

Patterns of intrinsic functional connectivity (iFC) in behaviorally inhibited children

Koraly Pérez-Edgar
Bradley Taber-Thomas
Santiago Morales
November 2014

This research is supported by grant R01 MH094633 and R21 MH103627 to KPE

Collaborators

U Maryland

Nathan A. Fox, PhD

Andrea Chronis-Tuscano, PhD

Kathryn Degnan, PhD

UC-Davis

Amanda Guyer, PhD

U Michigan

Jillian Hardee, PhD

Tel Aviv University

Yair Bar-Haim, PhD

Waterloo U

Heather Henderson, PhD

NIH

Daniel S. Pine, MD

Monique Ernst, MD/PhD

Ellen Leibenluft, MD

Eric Nelson, PhD

PSU

Kristin Buss, PhD

Rutgers-Newark

Vanessa LoBue



Behavioral Inhibition or Shyness

The child's initial behavioral reactions to unfamiliar people, objects and contexts, or to challenging situations

Reactions of an inhibited/shy child to novelty include:

- Becoming quiet and watchful
- Ceasing current activity
- Retreating from unfamiliarity
- Refusing to engage in interaction





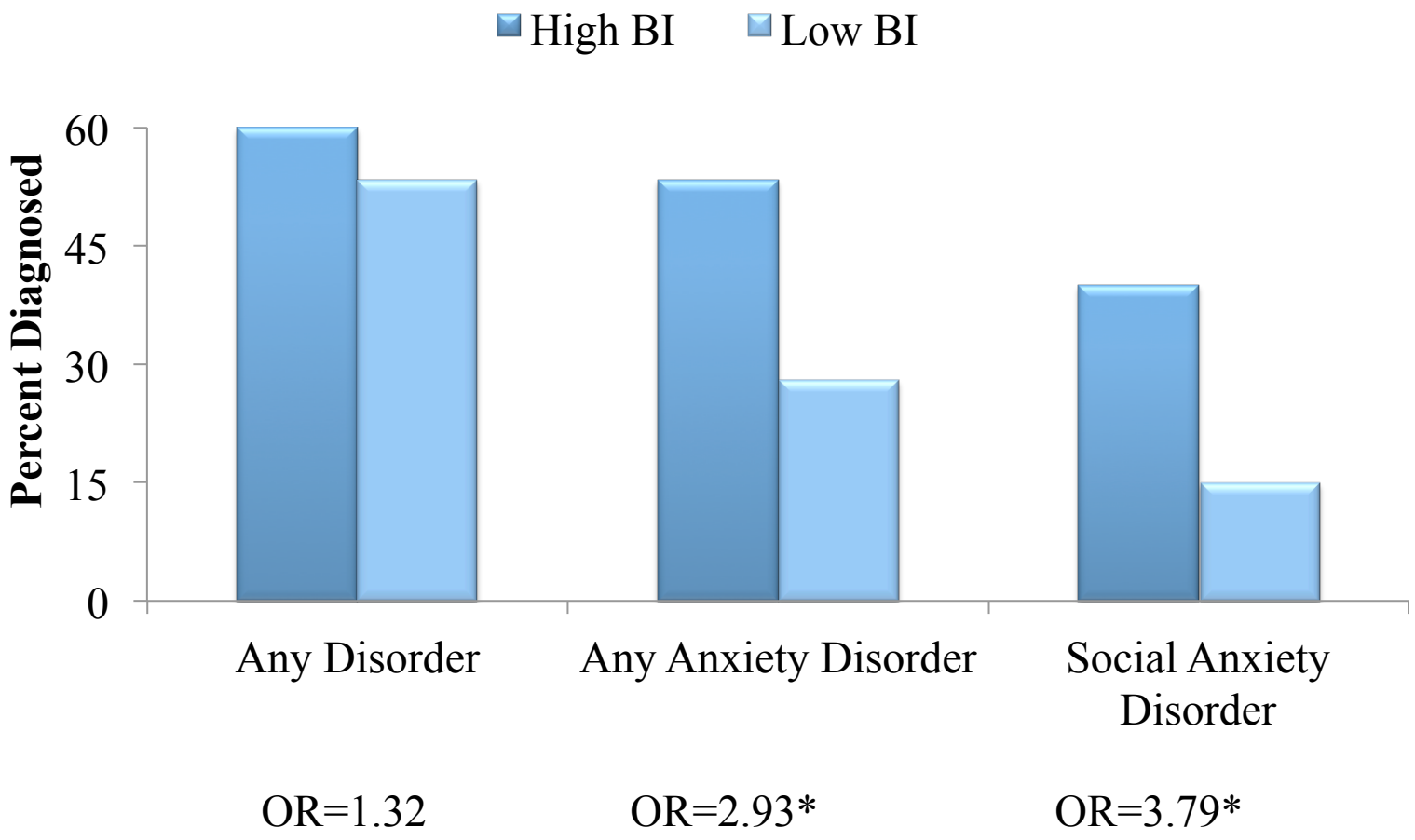


Infant Reactivity

Behavioral Inhibition

Social Anxiety

Behavioral Inhibition and Anxiety



Chronis-Tuscano et al, 2009, JAACAP

Amygdala Model of Behavioral Inhibition

Kagan (1994)

More reactive amygdala.

More visceral feedback to limbic sites.

A "special preparedness" to detect subtle differences in environment.

Such "preparedness" may involve sensitivity of the attention system to detect threat.

Amygdala-based Neural Perturbations in BI

The Physiology and Psychology of Behavioral Inhibition in Children

Jerome Kagan, J. Steven Reznick, and Nancy Snidman

Harvard University

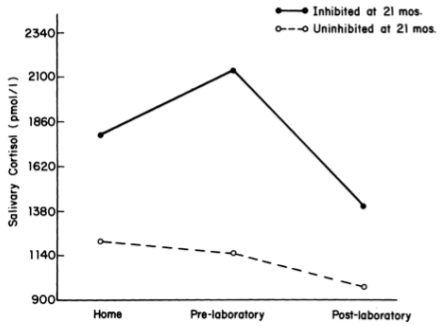
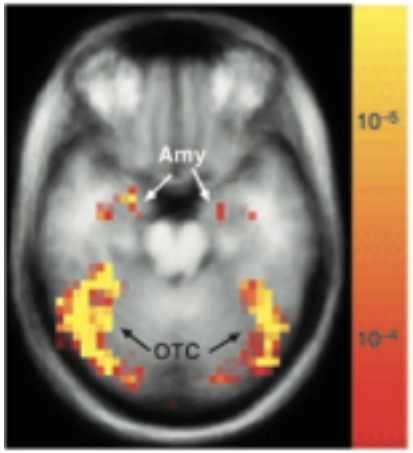


FIG. 3.—Mean cortisol levels at age 5½ in home and laboratory for children classified as inhibited or uninhibited at 21 months of age: Cohort 1.

