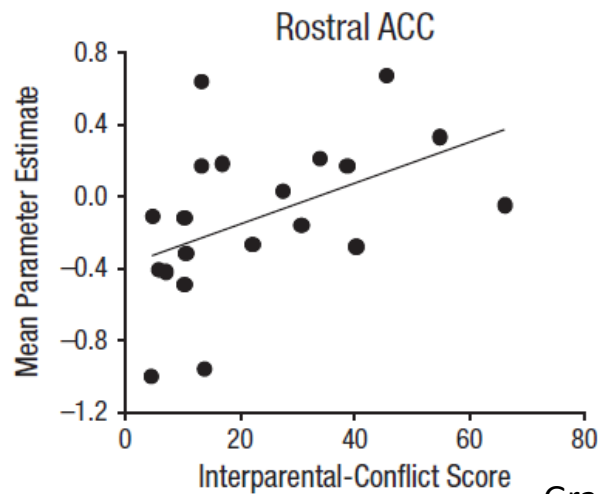
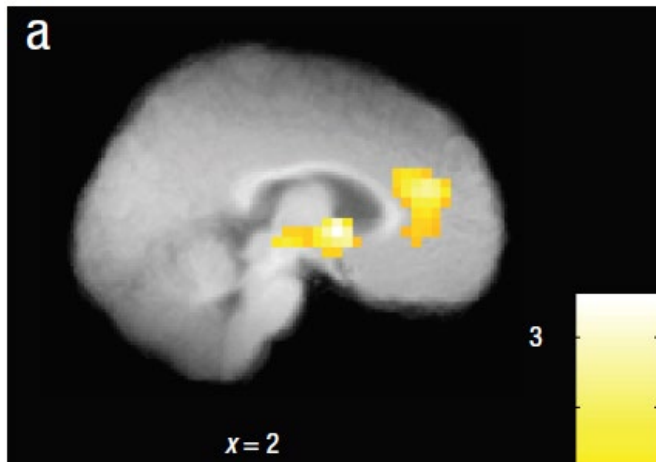


Figure 2.4 The expansion of myelinated fibers over early postnatal development as revealed by a new structural MRI technique.

Prenatal Adversity and Brain Development in infancy and beyond

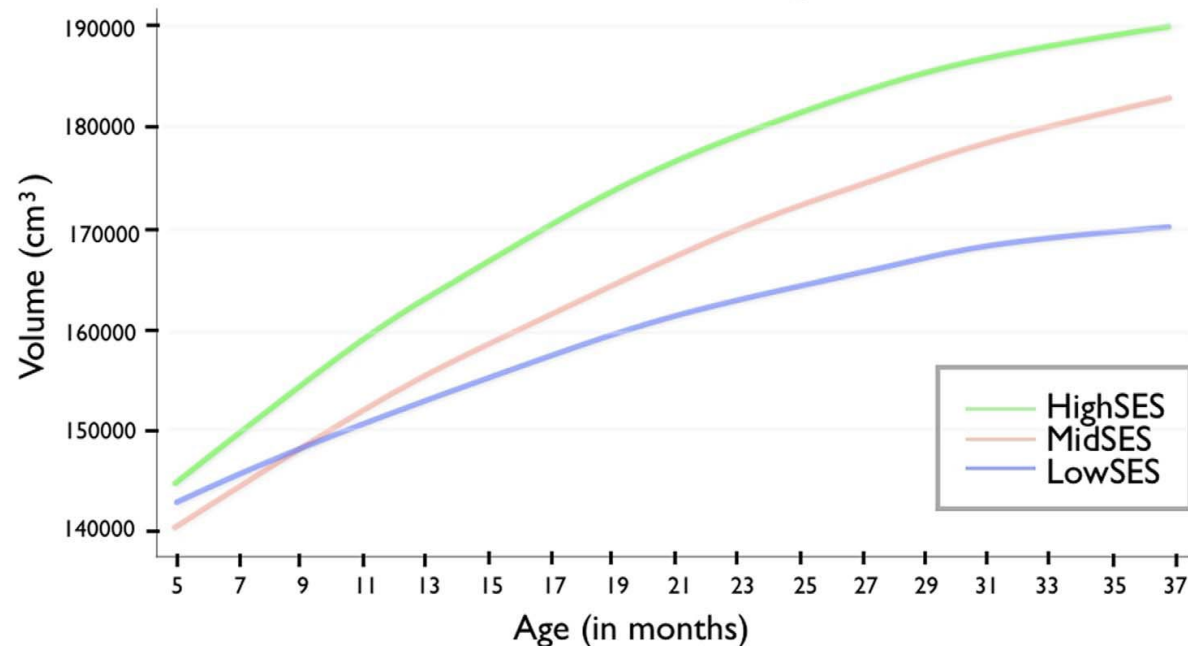
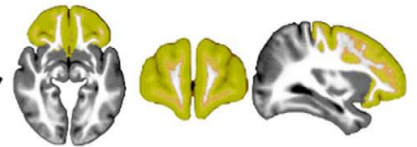
- Maternal anxiety, inflammation, cortisol levels during pregnancy
 - Greater amygdala functional connectivity with the medial PFC in 6-month-old infants (Qiu et al. 2015)
 - Larger amygdala and greater amygdala functional connectivity with insula in neonates (Graham et al 2018)
 - Larger amygdala volume and more affective problems in girls (Buss et al 2012)
- Maternal depression during pregnancy
 - Decreased amygdala functional connectivity with the medial PFC in neonates (Posner et al 2016), lower white matter organization in the amygdala (Rifkin-Graboi 2013)

