Transgenerational Risk Factors in the Transmission of Depression

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Acknowledgements

- Postdoc and Grad Students
  - Max Owens, PhD
  - Katie Burkhouse, PhD
  - Cope Feurer, PhD
  - Claire Foster, MS
  - Kelly Gair, BS
  - Andrea Hanley, PhD
  - Elana Israel, MS
  - Kiera James, PhD
  - Ashley Harrison Johnson, PhD
  - Anastacia Kudinova, PhD
  - Pooja Shankar, MS
  - Lindsey Stone, PhD
  - Aliona Tsypes, PhD
  - Mary Woody, PhD
- Postbacs
  - Celeste Beauvilaire, BS
  - Nia Cole, BS
  - Sara Buseman, BA
  - Amber Gan, BA
  - And many more…
- Undergrad RAs
  - Caroline Cahill
  - Catharine Carfagno
  - Jennifer Cunneen
  - Matthew Larocchia
  - Stefania Skaliotis
  - Francesca Varriano
  - And so many more!
- Additional Collaborators
  - Leslie Brick, PhD
  - Peter Gerhardstein, PhD
  - Sherryl Goodman, PhD
  - Paul Hastings, PhD
  - Andreas Keil, PhD
  - John McGeary, PhD
  - Jennifer Silk, PhD
- Families who made the research possible

NIMH National Institute of Mental Health

Eunice Kennedy Shriver NICHD National Institute of Child Health & Human Development

Outline

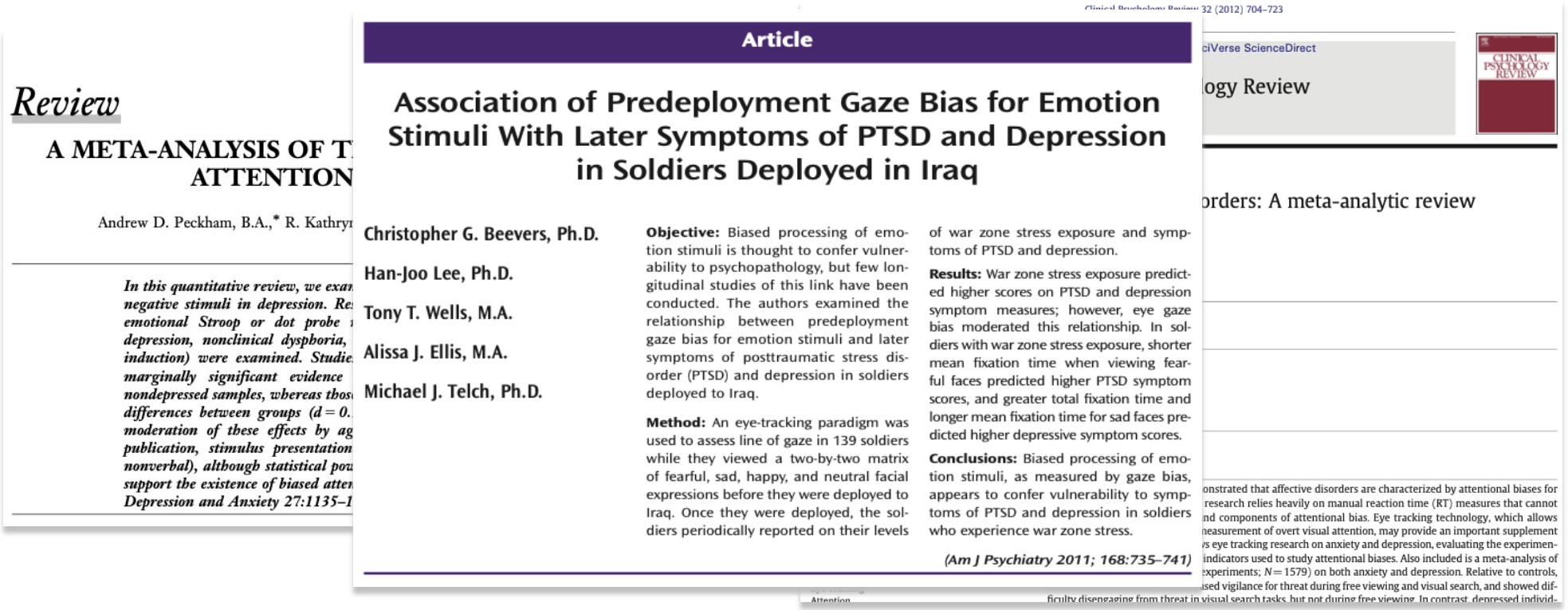
1. Attentional biases as a mechanism of risk for the intergenerational transmission of depression
   - How the form and function of these biases may change as children age into adolescence
2. The role of environmental stress
   - Family, peer, and neighborhood stress

1. Attentional Biases

Attentional Biases and Depression

- Depressed and at-risk individuals are hypothesized to exhibit preferential attention toward, or difficulty disengaging attention from, depression-relevant stimuli (e.g., sad faces)
  - Should be specific to depression-relevant stimuli
  - Should be specific to biases in sustained attention
- There is strong evidence for these biases in depressed and at-risk adults and adolescents

Attentional Biases in Adolescents and Adults



Review

A META-ANALYSIS OF T… ATTENTION…

Andrew D. Peckham, B.A.,* R. Kathryn…

In this quantitative review, we exam… negative stimuli in depression. Re… emotional Stroop or dot probe … depression, nonclinical dysphoria, … induction) were examined. Studie… marginally significant evidence … nondepressed samples, whereas thos… differences between groups (d = 0.… moderation of these effects by ag… publication, stimulus presentation … nonverbal), although statistical pow… support the existence of biased atten…
Depression and Anxiety 27:1135–1…

Article

Association of Predeployment Gaze Bias for Emotion Stimuli With Later Symptoms of PTSD and Depression in Soldiers Deployed in Iraq

Christopher G. Beevers, Ph.D.
Han-Joo Lee, Ph.D.
Tony T. Wells, M.A.
Alissa J. Ellis, M.A.
Michael J. Telch, Ph.D.

Objective: Biased processing of emotion stimuli is thought to confer vulnerability to psychopathology, but few longitudinal studies of this link have been conducted. The authors examined the relationship between predeployment gaze bias for emotion stimuli and later symptoms of posttraumatic stress disorder (PTSD) and depression in soldiers deployed to Iraq.

Method: An eye-tracking paradigm was used to assess line of gaze in 139 soldiers while they viewed a two-by-two matrix of fearful, sad, happy, and neutral facial expressions before they were deployed to Iraq. Once they were deployed, the soldiers periodically reported on their levels of war zone stress exposure and symptoms of PTSD and depression.

Results: War zone stress exposure predicted higher scores on PTSD and depression symptom measures; however, eye gaze bias moderated this relationship. In soldiers with war zone stress exposure, shorter mean fixation time when viewing fearful faces predicted higher PTSD symptom scores, and greater total fixation time and longer mean fixation time for sad faces predicted higher depressive symptom scores.

Conclusions: Biased processing of emotion stimuli, as measured by gaze bias, appears to confer vulnerability to symptoms of PTSD and depression in soldiers who experience war zone stress.

(Am J Psychiatry 2011; 168:735–741)

Clinical Psychology Review 32 (2012) 704–723

…iVerse ScienceDirect

…ogy Review

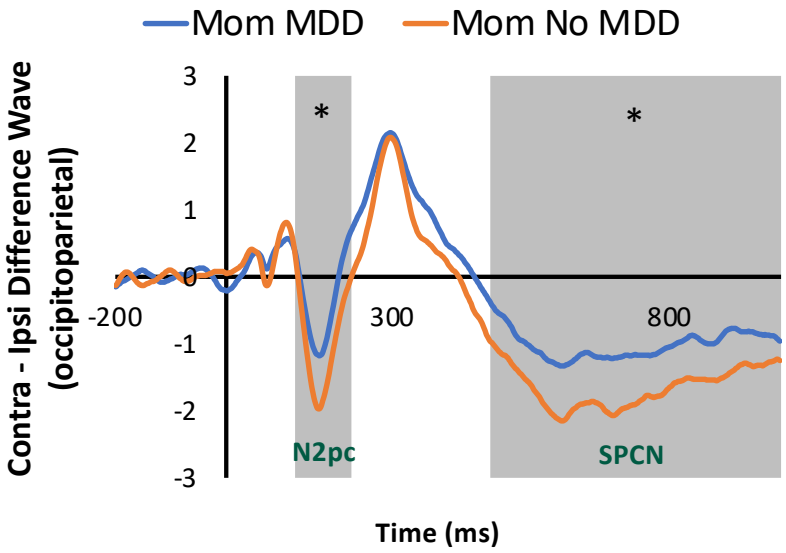
CLINICAL PSYCHOLOGY REVIEW

…orders: A meta-analytic review

…onstrated that affective disorders are characterized by attentional biases for … research relies heavily on manual reaction time (RT) measures that cannot …nd components of attentional bias. Eye tracking technology, which allows …measurement of overt visual attention, may provide an important supplement …s eye tracking research on anxiety and depression, evaluating the experimen… …indicators used to study attentional biases. Also included is a meta-analysis of …experiments; N = 1579) on both anxiety and depression. Relative to controls, …ised vigilance for threat during free viewing and visual search, and showed dif… ficulty disengaging from threat in visual search tasks, but not during free viewing. In contrast, depressed individ…