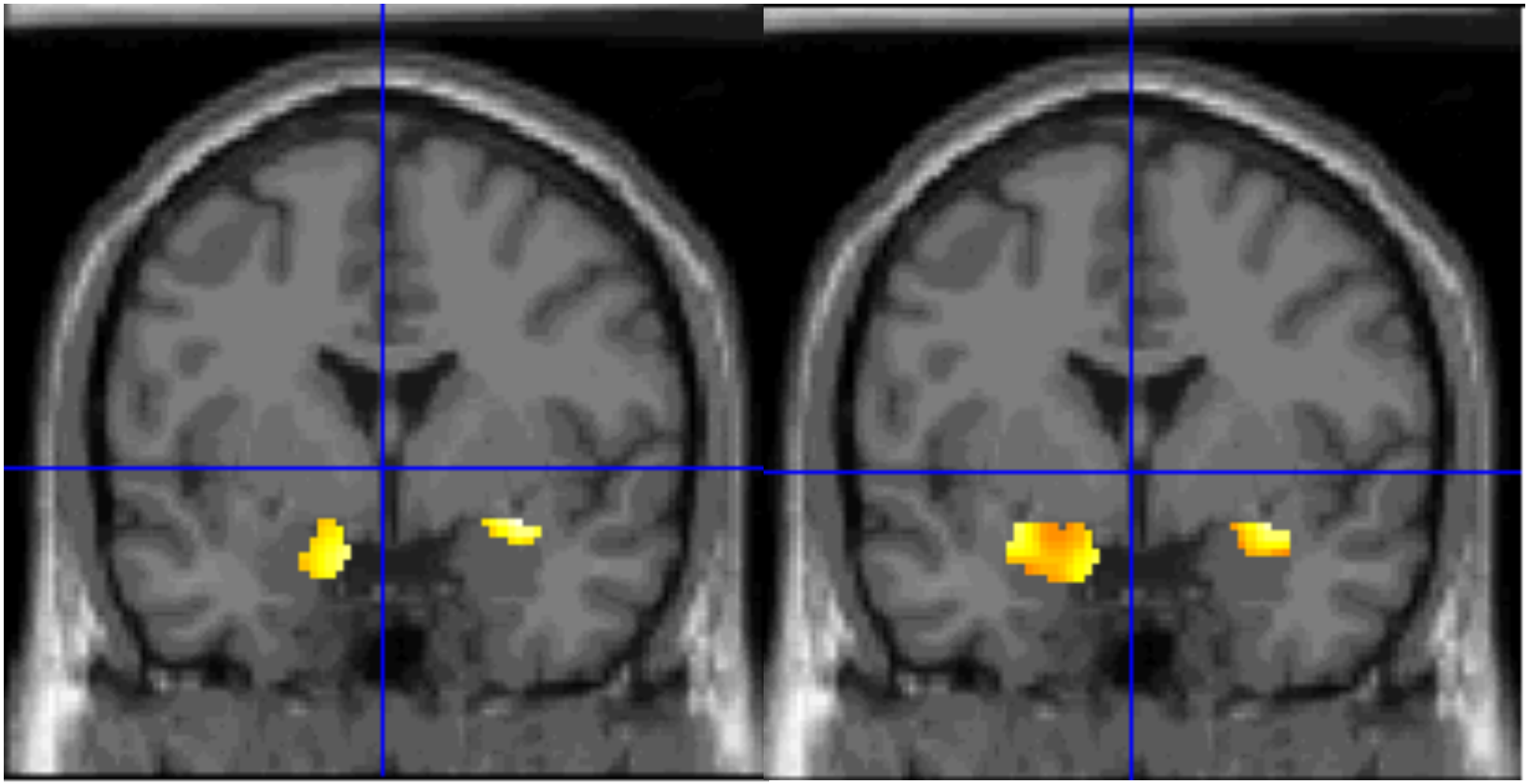


Inhibited and Uninhibited Infants "Grown Up": Adult Amygdalar Response to Novelty

Carl E. Schwartz,[1,2,3*] Christopher I. Wright,[2,3,4] Lisa M. Shin,[2,5] Jerome Kagan,[6] Scott L. Rauch[2,3]

