Early Maternal Deprivation and Human Amygdala-Prefrontal Cortex Development

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• No disclosures
Early-Life Stress Sample

- Timing of adversity exposure
- Previous institutional (PI) care
Emotional Phenotypes are Vulnerable to Adversity

- Infants reared in orphanages exhibit physical growth and behavioral delays (Hostetter et al., 1991; Rutter et al., 1998)
- Can show remarkable recovery in a number of cognitive and physical health domains (Hostetter et al., 1991; Rutter et al., 1998)
- Emotional behavior may show long-term effects (Nelson et al., 2002; Rosenblum; 2001)
  - Emotional reactivity
  - Stress reactivity
  - Increased fear/anxious behavior
  - Increased arousal
- Brain
  - Regionally specific effects
Hippocampus

Control

CIS

Control

Hippocampus

Amygdala

Amygdala

Mitra et al., 2005

Magarinos & McEwen., 1995

Vyas et al., 2002

Number of spines (per 10μm)

Control

CIS

D

0

2.5

5.0

7.5

*
Developmental Onset

Amygdala Functional Reactivity

Age (years)
Amygdala-mPFC connectivity development

Developmental Onset

Age (years)

Amygdala Functional Reactivity
• Assessing amygdala functional development in response to threat

• 45 healthy participants (4-22 years old)
• Passive viewing of fear faces (press to neutral)
  – Event-related design
  – 3T Siemens (UCLA)
Mock MRI Scanner
Amygdala reactivity to fear faces is highest in early childhood & declines with age

Gee et al., 2013, J Neuroscience

p=0.002, corrected

Negative correlation with age
Developmental *valence-switch* in amygdala-mPFC connectivity

Gee et al., 2013, *J Neuroscience*
Early Separation from Mother (in rodents)

Amygdala Structure

Ono et al., 2008

Amygdala Function

Moriceau et al., 2004

Connectivity (Amygdala-mPFC)

Callaghan & Richardson, 2011

Mediated by high levels of stress hormone (CORT)
Early-Life Stress in Humans: Maternal Deprivation
2 Samples – Cornell & UCLA

NYC Sample (Cornell)
93 children
- 51 PI
  - 78% female, 22% male
  - Mean age = 8 years old (4-12 years old)
  - 73% Asia, 27% Eastern Europe
  - Majority (94%) placed in orphanage within 1st year
  - Majority adopted within 1st 2 years (80%)
  - IQ = 101 (SD = 12)
- 42 Comparison
  - sex, age group matched

LA Sample (UCLA)
314 children/adolescents
- 109 PI
  - 68% female, 32% male
  - Mean age = 9 years old (3-17 year old)
  - 49% Eastern Europe, 40% Asia
  - Majority (81%) placed in orphanage within 1st year
  - Majority adopted within 1st 3 years (80%)
  - IQ=101 (SD=16)
- 205 Comparison
  - 53% female, 47% male
  - Mean age = 9 years old (3-17 years old)
Anxiety/Internalizing problems

(NYC - Cornell)

(Casey*, Glatt*, Tottenham* et al., 2009)

(UCLA)

Goff...Tottenham, in press
Early adversity associated with larger amygdala volumes

Tottenham, Hare, Quinn et al., 2010
Caregiving X Emotion

Tottenham, Hare, Millner et al., 2011

\[ Y = -5 \]

\[ p < 0.01, \text{corrected} \]
Amygdala Reactivity following Early-Life Stress

Gee et al., 2013, PNAS

Functional Activation within Anatomically Defined ROI

y = 5
Replication across two sites

NYC (Cornell)

Early Exp X Emotion, p < 0.01, corrected

Los Angeles (UCLA)

Early Exp Effect, p<.005, corrected
Early-Life Stress

Salivary Cortisol (Post-MRI Measure)

2.78(1.39)*

Amygdala-mPFC Connectivity

-.05(.02)**

-.41(.20)č*

-.28(.23)č'

**p<.01
*p<.05

Gee et al., 2013, PNAS
% with Negative Connectivity Valence

Children  | Adol
COMPARISON
23%  | 56%

61%  | 63%

Gee et al., 2013, PNAS
Main effect of Early Experience
Main effect of Amygdala-mPFC Connectivity

Gee et al., 2013, PNAS
Posited Sensitive Period for Experience (Amygdala Reactivity)

Early-Life Stress

Developmental Onset

Amygdala Functional Reactivity
Amygdala Hyperactivity

Functional emergence

Amygdala-mPFC Connectivity Development

Age (years)
Conclusions

- **Normative development:**
  - Amygdala functionally reactive to fear stimuli by early childhood
  - Developmentally normative high amygdala reactivity that declines with age
  - Amygdala-mPFC functional connectivity immature in childhood, switch to negative connectivity around transition to adolescence

- **Environmental influences:**
  - Early postnatal stress associated with structural and functional changes in amygdala
  - Emergence of adult-like amygdala-mPFC connectivity during childhood

- Amygdala-mPFC connectivity as long-term mediator of early postnatal stress and later emotional behavior
- Early-life stress may shift these curves earlier (ontogenetic adaptation)
- Childhood as a potential sensitive period for environmental shaping
Acknowledgements

Tottenham Lab (UCLA):

Christina Caldera
Dominic Fareri, Ph.D.
Jessica Flannery
Laurel Gabard-Durnam, M.A.
Bonnie Goff, M.A.
Kate Humphreys, M.A
Daniel Lumian, M.A.
Eva Telzer, Ph.D. (U Illinois)

Susan Bookheimer, Ph.D. (UCLA)
Elizabeth Sowell, Ph.D. (USC)
Ty Cannon, Ph.D. (Yale)
Regina Sullivan, Ph.D. (NYU)
John Piacentini, Ph.D. (UCLA)
BJ Casey, Ph.D. (Sackler/Cornell)

Funding Sources:
NIMH (R01MH091864) BRAINS R01 (NT)
Dana Foundation (NT)
NSF Graduate Research Fellowship (DGG)
APF Koppitz Child Psychology Fellowship (DGG)

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