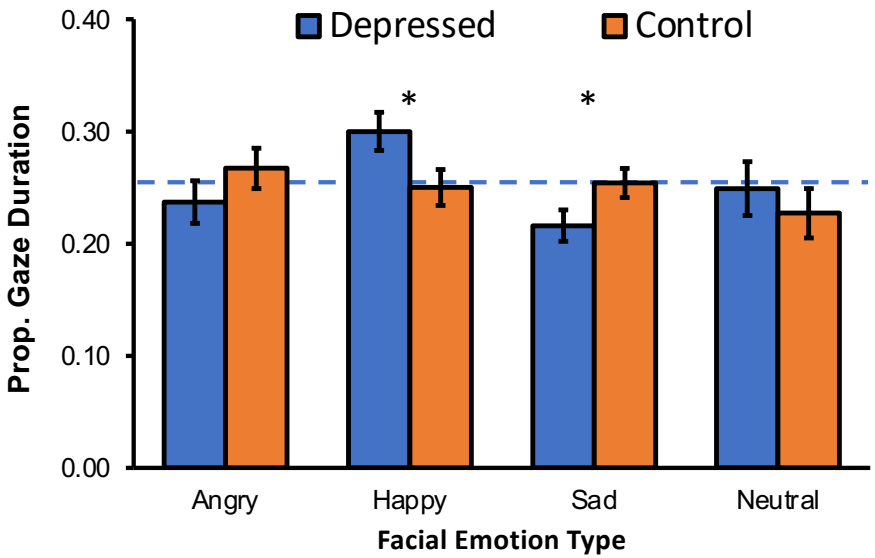
Depressed and At-Risk Children Exhibit Reduced Attention to Sad Faces

Posner: ERPs to Sad Faces



Gibb et al. (2016) J Abnormal

Passive Viewing: Eye Tracking

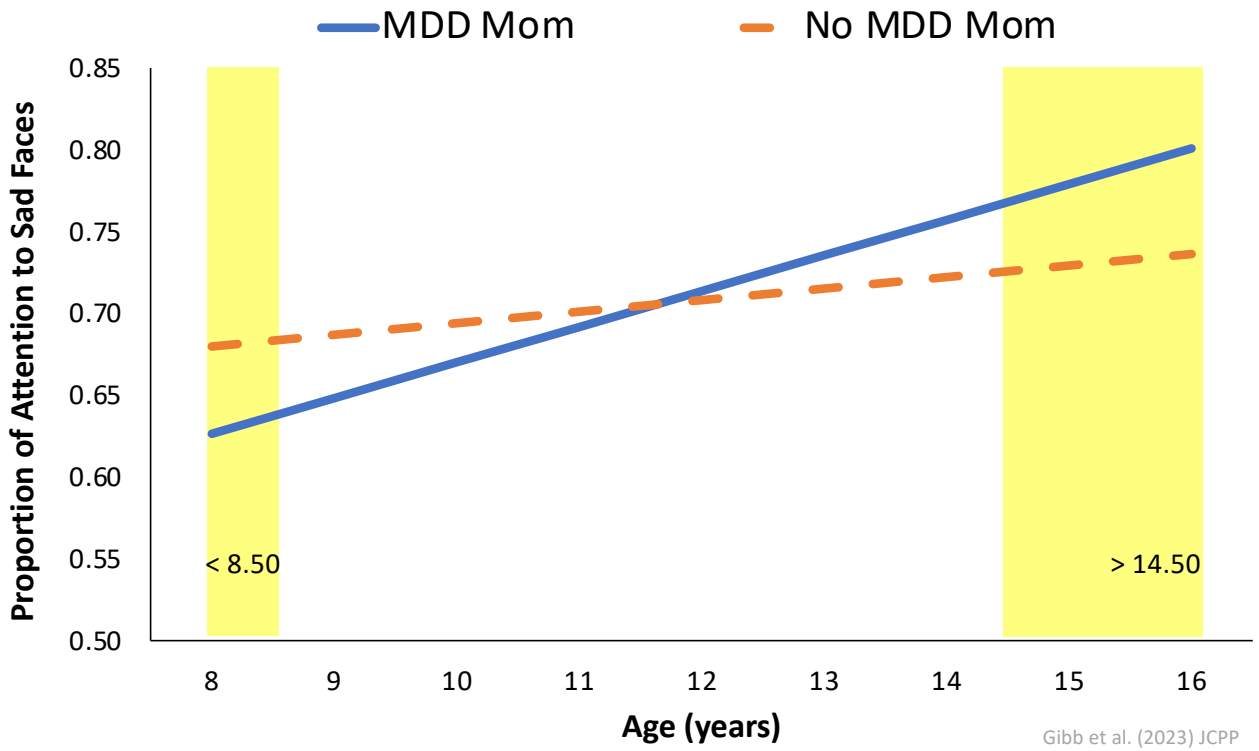


Harrison & Gibb (2015) JCCAP

Does the form or direction of attention bias change across development?

Trajectories of Gaze to Sad Faces among Children of Mothers with and without MDD

- 8–14-year-old children of mothers with (*n* = 123) and without (*n* = 119) a history of MDD during their child's life
- Attention biases to sad, happy, and angry faces assessed every 6 months for 2 years
- Effects were:
  - Specific to sad faces
  - Maintained when controlling for kids' concurrent dep sxs

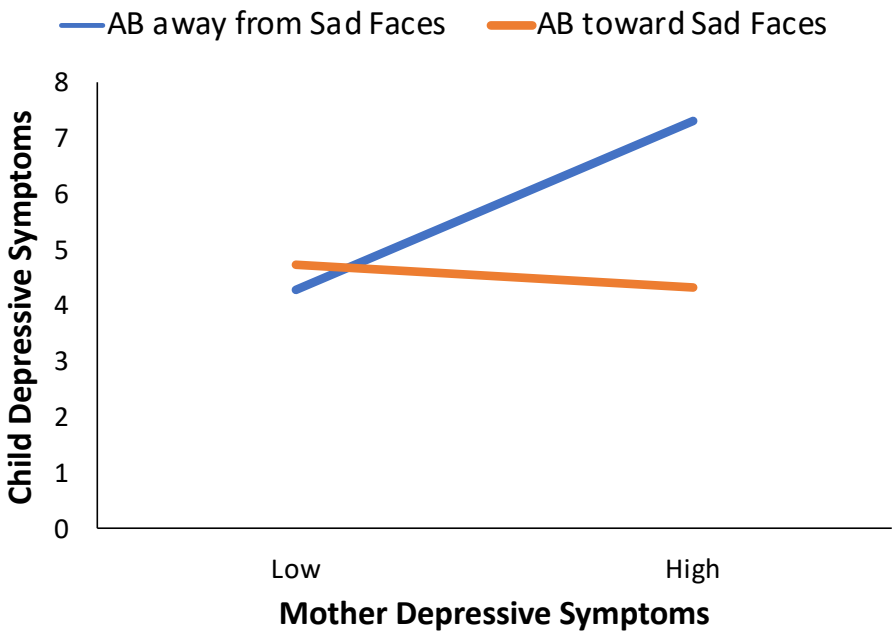


Gibb et al. (2023) JCPP

Developmental Shifts in the Impact of Attention Biases

8-12 year olds (*n* = 74)

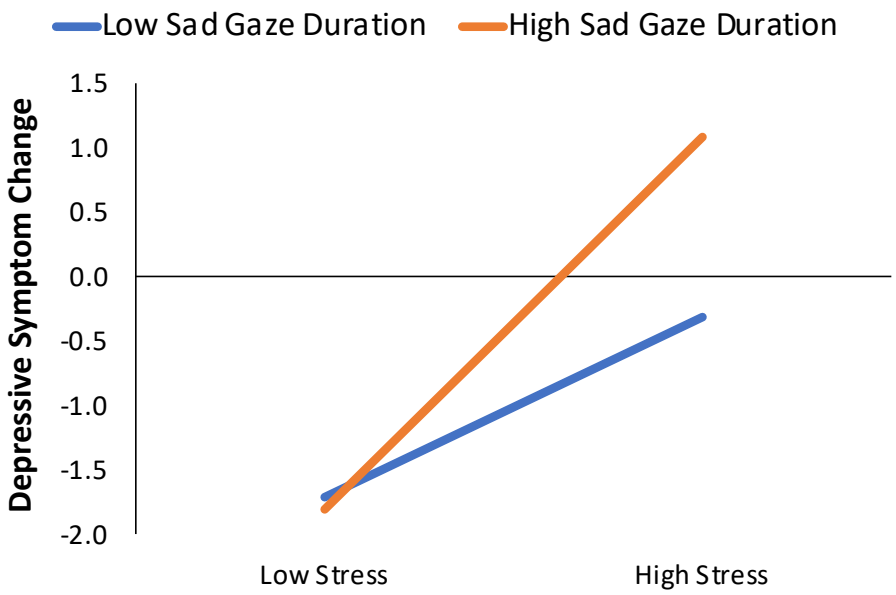
Assessments every 2 weeks for 6 weeks



Gibb et al. (2009) JCCAP

13-17 year olds (*n* = 95)

Assessments every 2 weeks for 8 weeks



Feurer et al. (2020) JCCAP

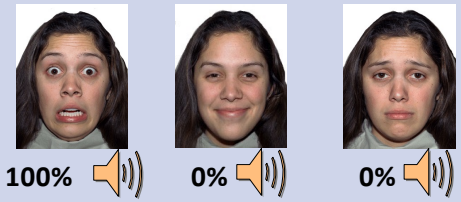
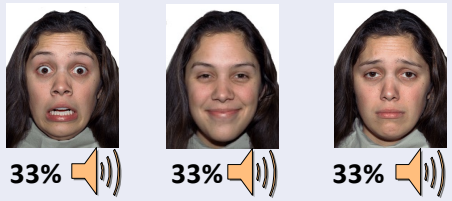
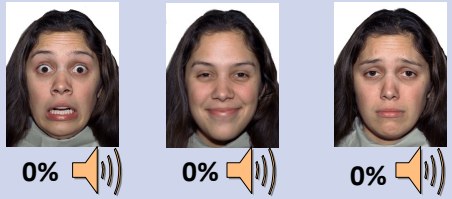
Gibb et al., (2016) J Abnormal

Can we model the development of attentional biases?