Fear Rating vs. Passive Viewing

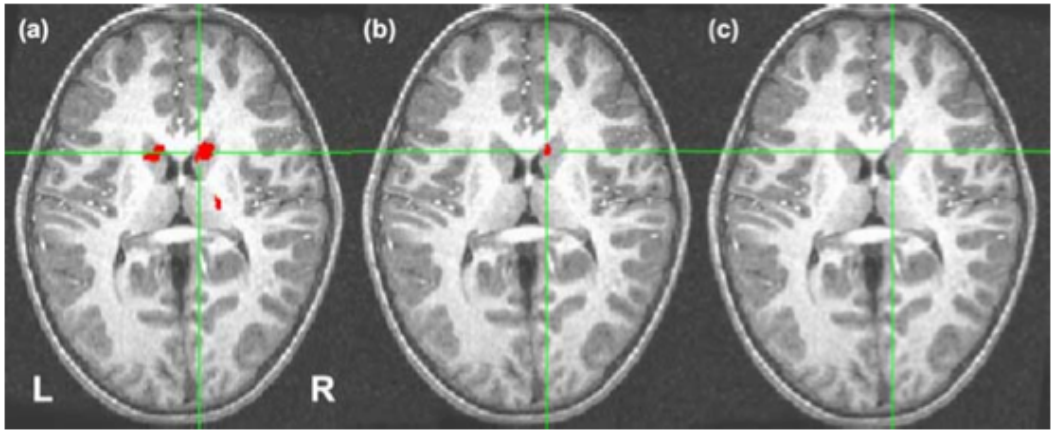
Fearful Faces ***Happy Faces***



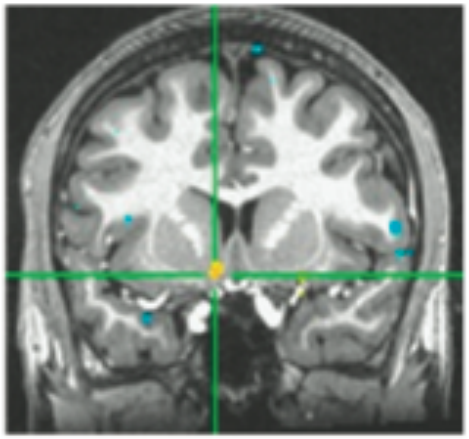
Perez-Edgar et al, 2007, NeuroImage

Striatum Based Neural Perturbations in BI

- Recent studies have also shown BI is related to enhanced striatal sensitivity to monetary reward