Adversity exposure during infancy and brain development



Graham et al 2013

Frontal Gray Matter



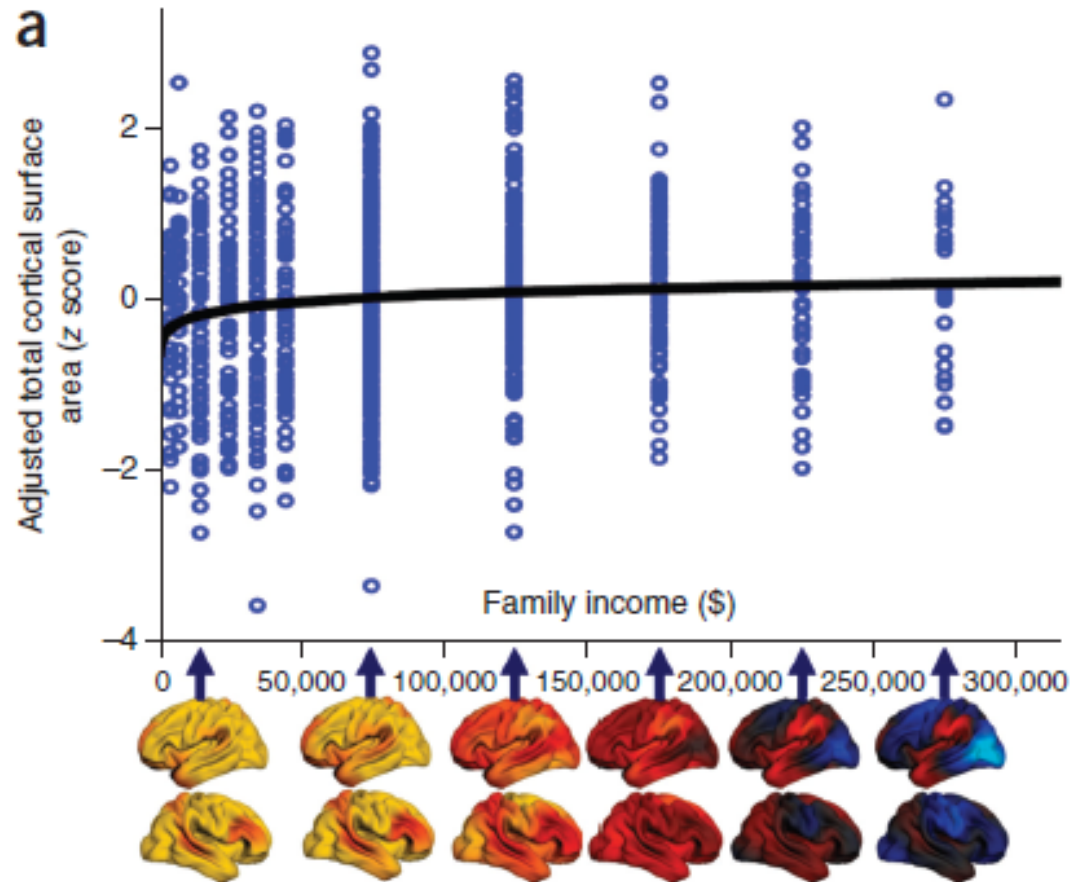
Hanson et al 2013

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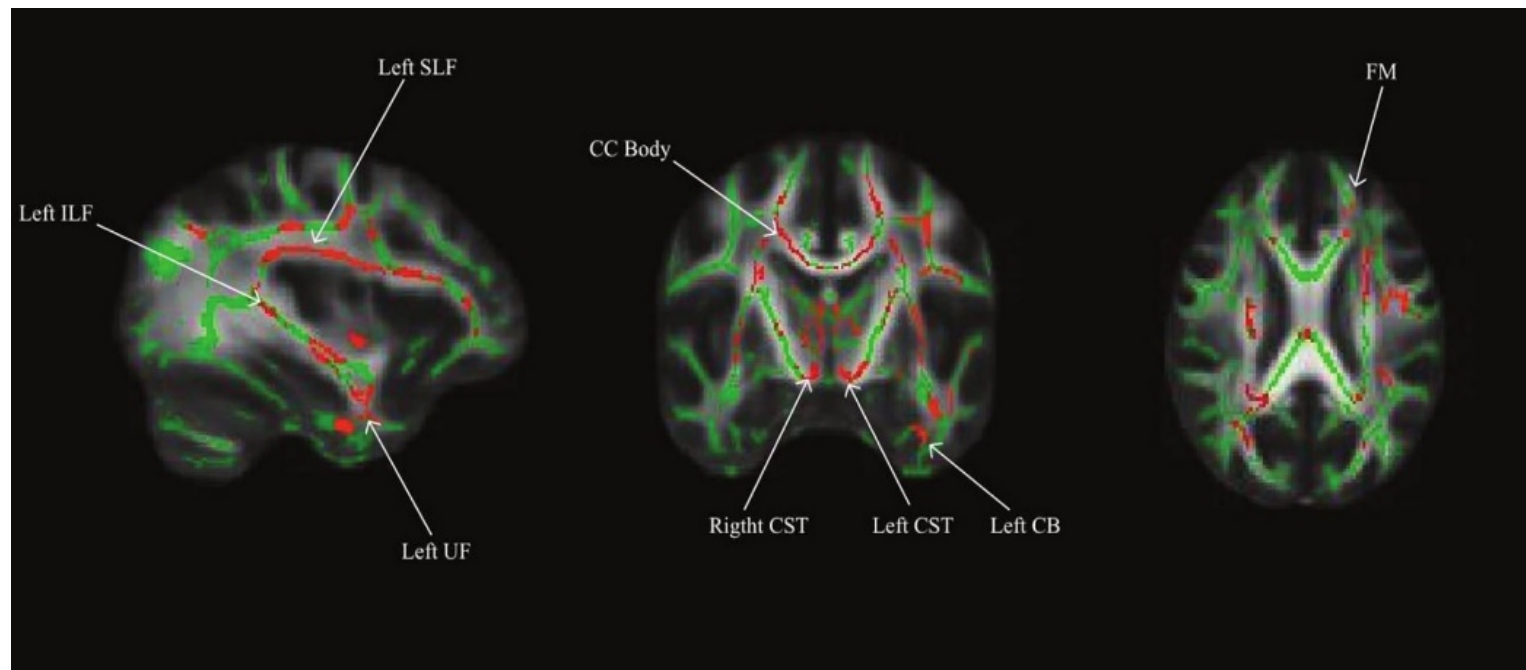
Poverty and Brain Development during Childhood and Adolescence

- Family income was associated with smaller cortical surface area, which was further linked to poor cognitive development among children.