Conditioning Model for the Development of Attentional Biases

- Children's attentional avoidance is thought to reflect an emotion regulation strategy (cf. Gross)
- Children's age may be relevant in at least two ways:
  - Conditioning effects may be stronger for younger children
  - The direction of attentional biases may change across development

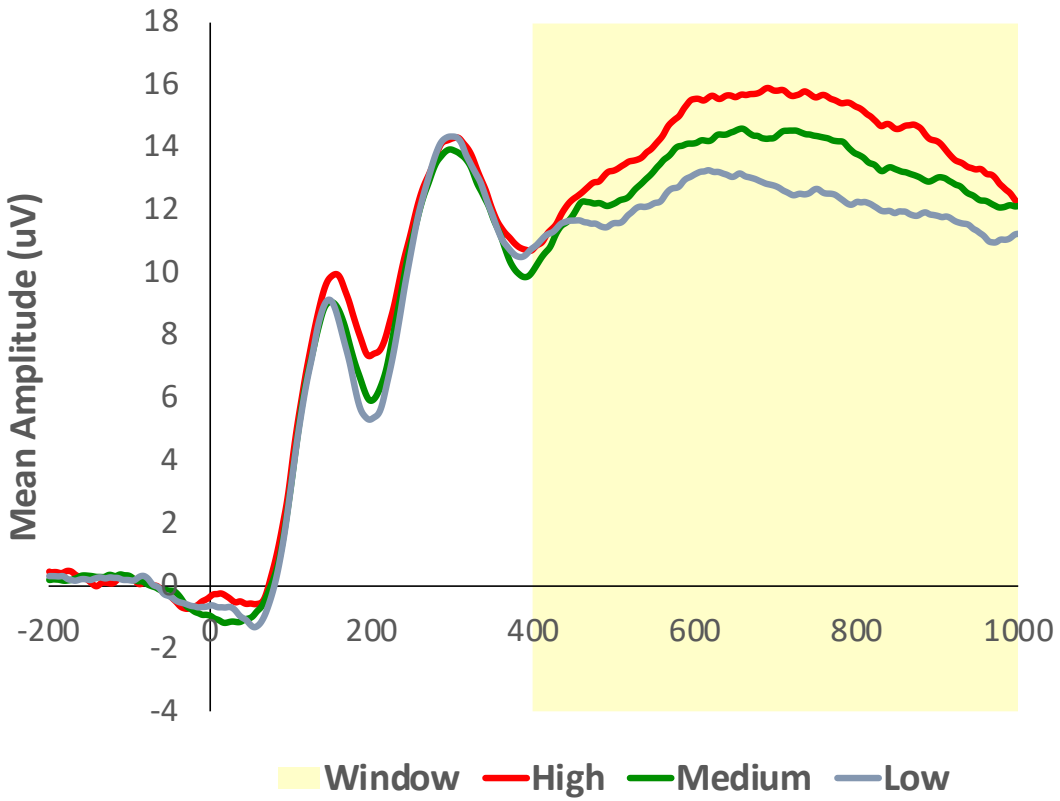
Experimental Tasks

	Conditioning Task (Dot Probe)
Active Training (*n* = 44)	
Active Control (*n* = 42)	
No Sound (*n* = 61)	

Generalization Task (Morphed Faces)	
All Participants	Facial stimuli from a novel set morphed in 10% increments from neutral to full emotion (afraid, happy, sad)
	Presented on the screen for 3 seconds during which EEG was recorded
	Following this, asked to provide a behavioral response to indicate the emotion conveyed by each expression

Sample Neutral > Afraid Continuum

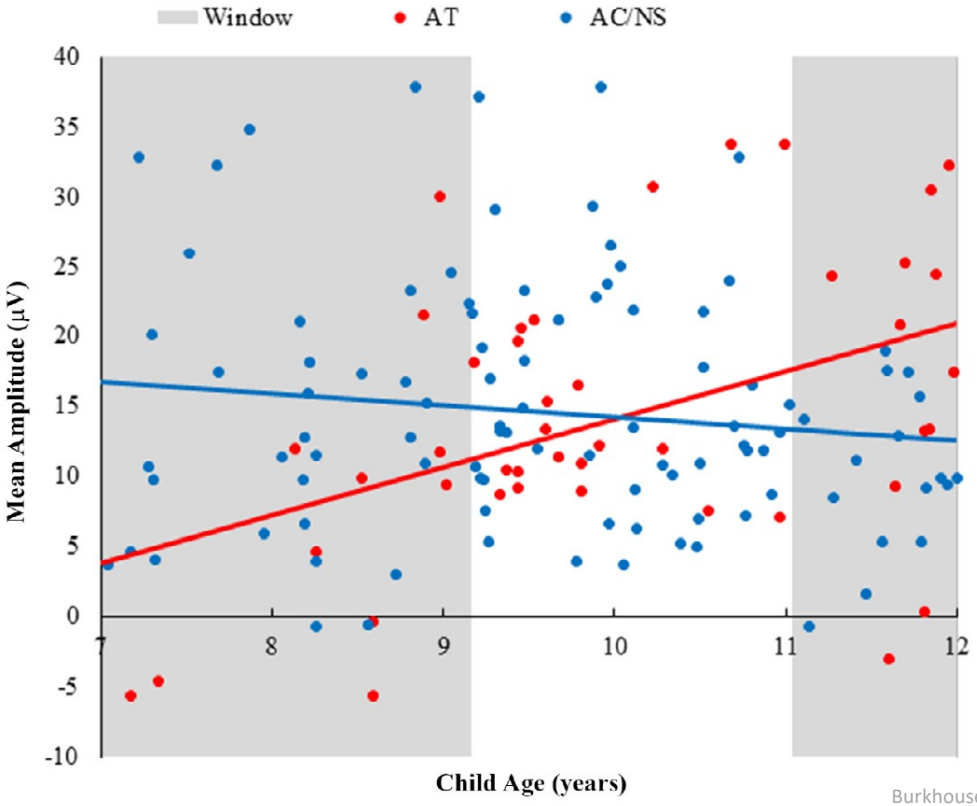
LPP: Afraid Faces



Burkhouse et al. (2019) *JECP*

Regions of Significance: High Morph Afraid Faces

- Results maintained when statistically controlling for:
  - Children's state anxiety and sadness before or after the conditioning task
  - Children's symptoms of anxiety and depression
  - Parents' symptoms of anxiety and depression
  - Parents' history of anxiety disorders and MDD



Burkhouse et al. (2019) *JECP*

How early in development can we detect these biases?

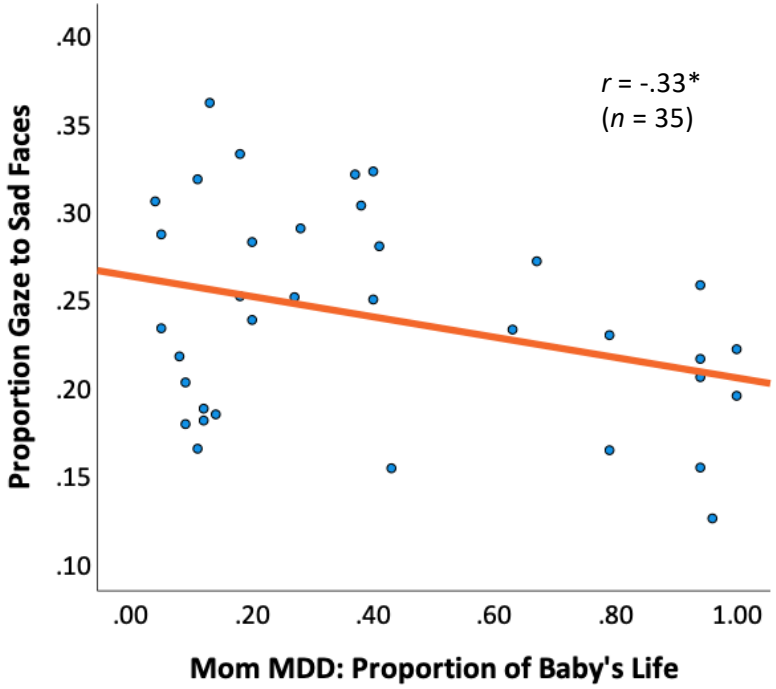
Attention Biases in 6-12 month olds

Two eye-tracking tasks
- Passive Viewing: 4 faces (5 s trials)
- Visual Paired Comparison: 2 faces (1.5 s trials)