large reward medium reward small reward



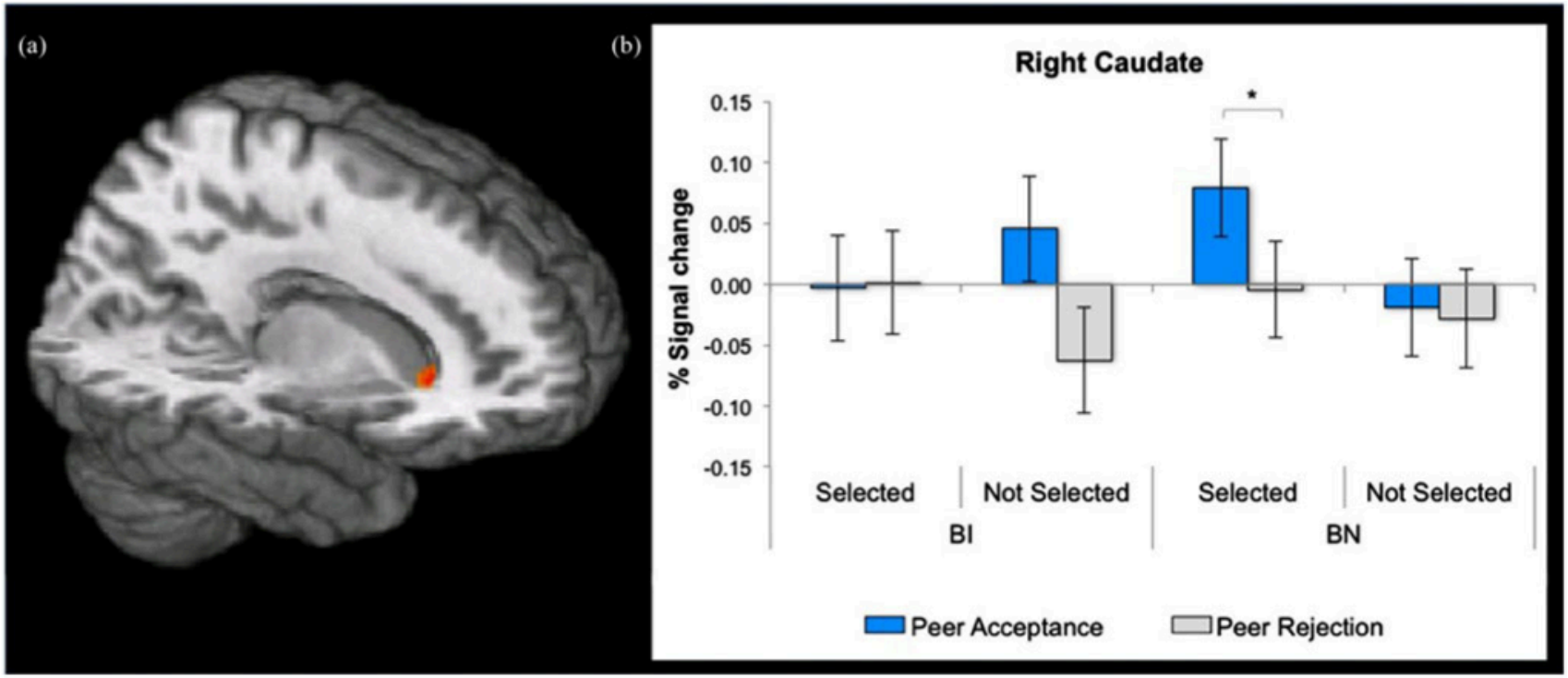
contingent>noncontingent reward

Guyer et al, 2006, Neuroscience

Bar-Haim et al, 2009, Psych Science

Neural Perturbations Encompass Social Reward

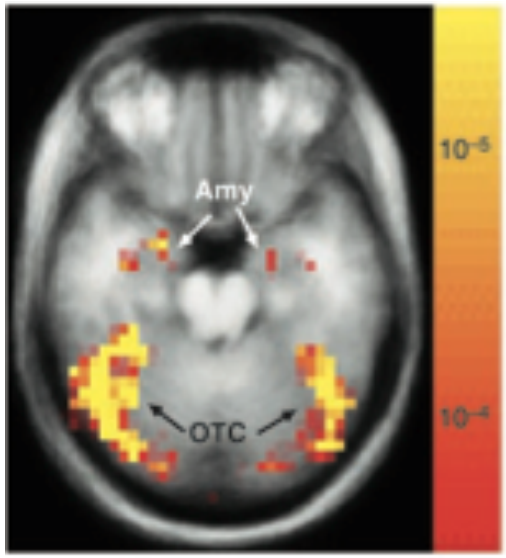
- Pattern of reward sensitivity also seen with social feedback



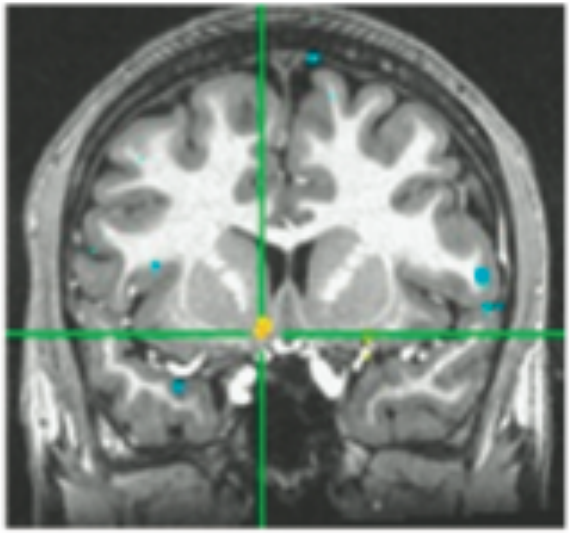
Guyer et al, 2014, Depression & Anxiety

Neural perturbations in BI

- How do we reconcile these emerging storylines?