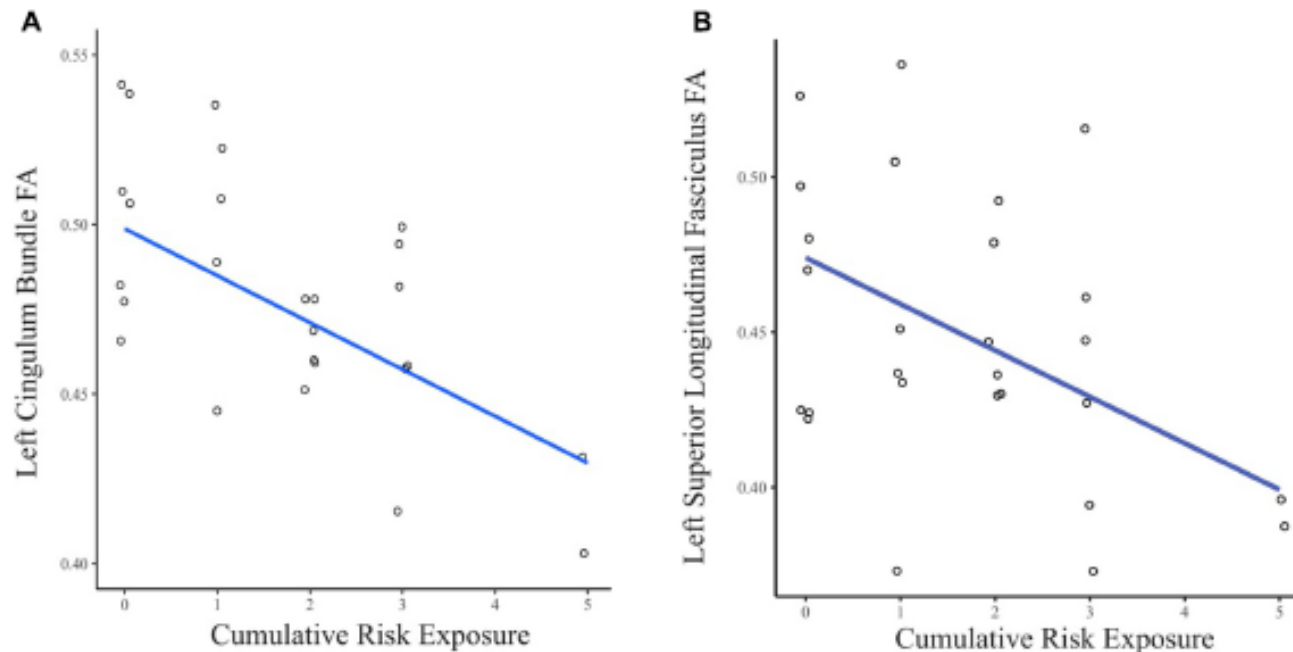
At age 9, low family income was associated with lower white matter organization.

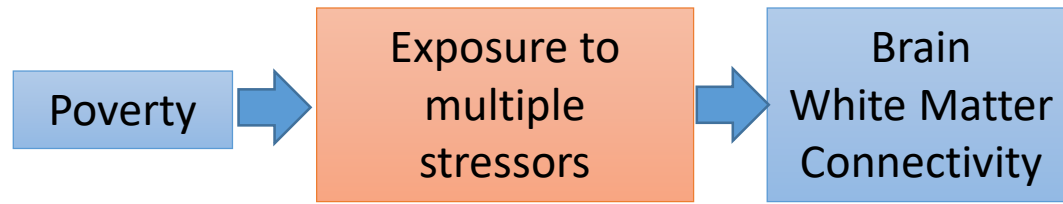
- Low family income-to-needs ratio was associated with lower fractional anisotropy for several clusters including uncinated fasciculus and cingulum bundle.



At age 9, exposure to multiple stressors was associated with the lower white matter organization.