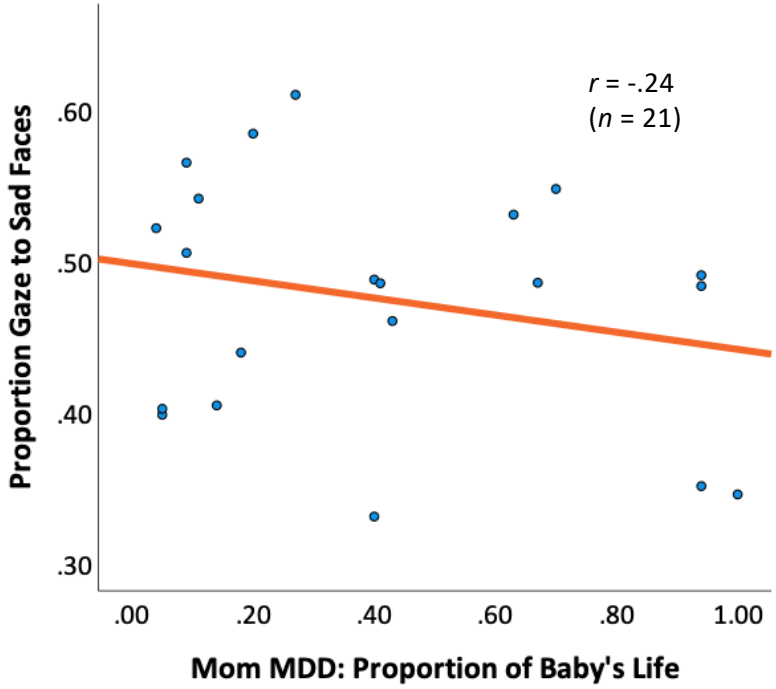
Two interaction tasks: Free Play and Sad (3 min)
- Behavioral coding of infant attention (coded)
- Infant and mom psychophysiology (e.g., ECG)

Computer Tasks

Passive Viewing Task

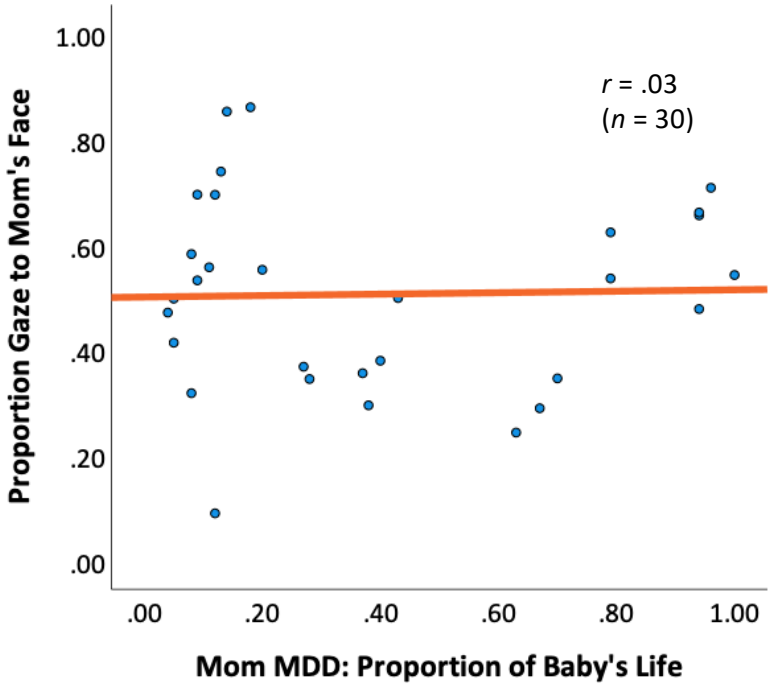


Visual Paired Comparison Task

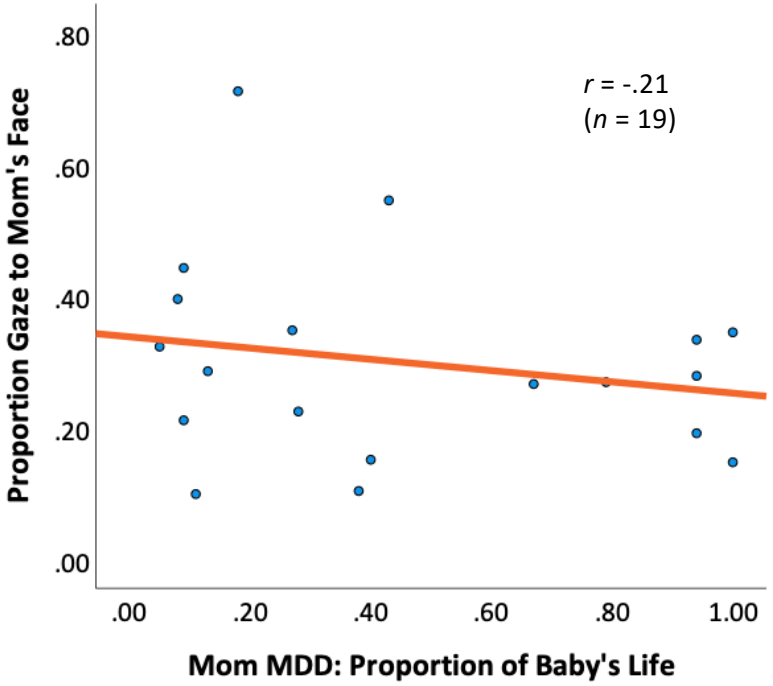


Interaction Tasks

Free Play



Sad Interaction



Current Project

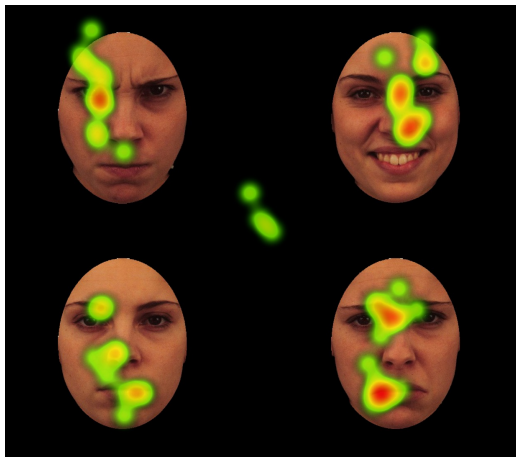
Aims

- Fine-grained assessment of attention biases in offspring of mothers with a history of MDD during the child's life vs. no history of depression
- Determine how the biases may change as children age into adolescence
  - 7-15 years old at baseline with assessments every 6 months for 2 years
- Evaluate potential contributors to developmental shift in bias
  - E.g., pubertal development, rumination, sleep
- Examine links with youth depression and how this may change from childhood to adolescence