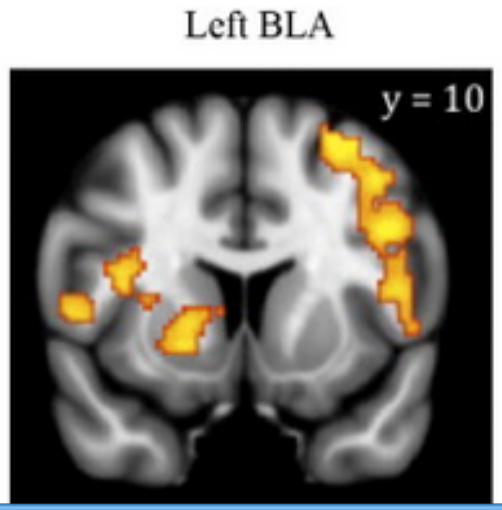


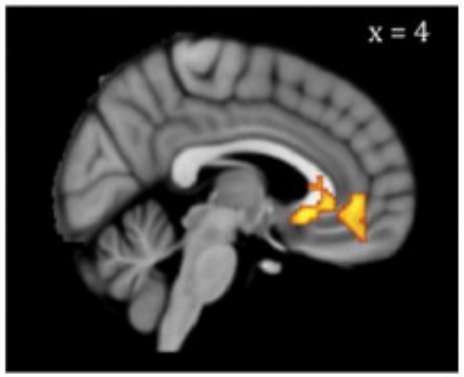


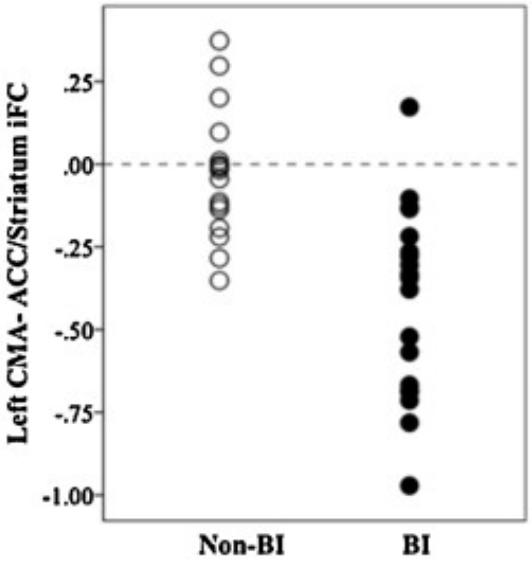
- Perhaps these data reflect patterns of activation across Intrinsic Neural Networks

Intrinsic networks in BI

- iFC measures correlations in slow fluctuations (<1 Hz) between regions
- In otherwise healthy young adults characterized as BI in childhood, altered iFC from amygdala subregions to subgenual ACC, striatum, and insula





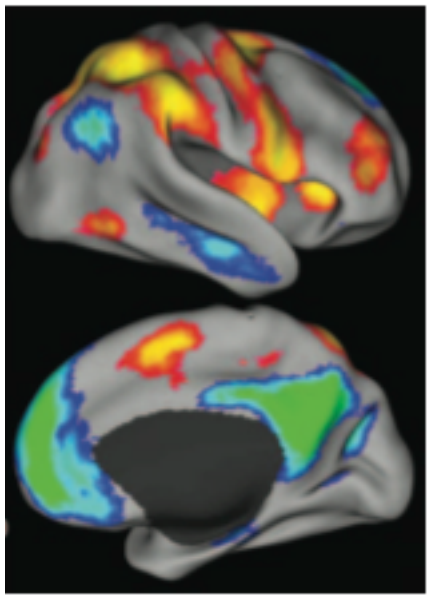


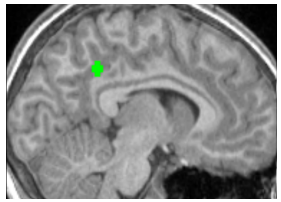
Roy et al, 2014, Biological Psychology

Intrinsic networks

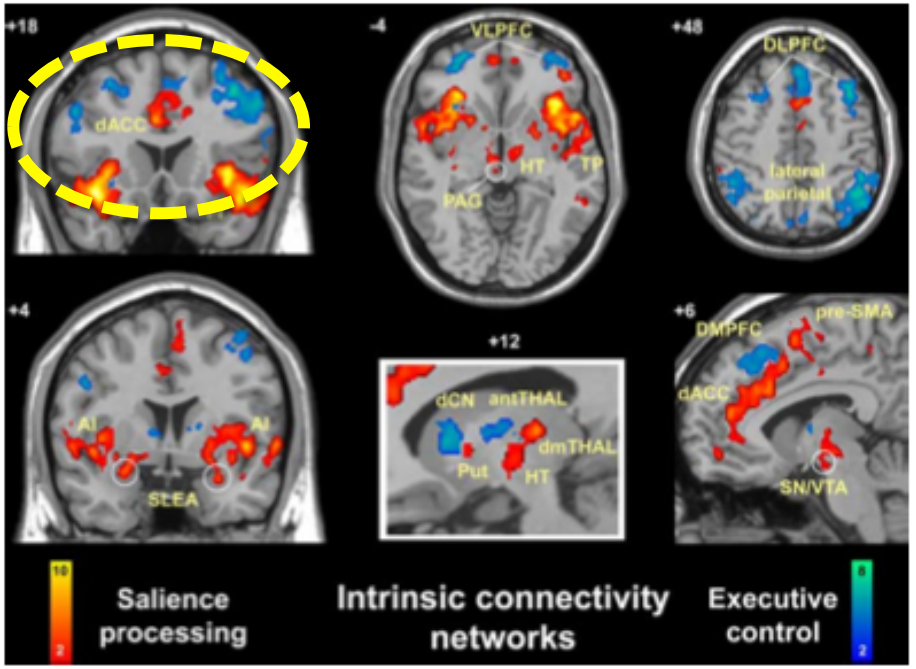
- Intrinsic neural networks—task-positive (Salience; Executive) anticorrelated with task-negative (DMN) networks