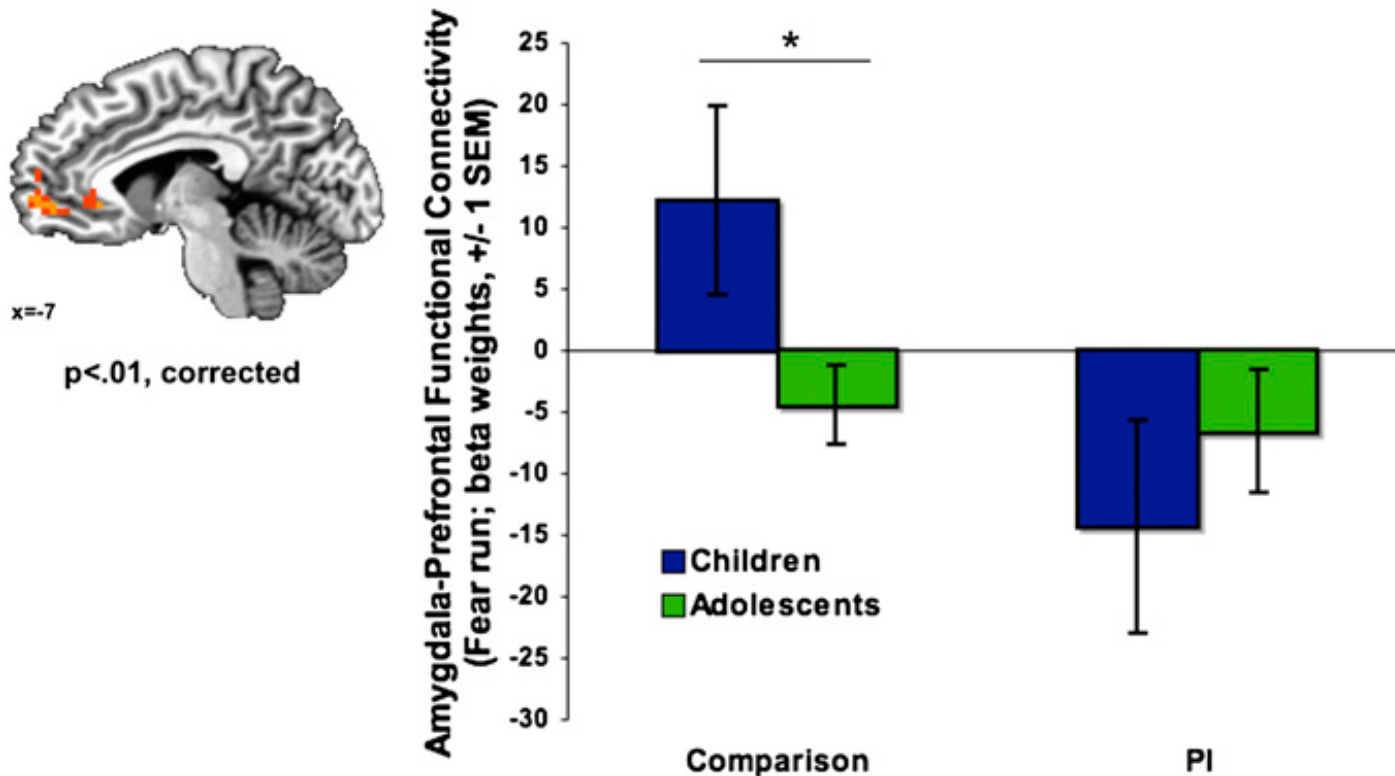
- Exposure to exposure to multiple stressors (exposure to violence, family conflict, child separation, noise, housing problem, crowding) was associated with lower FA.

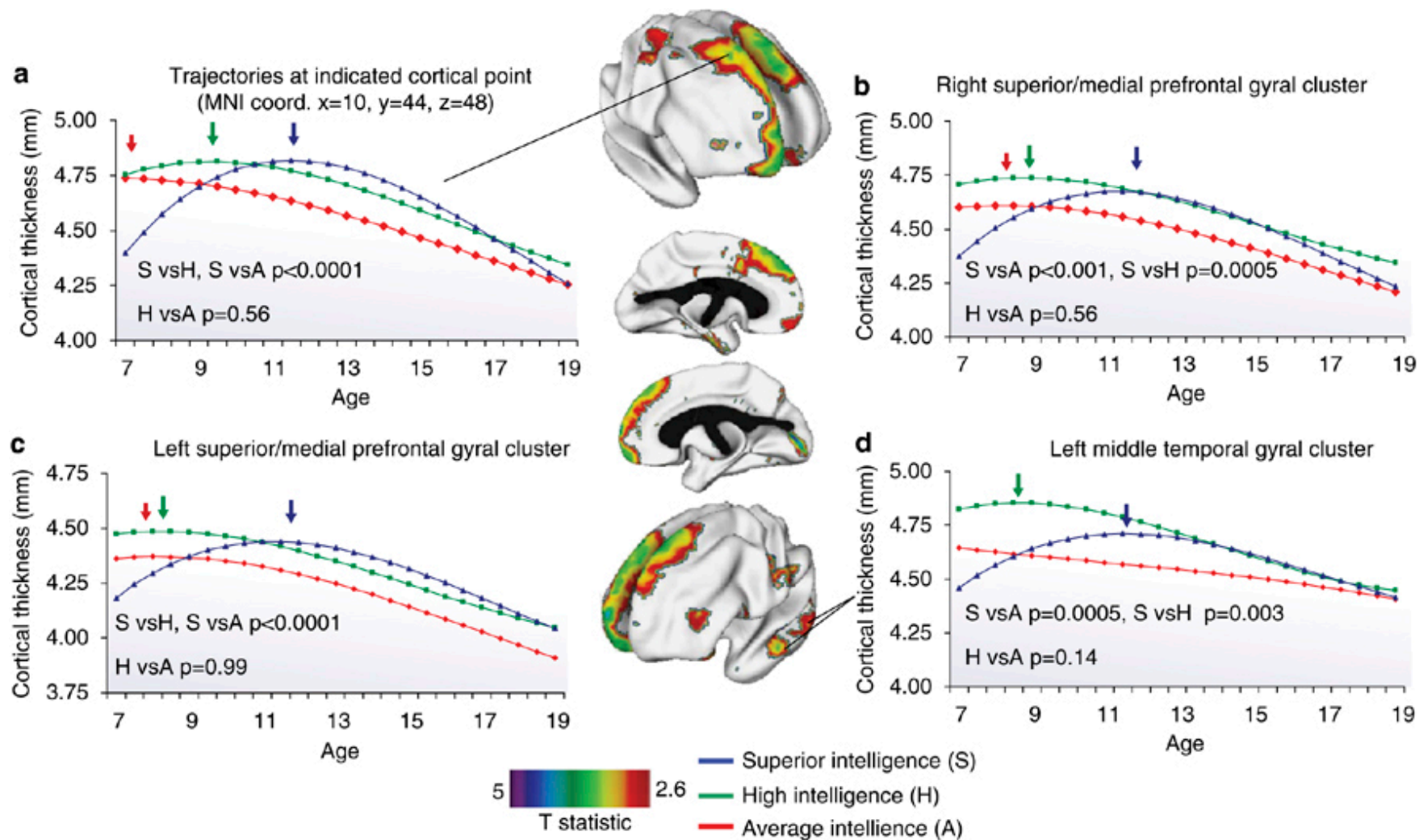




Maternal deprivation and brain development

- Transitions from childhood to adulthood is associated with a shift in amygdala-mPFC connectivity related to top-down control (usually in response to emotional stimuli).