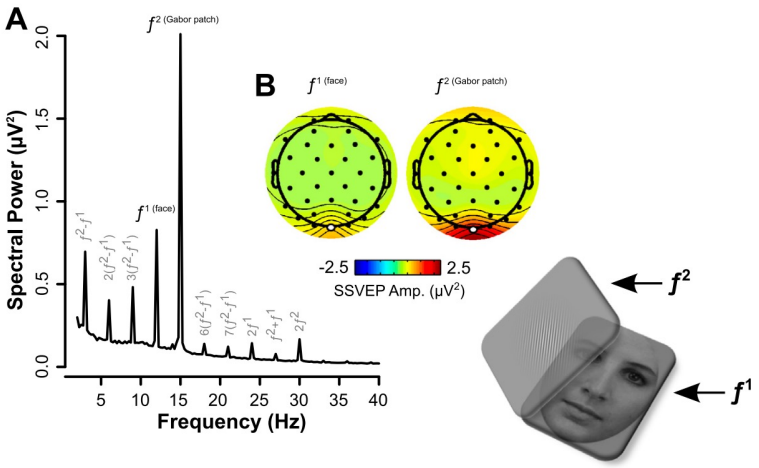
Assessments

Computer-based Tasks

Screen-based Eye Tracking



SSVEPs derived from EEG



Mother-Child Interaction Tasks

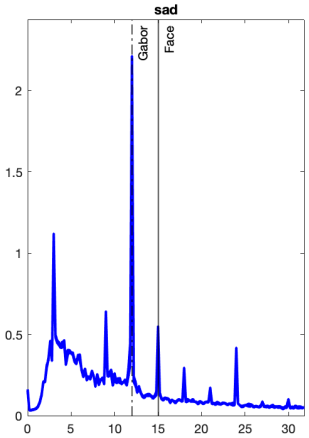
Mobile Eye Tracking

SSVEPs: Difficulty Inhibiting Attention to Sad Faces

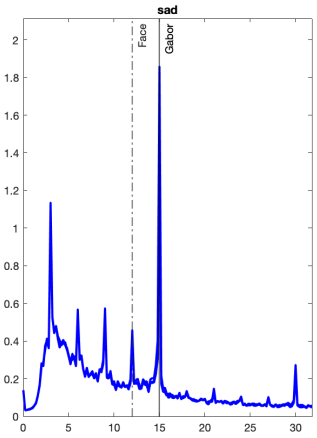
From James et al. (2022) *SLTB*

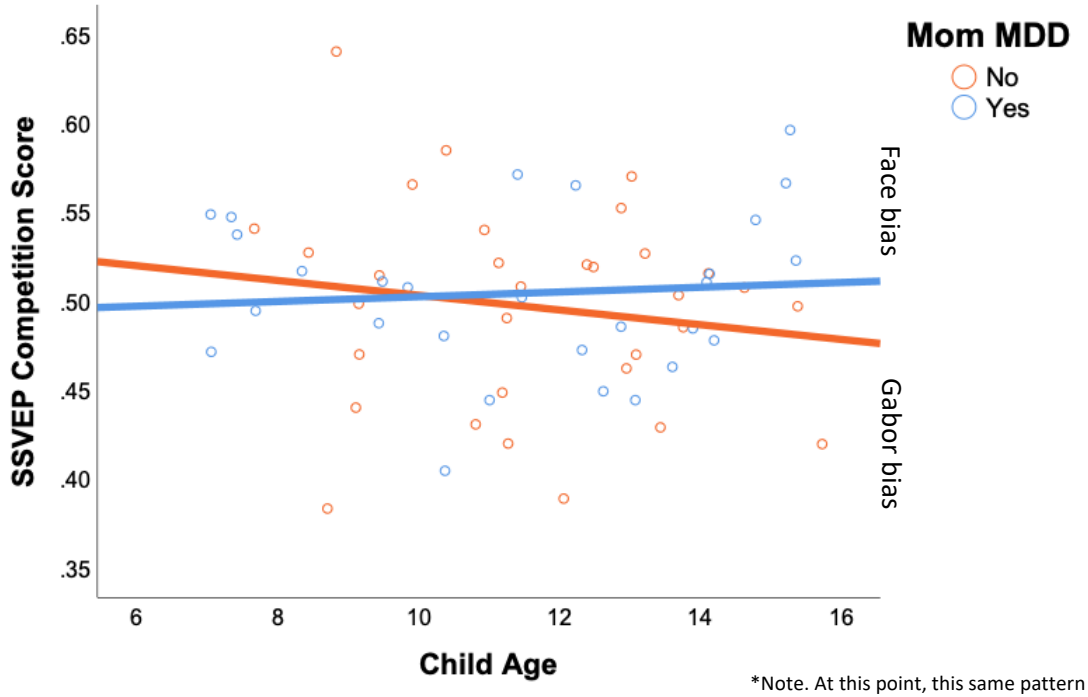
SSVEPs: Ability to Inhibit Attention to Sad Faces

Gabor: 12Hz
Face: 15Hz
(*n* = 30)



Face: 12Hz
Gabor: 15Hz
(*n* = 31)



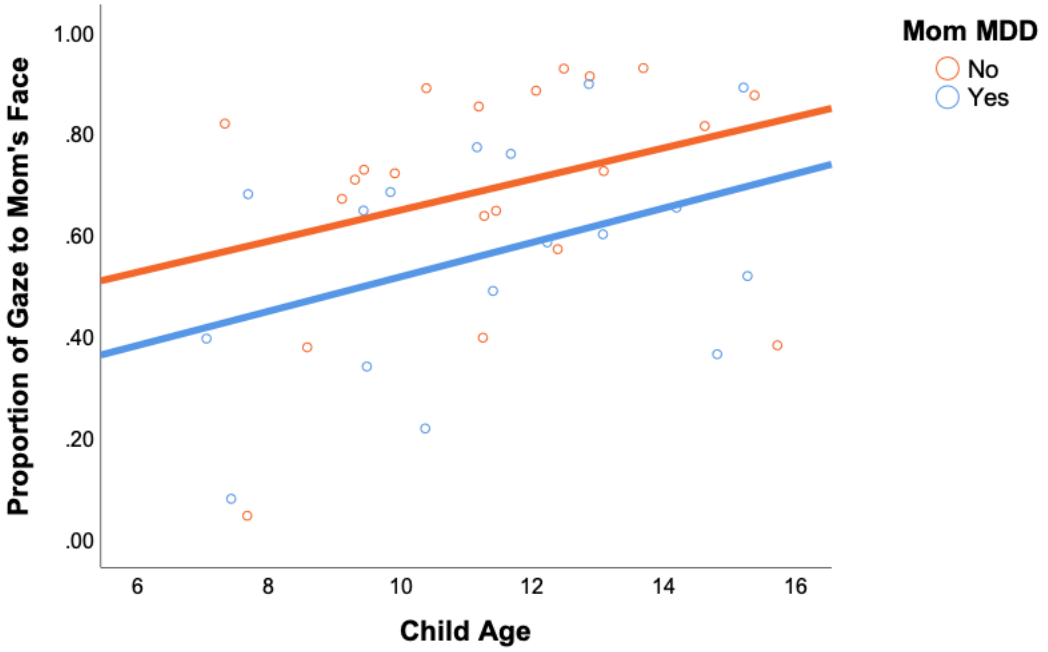


*Note. At this point, this same pattern is also seen for Angry and Happy faces

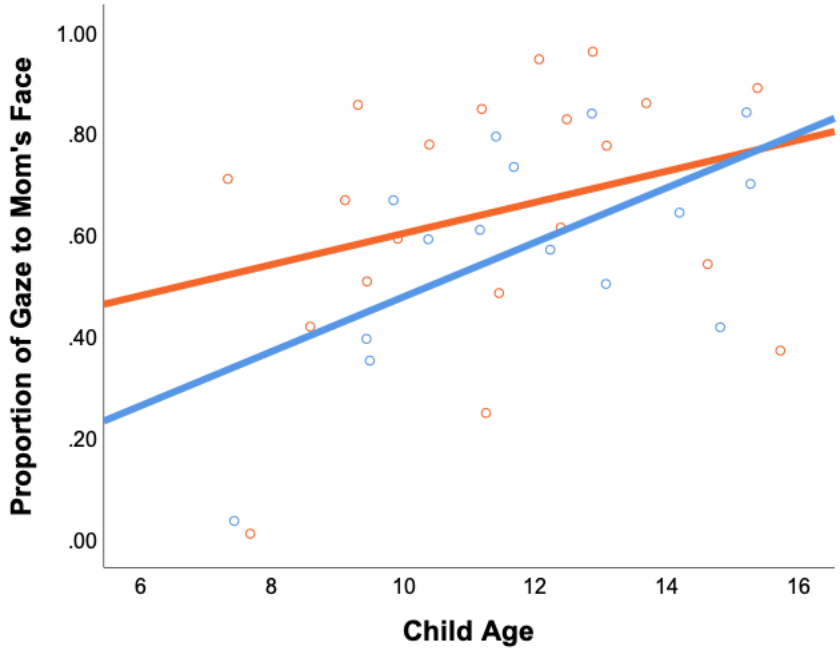
Eye Tracking Glasses: Attention to Mom During Mother-Child Interactions

Eye Tracking Glasses: Attention to Mom During Mother-Child Interactions

Vacation Planning
(*n* = 38)



Conflict Discussion
(*n* = 35)



Interim Conclusions: Attention Biases

- Overall, the findings support the hypothesis that form and function of attentional biases changes across development
- In children and infants, attentional avoidance may represent an emotion regulation strategy used to reduce arousal/negative affect associated with exposure to emotionally salient negative facial expressions
- During late childhood/early adolescence, however, the direction of attentional biases appears to shift to that observed in adults

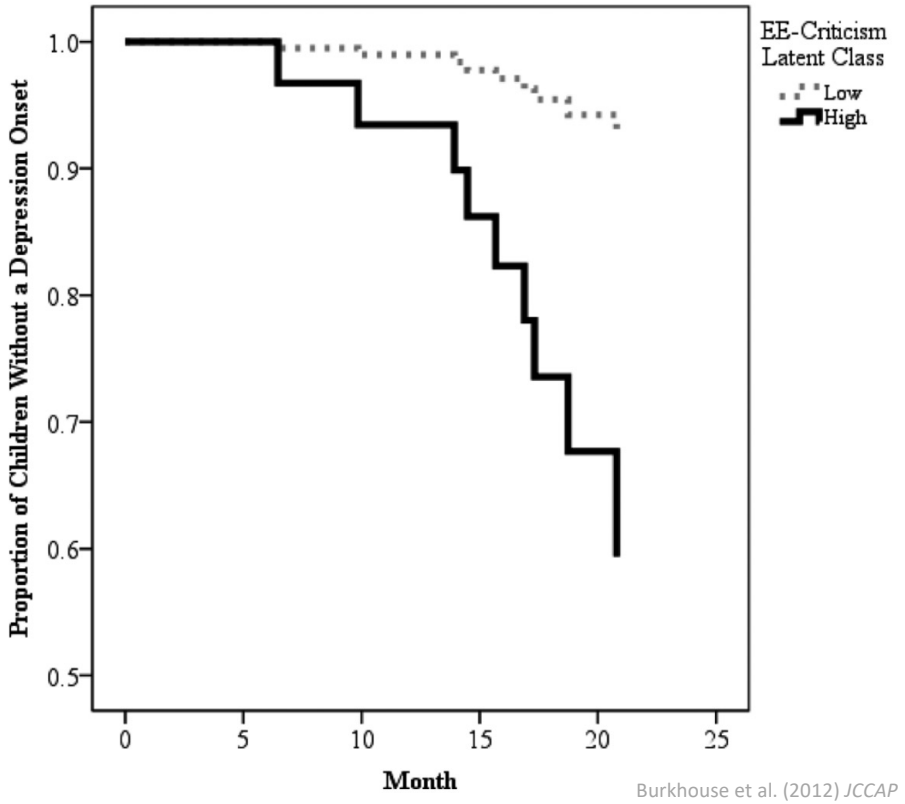
Interim Conclusions: Attention Biases

- Next steps
  - Examine infant/child ECG, time-locked to attention shifts, to test our hypotheses regarding the role of arousal
  - Using fEMG and computer-coded facial affect to examine mothers' facial expressions during the interactions
  - Examine mothers' attentional biases during the interactions

