Neurobiology of Emotion Regulation Development & the Role of the Early Environment

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Emotion Regulation

• Def: The ability to control strong emotional impulses for the sake of achieving alternative goals

Poor Emotion Regulation is associated with:

• Mental Health Difficulties (Anxiety, Depression, ADHD)
• Low Academic Achievement
• Increased risk for Drug Abuse/Obesity
• Increased aggression/violence
• Risky sexual behaviors

• Development:
  • Emotion Regulation takes a LONG time to develop
• Nurture:
  • Emotion Regulation skills are highly dependent on early experiences
Association between Adversity and Later Socio-Emotional Outcomes
Prefrontal Cortex

Emotion & Regulation

Infancy
Childhood

Sensitive Periods:

Coordination of Amygdala Inputs

Emotional Attention and Learning
The child is father of the man.
(William Wordsworth)

**Developmentally, Amygdala is Driver**
Emergence and peak in mental disorders during adolescence

One in five adolescents have a mental illness that will persist into adulthood

- ADHD, conduct disorder
- Anxiety disorders
- Mood disorders
- Schizophrenia
- Substance abuse
- Any mental illness

Age in years

Lee et al., 2014
• *Why* are early caregiving environments important for later behavior?
• How can later experiences *rescue/protection* brain development following adversity?
Amygdala-mPFC Aims

- Normative changes occurring during development
- Role of caregiving
- Early caregiving adversity during development
Human Amygdala Development

- Anatomical: Significant development postnatally
  (Gilmore et al., 2011; Giedd et al., 1996; Humphrey, 1968; Ulfig, et al., 2003)

<table>
<thead>
<tr>
<th>Year 0</th>
<th>Year 1</th>
<th>Year 2</th>
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<tbody>
<tr>
<td>Amygdala_R</td>
<td>515.4 mm$^3$</td>
<td>1057.0 mm$^3$ (change 105%)</td>
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Uematsu et al., 2012
Amygdala Function

- **What is the course of amygdala functional reactivity to threat cues across development?**

- **45 healthy participants (4-22 years old)**

- **Passive viewing of fear faces (press to neutral)**
Early Amygdala Functional Response in development:

Negative correlation with age

Gee et al., 2013 J Neuroscience
Emotional Attention and Learning

Prefrontal Cortex

Regulation/Coordination of Amygdala Inputs

mPFC

BOLD Signal

Amygdala

Emotional Attention and Learning

Hare et al., 2008

mPFC-Amygdala Functional Connectivity
Slow Maturation of Amygdala-mPFC functional connectivity:

Functional connectivity (psychophysiological interaction) – Amygdala seed (functionally defined):

Negative correlation with age

Developmental Valence-Switch

Gee et al., 2013 J Neuroscience
In response to emotional stimuli:
Tracing studies (Rodents): amygdala-originating inputs to the mPFC earlier than mPFC-originating inputs to the amygdala

(Cressman et al., 2010; Bouwmeester, Wolterink, Van Ree, 2002; Bouwmeester, Smits, Van Ree, 2002)
Effects of mPFC Manipulation on amygdala reactivity: Children vs Adolescents

Task 1: Stroop

Task 2: Fear Faces

Gee et al., in prep
IMaGES: Graph Theoretical Approach
(Ramsey et al., 2010)

w/Steve Hanson & Catherine Hanson
Scan 1:

Resting-state Connectivity

Stimulus-elicited Connectivity

\[ r_{mPFC} = 0.292 \]
\[ r_{rPFC} = 0.291 \]

Scan 2:

Resting-state Connectivity

Stimulus-elicited Connectivity

\[ r_{mPFC} = 0.401 \]
\[ r_{rPFC} = n.s. \]
\[ r_{rPFC} = 0.495 \]
\[ r_{rPFC} = 0.521 \]

Amygdala-mPFC connectivity associations

Amygdala seed

\[ Y = -3 \]

Effect of stimulus-elicited connectivity on future resting-state connectivity across development

A

Predicted change (beta weight in resting-state 2 years later)

Age 7 years  
Age 11 years  
Age 15 years

B

Amygdala-mPFC connectivity stabilization

plastic  
adolescence  
stable
Childhood Sensitive Periods:
Emotional Learning in Childhood is Enduring and Potent

*Efficacy of Stimuli Learned during Development*

Learning

Usage (Anxiolytic Properties)

(Early in Life) (Maturity)