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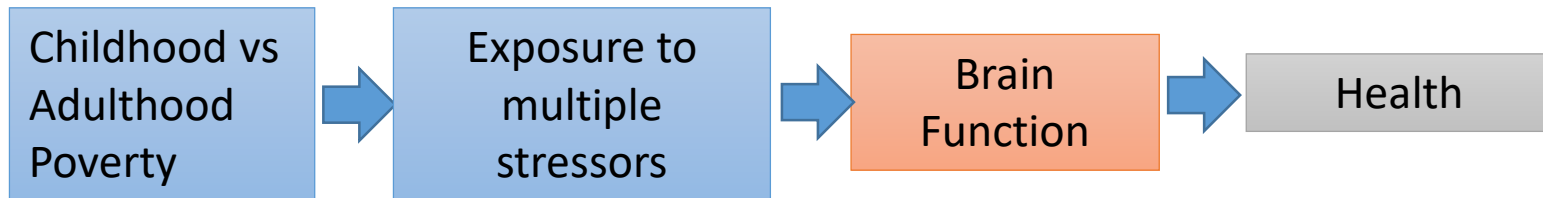
Childhood as a sensitive period

- Childhood socioeconomic disadvantages are associated with adulthood health outcomes
 - increased risk of physical illnesses including coronary heart disease (Cohen et al, 2010)
 - increased risk for mental illnesses including mood, anxiety, and substance abuse (McLaughlin et al 2012)

independent of adult-level SES

The aggregate cost of childhood poverty to the US is estimated at \$500 billion (Holzer et al, 2008)

- When and how does poverty get into a brain?
 - Childhood vs. Adulthood poverty exposure
 - Brain function in the amygdala and PFC for emotion regulation



Participants

- 49 participants
 - Age: 23.6 years (SD = 1.3)
 - Gender: 55% males
- Family income-to-need ratio (1 = poverty line)
 - Age 9: 1.8 (SD = 1.1)
 - Age 24: 3.2 (SD = 3.0)

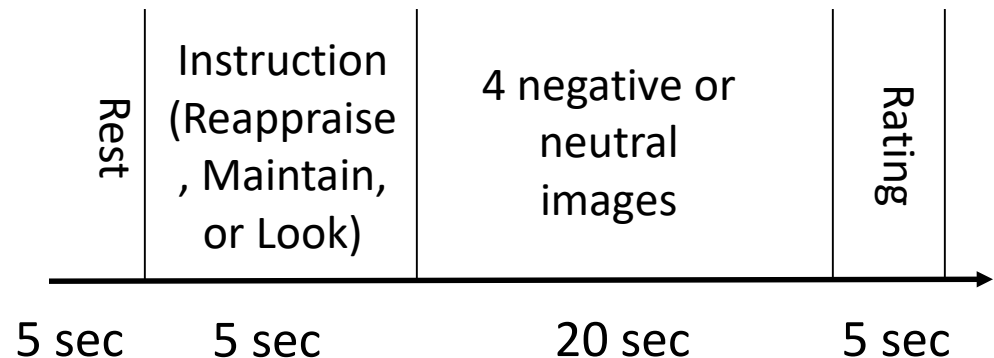
The Emotion Regulation Paradigm

Maintain

- attend to and experience naturally (without trying to change or alter) the emotional state elicited by negative pictures

Reappraise

- voluntarily decrease the intensity of their negative affect by using the cognitive strategy of reappraisal