2. Environmental Influences

Maternal Criticism (EE-Criticism)

- 48 children (8-12 years old) of mothers with a history of MDD during their child's life
- EE-criticism coded from the Five-Minute Speech Sample (FMSS)
  - Mothers asked to "speak for 5 minutes, telling me what kind of a person [child's name] is and how the two of you get along together"
  - Assessed every 2 months for 6 months and LCA used to identify High vs Low EE-Crit classes
- New diagnoses of major and minor depression in the children assessed at a 20-month follow-up

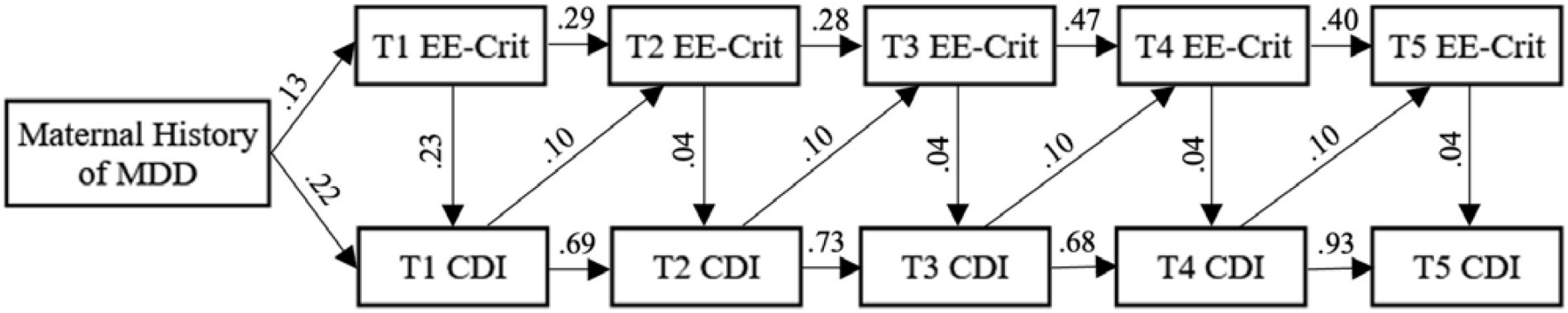


Burkhouse et al. (2012) *JCCAP*

Maternal Criticism (EE-Criticism)

255 children (8-14 years old) of mothers with and without a history of MDD

Assessments every 6 weeks for 2 years



Israel & Glbb (in press) *D&P*

Mother MDD and Children's Episodic and Chronic Life Stress

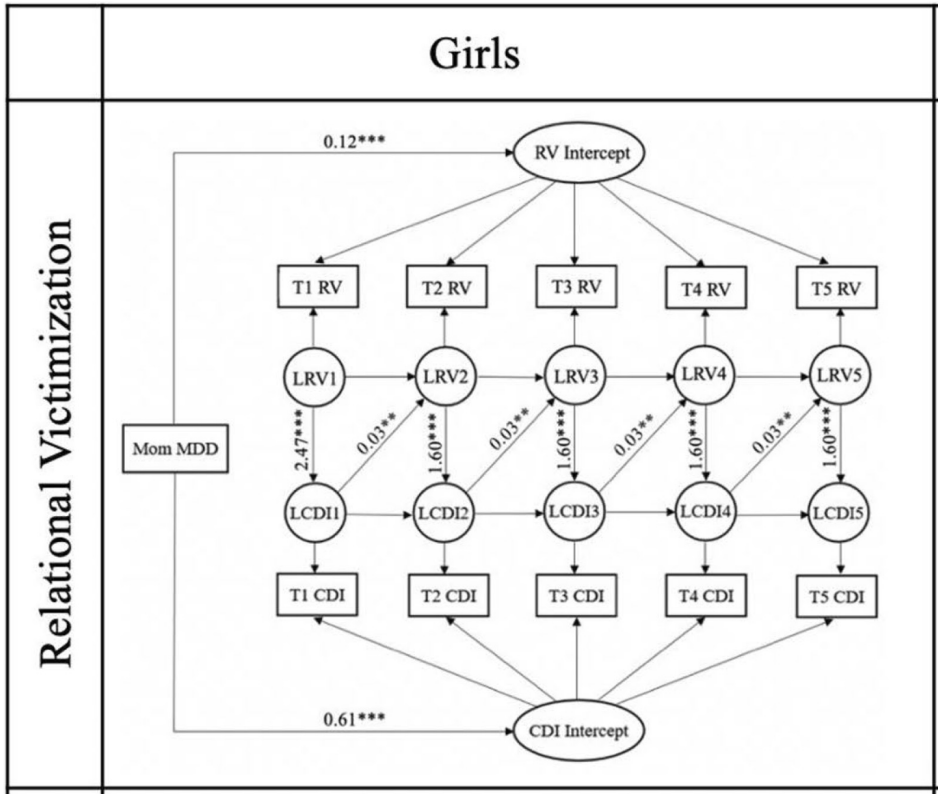
	Never Depressed Moms (n = 126)	Moms with Single MDD (n = 71)	Moms with Recurrent MDD (n = 58)
CS: Academic	1.91 (0.67)	2.20 (0.76)	2.03 (0.75)
CS: School Behavior	1.67 (0.43)	1.82 (0.53)	1.94 (0.67)
CS: Peer	2.26 (0.58)	2.44 (0.65)	2.70 (0.64)
CS: Mother-Child	2.07 (0.46)	2.22 (0.64)	2.42 (0.66)
CS: Other Family Members	2.35 (0.54)	2.71 (0.75)	2.81 (0.72)
ES: Dependent Interp.	0.53 (0.80)	*0.87 (1.05)*	1.33 (1.60)
ES: Independent Interp.	1.21 (1.25)	1.77 (1.90)	1.85 (2.46)
ES: Non-interpersonal	0.15 (0.30)	0.16 (0.37)	0.22 (0.41)

* All significant relations were maintained when (i) excluding children with a history of MDD, and (ii) statistically controlling for children's current depressive symptoms

Peer Victimization

255 children (8-14 years old) of mothers with and without a history of MDD

Assessments every 6 months for 2 years



Israel & Glbb (2023) RCAP

What about genetic influences?

Polygenic Risk Scores and Episodic Life Stress

- 180 children (8-14 years old; European ancestry) of mothers with (*n* = 81) or without (*n* = 99) MDD
- PRS derived from UK Biobank broad depression GWAS (Howard et al., 2018)
- Dependent and independent life stress assessed with the UCLA Life Stress Inventory for Children

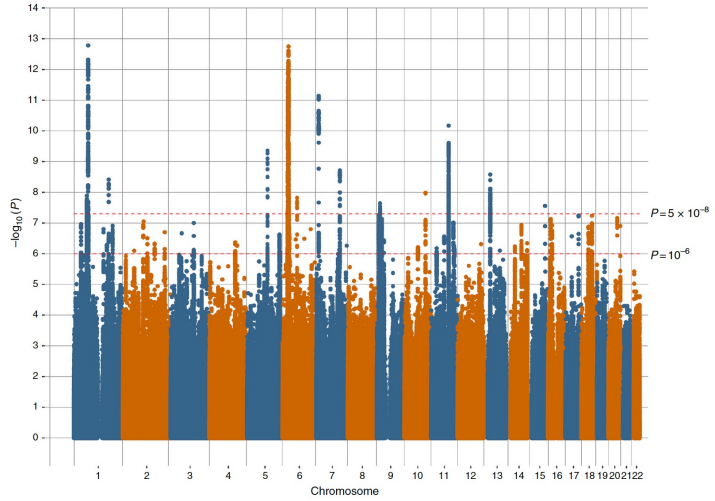
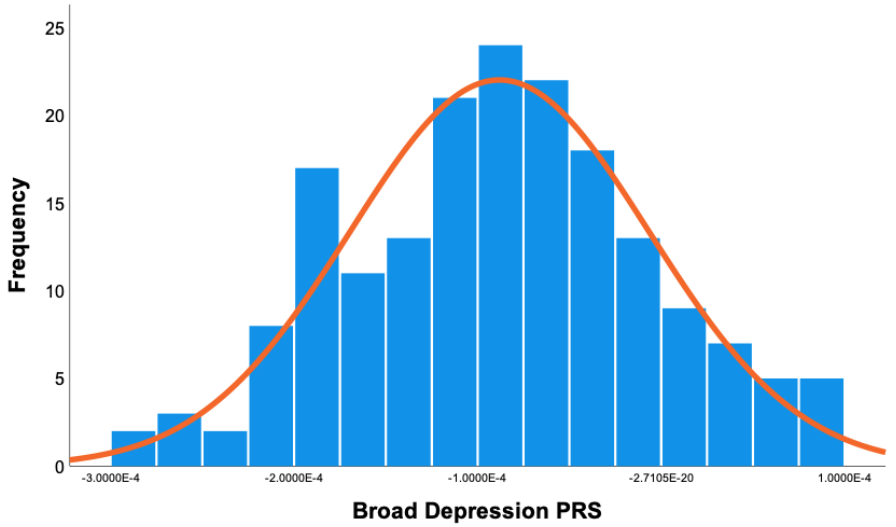