(Yang et al., 2012, PNAS)
(Raineki et al., 2012, J Neuro)
Parent as an ingredient for Brain development
Mother’s regulated presence blocks amygdala activity & Fear Learning
Parent support is less effective in buffering cortisol stress reactivity for adolescents compared to children

Hostinar, Johnson, & Gunnar, 2015
Regulated Parents Buffer Stress Neurobiology in Children

Fear Faces

Fear Learning

Amygdala Reactivity (Parent–Stranger)

Parent Buffering

Amygdala Reactivity to Fearful Faces

Childhood, Adolescence, Young Adulthood

Parent−Stranger

CHILD ADOL

Amyg−mPFC Connectivity

STRONGER

Moderated by attachment security

Gee*, Gabard-Durnam et al., 2014 Psych Science
Parent Unavailable

CORT → Amygdala → Fear

Parent Available

mPFC → CORT → Amygdala → Fear
Parent-Child Neuro-Environmental Loop

Putative mechanisms of parental buffering

Parent unavailable

↑ CORT

↑ Amygdala

↑ Fear

Parent available

↓ CORT

↓ Amygdala

↓ Fear

Sensitive period

Amygdala reactivity & fear

Phasic modulation by parent

Parent CAN influence

Reduced parental regulation

Childhood Adolescence Adulthood

Callaghan & Tottenham 2016 Neuropsychopharmacology
Severe Parental Neglect
Hypothalamic-Pituitary-Adrenal (HPA) Axis
Amygdala

Mitra et al., 2005

Vyas et al., 2002

Magarinos & McEwen., 1995
Developmental Rate and Vulnerability

• Periods of the most rapid change heighten the vulnerability of a particular brain region to environmental exposure (Lupien et al., 2009)
Early-life Stress can accelerate the Development of Emotion Regulation Neurobiology

(Ono et al., 2008; Moriceau et al., 2004; Callaghan & Richardson, 2011)

Developmental Adaptation  >> change in brain development to meet immediate needs

Trade-offs: benefits/costs
Absence of Parental Care

- Significant rebound upon adoption
- Significant heterogeneity
- Significantly elevated risk for emotion regulation difficulties
## 2 Samples – Sackler/WCMC & UCLA

### NY Sample (Sackler/WCMC)
- **N=93**
  - 51 PI
    - 40 female, 11 male
    - Mean Age = 8 years old; 4-12 years old
    - 73% **Asia**, 27% Eastern Europe
    - Majority (94%) placed in orphanage within 1st year
    - Majority (80%) adopted within 1st 2 years
    - IQ = 101 (SD = 12)
- 42 Comparison group
  - Sex, age matched

### LA Sample (UCLA)
- **N=243**
  - 94 PI
    - 61 female, 33 male
    - Mean age = 8.7 years old (4-17 year old)
    - 49% **Eastern Europe**, 35% Asia
    - Majority (81%) placed in orphanage within 1st year
    - Majority (80%) adopted within 1st 3 years
    - IQ=101 (SD=16)
- 149 Comparison
  - Sex, age matched
Anxiety/Internalizing problems
(NYC - Cornell)

Casey et al., 2009, Dep & Anxiety

(UCLA)

Goff et al., 2013 Neuroscience
Anxiety & Institutional Care
Random assignment
Zeanah et al., 2009

% with Internalizing Disorder

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<thead>
<tr>
<th></th>
<th>Institutionalized</th>
<th>Foster Care</th>
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<tr>
<td></td>
<td>50</td>
<td>20</td>
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Amygdala Development following Maternal Deprivation
Adjusted Volume (relative to Cortical Volume)

- Amygdala
- Hippocampus
- Caudate

Comparison to Early Adopted
Comparison to Later Adopted

* Early adversity associated with larger amygdala volumes

Tottenham, Hare, Quinn et al., 2010
Amygdala volume (adjusted for cortical volume)

Age adopted out of orphanage (mos)

$F(1,33) = 8.37, p < .007$

Tottenham, Hare, Quinn et al., 2010
Amygdala Volume Associated with More Trait Anxiety

Toenham, Hare, Quinn et al., 2010
Elevated Amygdala Reactivity Following Early Deprivation

New York (Sackler/WCMC)
*Tottenham et al., 2011 Dev Science

Los Angeles (UCLA)
Gee et al., 2013 PNAS
Face Go/Nogo Task

Accuracy

- Children
- Adolescents
- Adults

**Accuracy**

- pos
- neg
- PI_pos
- PI_neg

*To*enham, (Hare, (Quinn, et al., 2011)

Tottenham, Hare & Casey, 2011
Tottenham, Hare, Quinn, et al., 2010
Appraisals of Trustworthiness

Green et al., 2016 J Child Psychology and Psychiatry
Amygdala discrimination of trustworthiness is associated with age of adoption

Green et al., 2016 J Child Psychology and Psychiatry
Behavioral and neural discrimination of trustworthiness is associated with future separation anxiety.