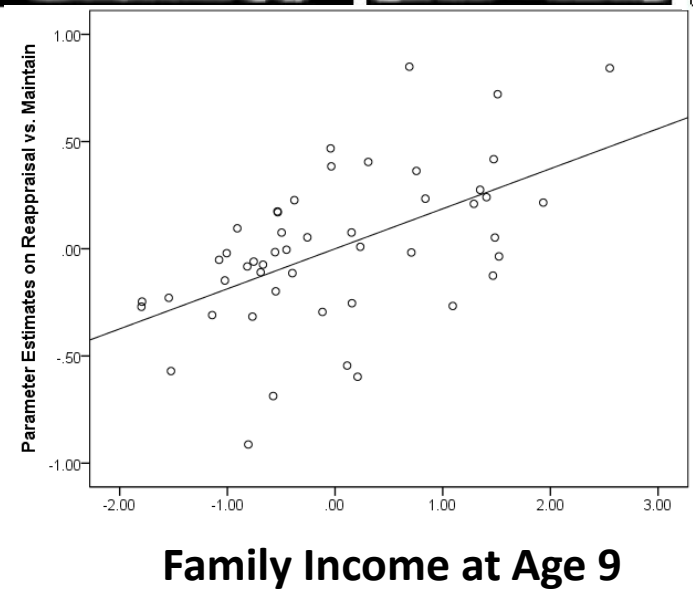
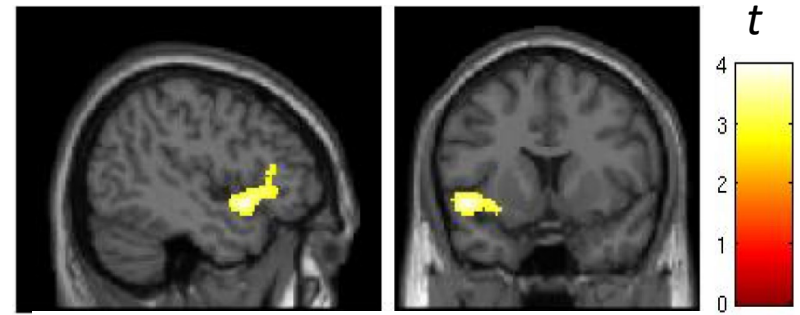
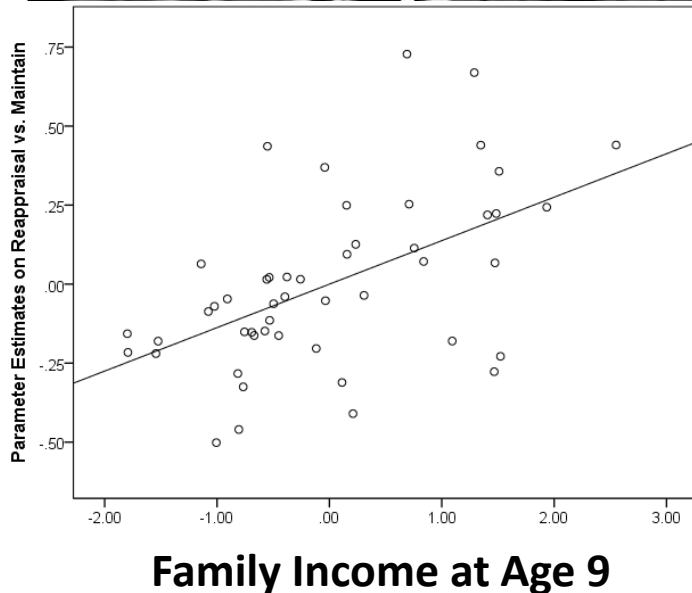
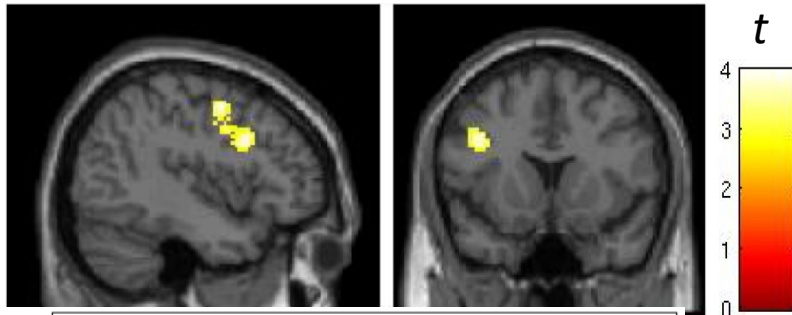
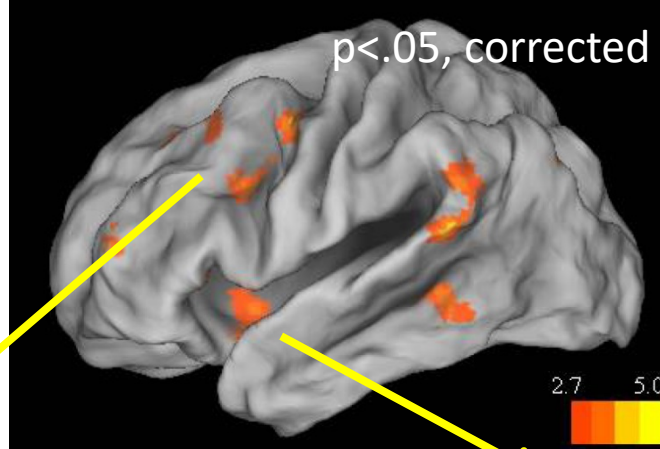