Fig. 1 Manhattan plot of the observed $-\log_{10}$ *P*-values of each variant for an association with broad depression ($n = 322{,}580$) in the UK Biobank cohort. Variants are positioned according to the GRCh37 assembly



Feurer et al. (2022) *JoPCS*

Polygenic Risk Scores and Episodic Life Stress

- 180 children (8-14 years old; European ancestry) of mothers with (*n* = 81) or without (*n* = 99) MDD
- PRS derived from UK Biobank broad depression GWAS (Howard et al., 2018)
- Dependent and independent life stress assessed with the UCLA Life Stress Inventory for Children

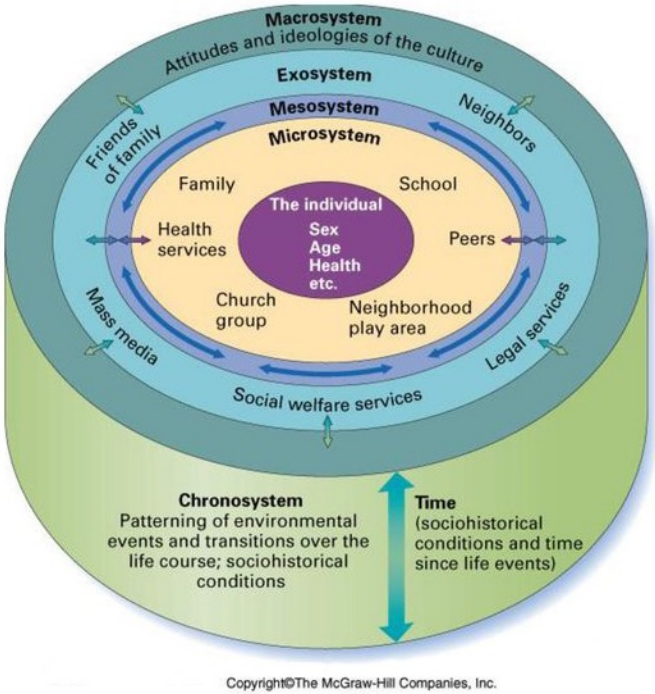
	Dependent Stress					Independent Stress				
Fixed effects	*B*	*SE*	*t*	$r_{\text{effect size}}$	*p*	*B*	*SE*	*t*	$r_{\text{effect size}}$	*p*
Step 1:										
Youth DEP-PRS	0.46	0.17	2.77	.20	.006	0.96	0.38	2.50	.18	.013
Step 2:										
Youth DEP-PRS	0.43	0.16	2.75	.20	.007	0.92	0.38	2.45	.18	.015
Mother MDD	0.12	0.03	4.53	.32	<.001	0.19	0.06	3.08	.23	.002

Note. DEP-PRS = Depression polygenic risk score; MDD = major depressive disorder (coded as follows: yes = 1, no = 0).

Feurer et al. (2022) *JoPCS*

Neighborhood Context

Brofenbrenner's Ecological Model

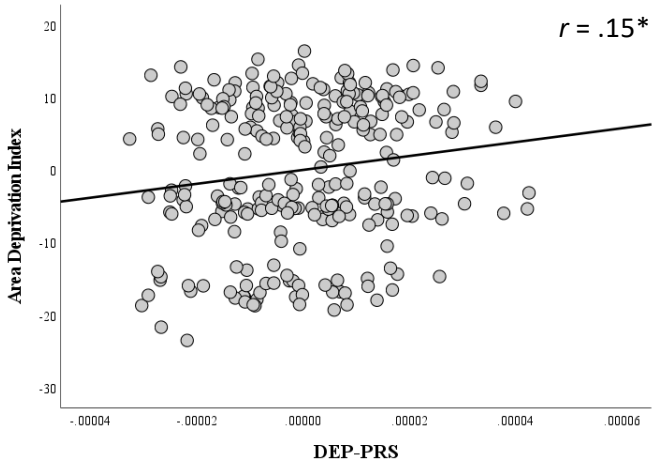


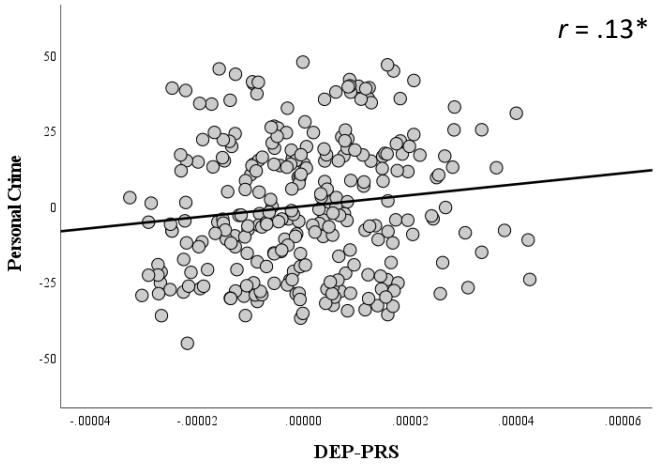
Neighborhood Characteristics

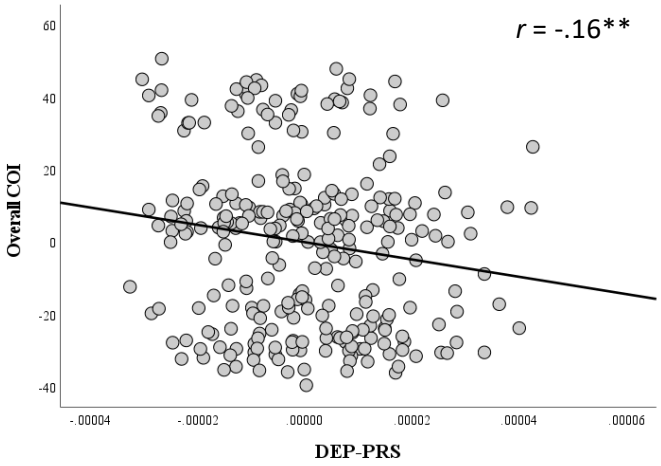
- Area Deprivation Index
  - Incorporates factors such as income, education, employment, and housing quality
- Neighborhood Crime
  - Personal and Property Crime
- Child Opportunity Index
  - Includes education, health and environment, and social and economic opportunities
- Zip-code level, nationally normed data based on participant address

Polygenic Risk Scores and Neighborhood Disadvantage

- 278 children (7-11 years old) of European ancestry
- PRS derived from UK Biobank GWAS (Howard et al., 2018)
- Census-derived indices: Area Deprivation, Neighborhood Crime, Childhood Opportunities





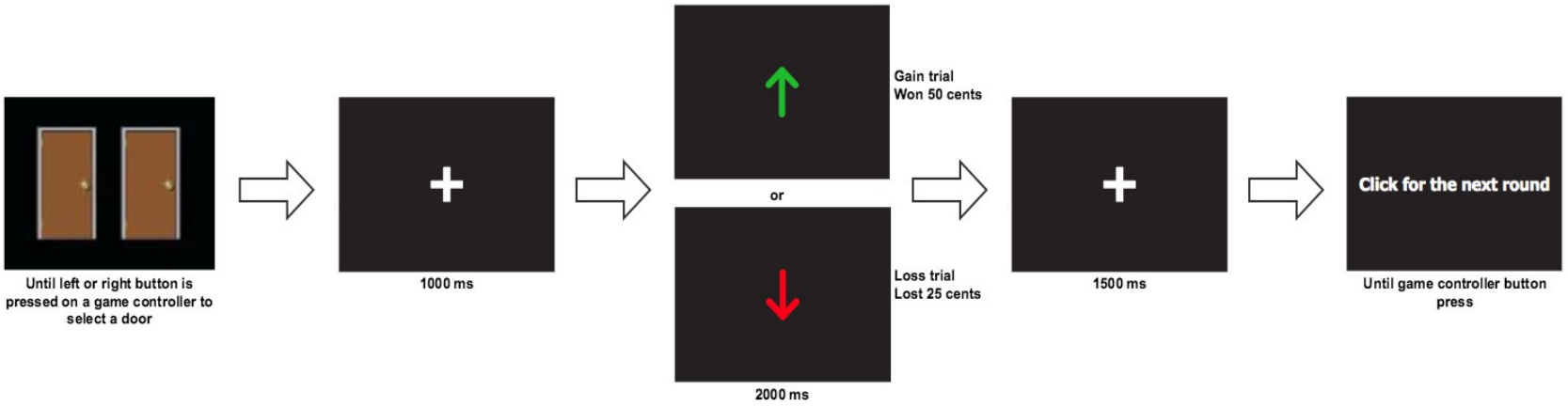


* All relations maintained when statistically controlling for family income and parent and child lifetime diagnoses of MDD and/or anxiety disorders

Feurer et al. (in preparation)