Green et al., 2016 J Child Psychology and Psychiatry
Maternal Deprivation results in decreased eye contact

Comparison

% of time making eye contact

0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1

Eye-tracking       Dyadic Interaction

To*enham,(Hare,(Millner(et(al.,(2011((Dev(Science((

Tottenham, Hare, Millner et al., 2011 Dev Science
Amygdala activity predicts amount of eye contact

![Graph showing the relationship between Right Amygdala Signal (Beta Value) and eye tracking and live interaction. The graph includes data points for Eye Tracking (solid circles) and Live Interaction (dashed circles). The R² values for Eye Tracking and Live Interaction are 0.22 and 0.28, respectively.]

Tottenham, Hare, Millner et al., 2011 Dev Science
Decision Making under Risk:

Exploration vs. Exploitation Choice:

Keep pumping (risk explosion & loss of earnings)
OR
Cash-In (keep earnings thus far)
Early care group → Exploitation “Cash-Ins” → Anxiety

Humphreys et al., in press, Dev Psychobio
Parental Deprivation and Amygdala-mPFC Connectivity

PPI: Fear>BL

Short-term Adaptation

Gee et al., 2013 PNAS
Early Caregiving Experience

Salivary Cortisol (Post-MRI Measure)

- 2.78(1.39)*
- .41(.20)_c*
- .28(.23)_c

Amygdala-mPFC Connectivity

- -.05(.02)**

**p < .01
*p < .05

Gee et al., 2013 PNAS
Amygdala hyperactivity

Functional emergence

Amygdala-mPFC connectivity development
% with negative connectivity valence

COMP

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<tr>
<th>Children</th>
<th>Adol</th>
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<tr>
<td>23%</td>
<td>56%</td>
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PI

<table>
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<tr>
<th>Children</th>
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<tr>
<td>61%</td>
<td>63%</td>
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Gee et al., 2013 PNAS
Adult-like neural phenotypes associated with lower CURRENT trait anxiety in PI group

Controlling for age

Gee et al., 2013 PNAS
Telomere Length

- **Younger Children** (3-5 years old) - n = 132
- **Children** (6-10 years old) - n = 115
- **Adolescents** (11-17 years old) - n = 93

Comparison of Telomere Length (T/S; normed; mean ± 1SE)
Depression in PI Youth
Telomere Length and Depressive Symptoms

Future MDD T-scores vs. Telomere length (T/S; normed)
Telomere Length and NAcc Reactivity

Parameter estimates (beta weights; mean ± 1 SE)

Comparison
PI

Children
Adolescents

MDD t-scores

NAcc response to happy faces (parameter estimates)
Parent-child relationships

Comparison

PI

RCADS Internalizing Symptoms

Security Scale

VanTieghem et al., 2016, Dev & Psychopathology
Parental Buffering of Stress Responses

Callaghan et al., in prep
Parental “buffering” of amygdala associated with decreased future internalizing problems
"Neuro-Environmental Loop of Plasticity"

Premature Exposure to "Independence"

Parent unavailable

↑ CORT

Parent available

↓ mPFC

↓ CORT

↑ Amygdala

↓ Amygdala

↑ Fear

↓ Fear

Sensitive period

Amygdala reactivity & fear

Phasic modulation by parent

Parent CAN influence

Reduced parental regulation

Childhood  Adolescence  Adulthood
Conclusions

• Human amygdala-mPFC circuitry develops very slowly
  – Value of Childhood/Juvenile Period

• Early caregiving experiences shape the neurobiology of emotion regulation
  – Social Regulators during Immaturity
  – Perhaps helping to maintain an immature neural state

• Early caregiving adversity may change developmental pacing through activity-dependent processes (short-term benefits/longer-term costs) >> understanding through lens of adaptations
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- Christina Caldera
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