**Reappraise >
Maintain**

Dorsolateral PFC

$p < .05$, corrected

**Ventrolateral
PFC/Insula/Temporop
olar Area**

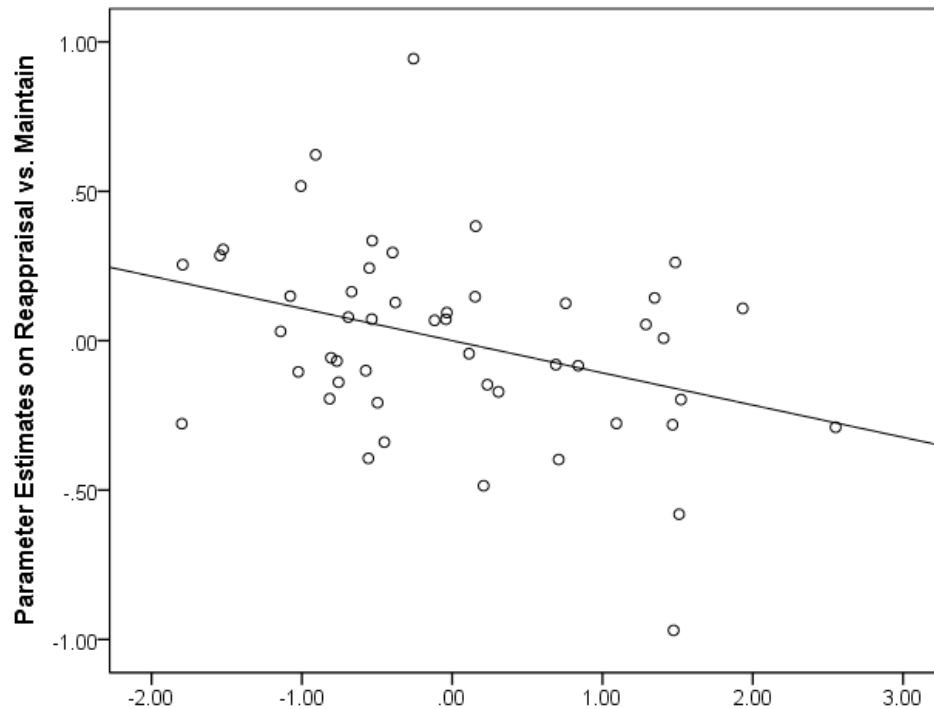


Amygdala



$p < .05$, uncorrected

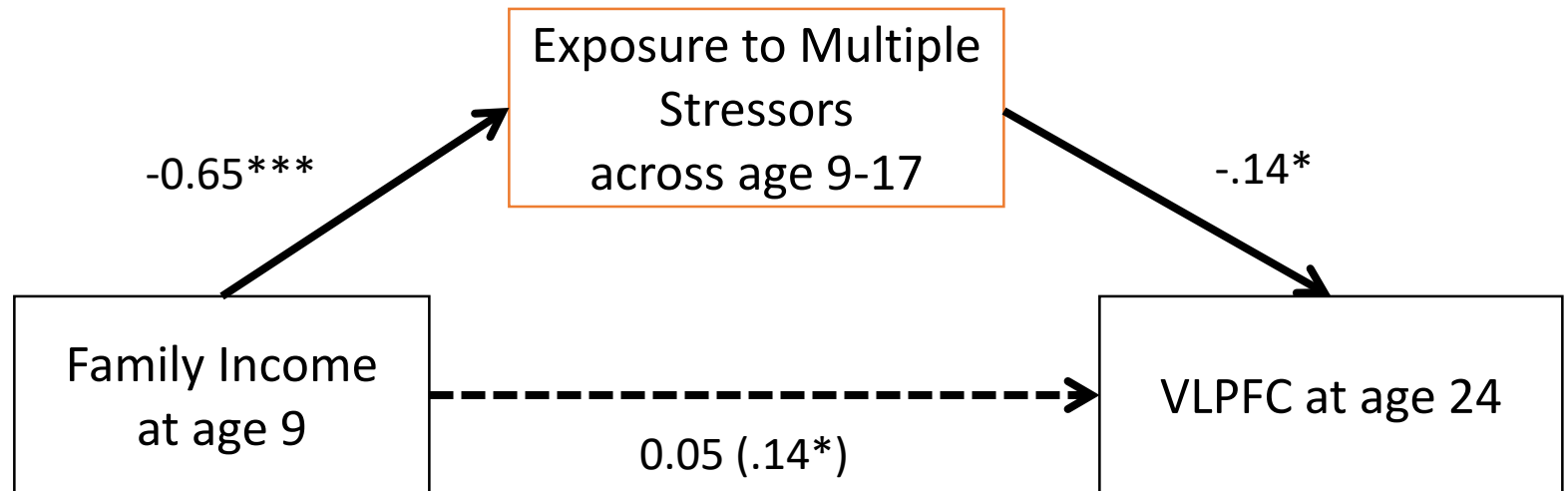
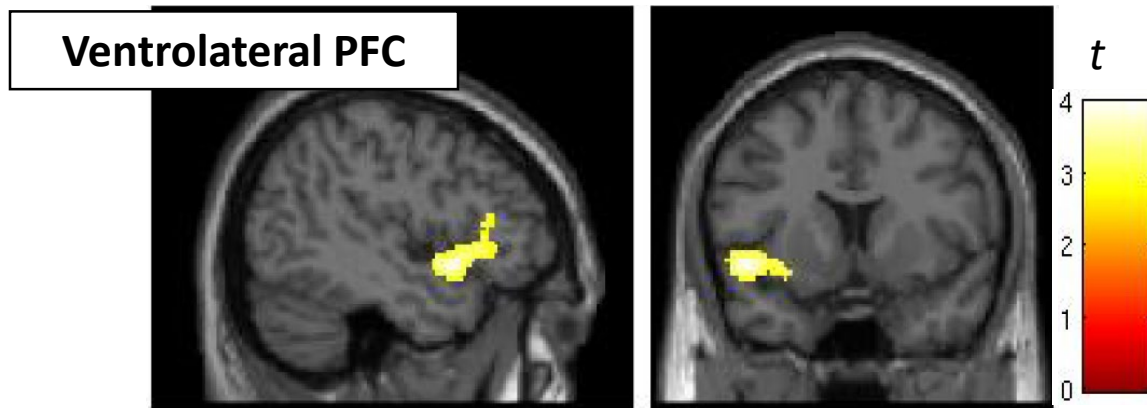
Reappraise >
Maintain