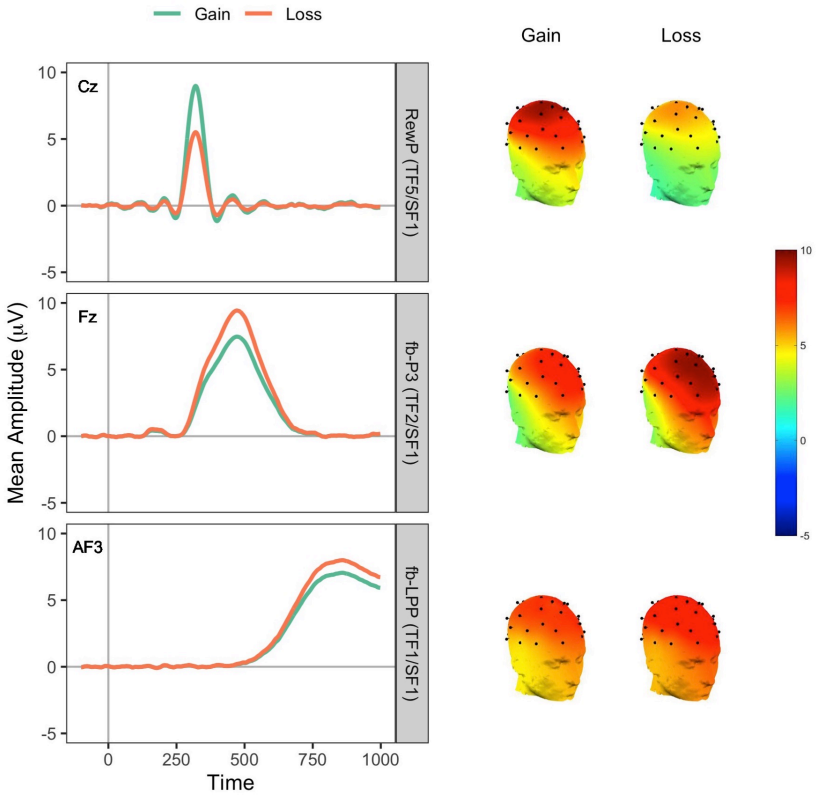
Neighborhood Disadvantage and Reward Processing

- *N* = 278 children (7-11 years old) of European ancestry (same sample as previous slide)
- Census-derived indices: Area Deprivation, Neighborhood Crime, Childhood Opportunities
- Reward outcome processing: RewP ERP component during Doors Task



Israel et al. (in preparation)

Neighborhood Disadvantage and Reward Processing



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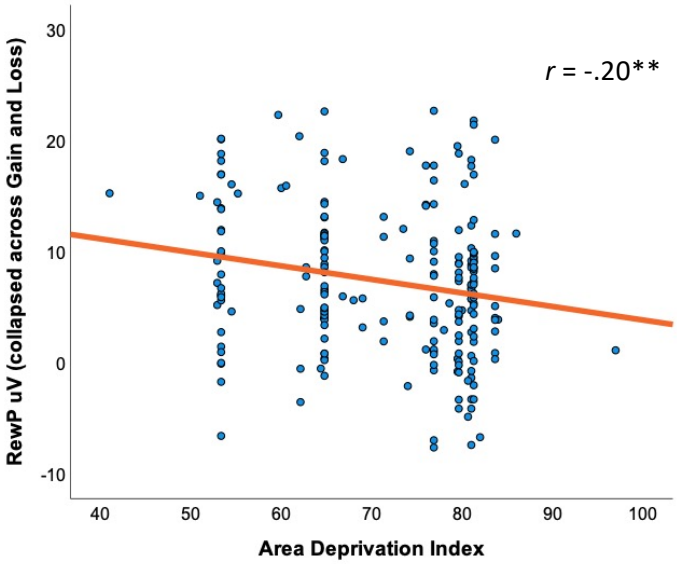
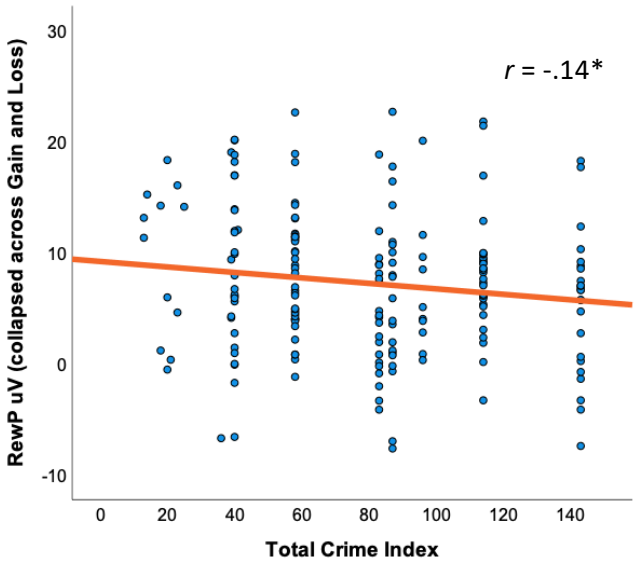
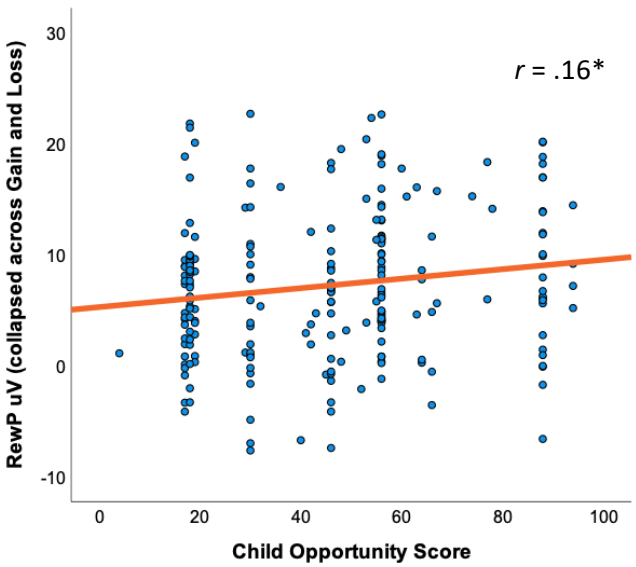
Neighborhood Disadvantage and Reward Processing

- Higher levels of neighborhood disadvantage are associated with reduced RewP for both gain and loss feedback







* All relations maintained when statistically controlling for children's depressive symptom levels

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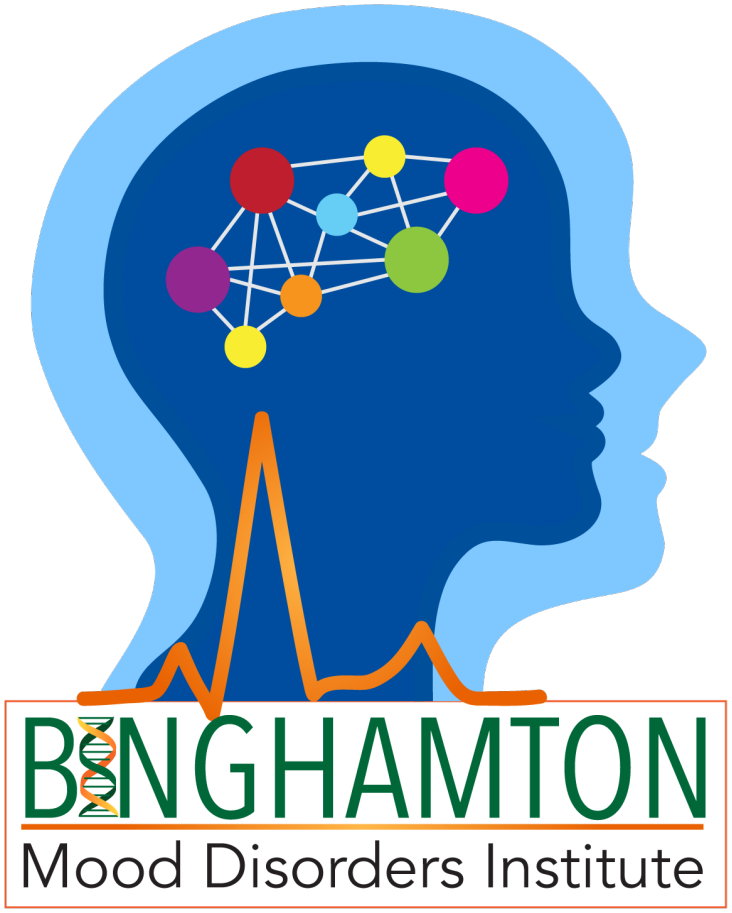
Interim Conclusions: Environment

- Depression in mothers is associated with elevated chronic and episodic stress for the child both inside and outside of the home
- At risk children are vulnerable to vicious cycles of risk in which heightened interpersonal stress and depression exacerbate each other over time (including stress generation effects)
- This risk extends to the community context in that genetically high-risk children grow up in areas characterized by greater adversity and crime and lower levels of opportunity (effects that are at least partially independent of family income and mother/child depression)

Discussion

Final Points

- There are a number of pathways by which a family history of depression can increase risk in the child
- Influences across various units of analysis – from genetic and neural to interpersonal and environmental – operate simultaneously
- I highlighted attentional biases as an illustration of a fine-grained process and contrasted that with neighborhood characteristics, which reflect more macro-level influences
- We are still working to understand how these factors across units of analysis intersect and how mechanisms of risk change across development from infancy to adolescence



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