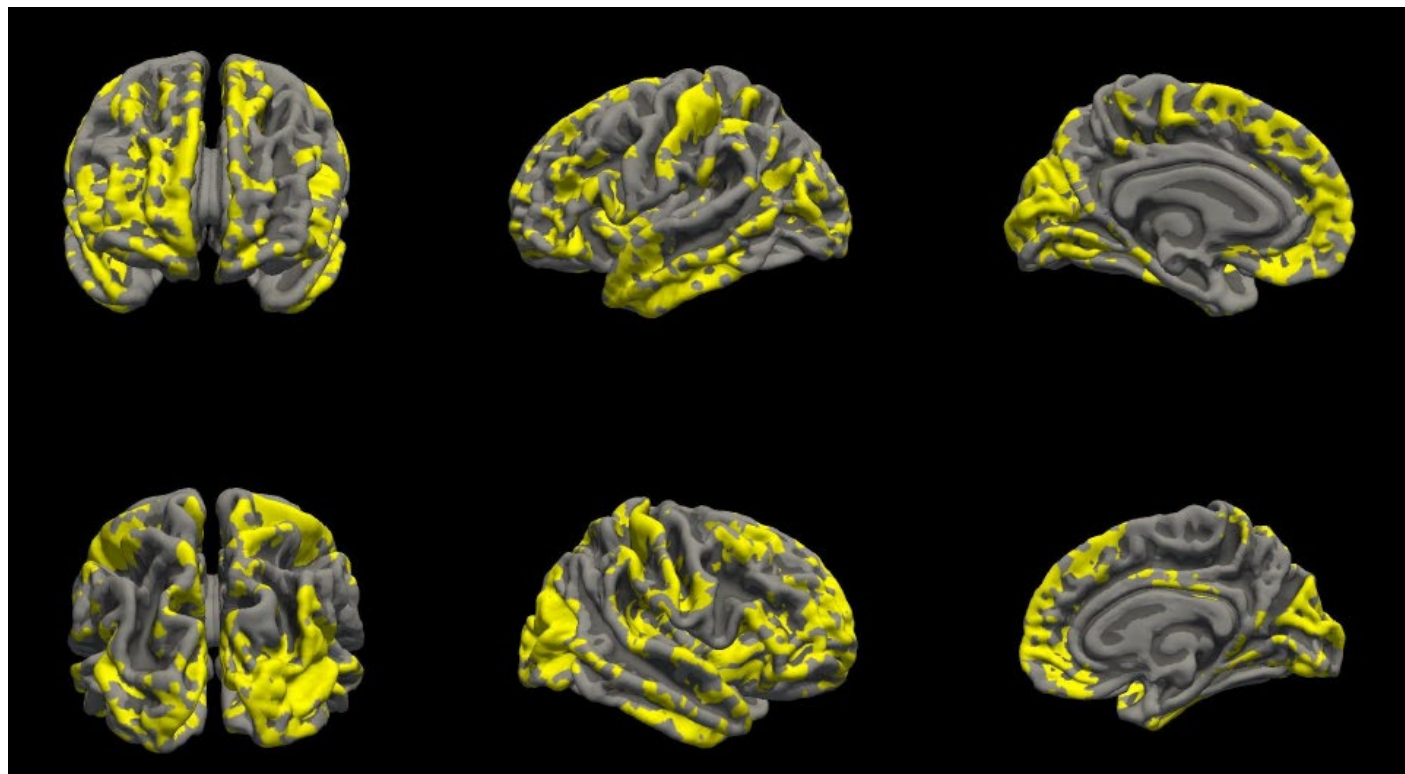
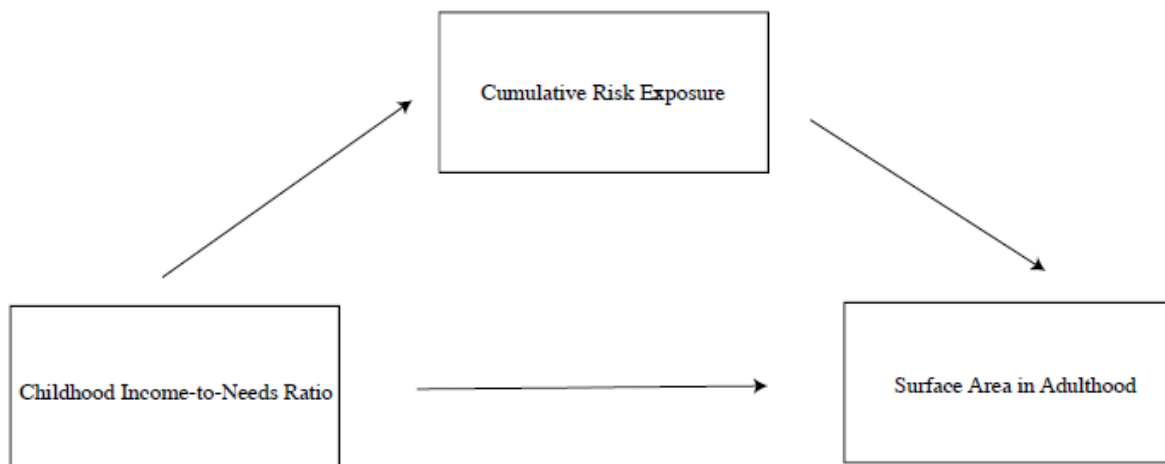


Family Income at Age 9

- Current (adulthood) income was not associated with neural activity

Mediating Role of Childhood Exposure to Multiple Stressors





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Overall Discussion

- **Developmental Origins of Mental Health Disorders**
 - Neural embedding of childhood adversity
 - Childhood adversity such as poverty and exposure to multiple stressors
 - Altered morphology, function, and connectivity among the amygdala and prefrontal cortex
 - Increase risks for emotion and behavioral regulation abilities across lifespan
 - Childhood as a sensitive period
 - Prevention for reducing early life adversity

Modification of the Environment through Interventions

- Amount of years living in poverty from ages 11-18 were associated with lower amygdalar volumes and more negative association with resting –state functional connectivity in emotion regulation networks.
- Participants of parents that had participated in the supportive parenting intervention did not have the association between number of years living in poverty and amygdalar gray matter volume and emotion regulation network functional connectivity at age 25.

Timing vs. Duration of Adversity Exposure

- **Biological embedding model** (Finch & Crimmins, 2004; Hertzman, 1999)
 - Developmental timing (sensitive period) of risk exposures and brain development would be valuable for informing interventions
- **Accumulative models** (Kuh & Ben-Shlomo, 2004)
 - Adversity begets adversity: longer exposure to adversity may contribute to an accumulation of chronic stress and lead to more severe damage in neurobiological systems.

Adaptive or Maladaptive Plasticity?

- **Allostatic Load Model** (McEwen, 2012)
 - Chronic stress causes disruptions of brain structure and function that are the precursors of later impairments in learning and behavior and chronic physical and mental illnesses
- **Active Calibration Model** (Ellis & Del Giudice, 2014)
 - Processes to optimize the individuals' adaptation to and resulting fitness for a particular environment, whether threatening or nurturing



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 - National Institute of Child Health and Human Development (NICHD) R01 HD090068, R21 HD078797 (PI: Kim)
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