DMN

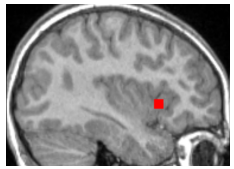




Salience



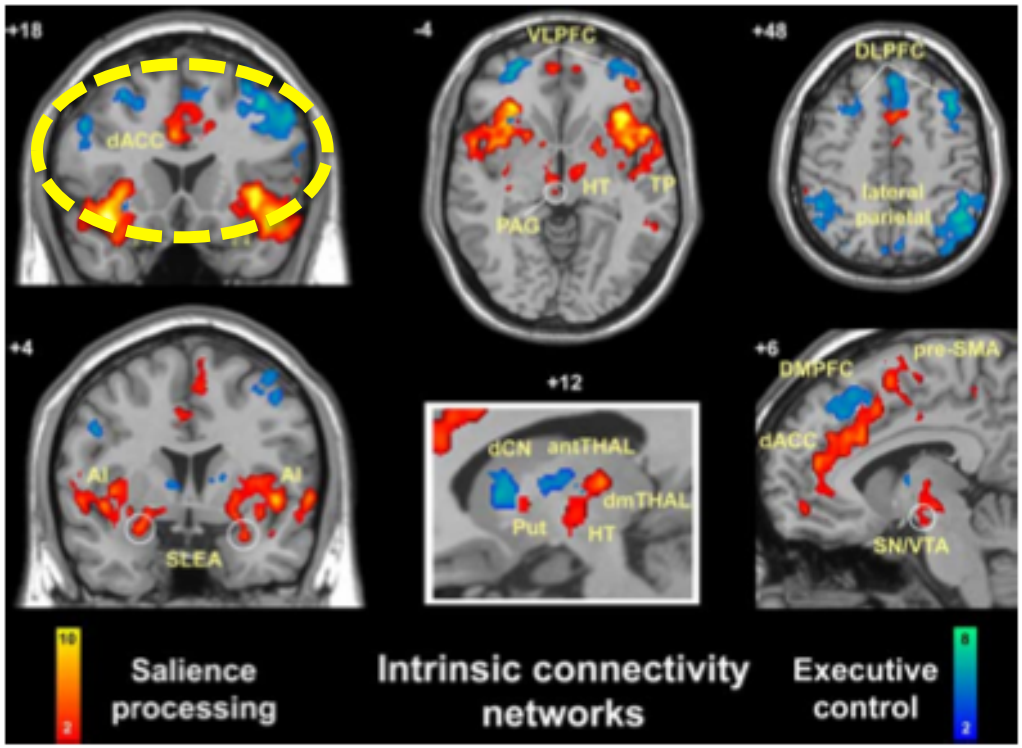
Executive



Fox et al, 2005
Seeley et al, 2007
Sridharan et al, 2008

Salience network

- "These regions coactivate in response to varied forms of salience, including the emotional dimensions of **pain**, **empathy** for pain, metabolic **stress**, hunger, or **pleasurable touch**, **enjoyable "chills"** to music, **faces** of loved ones or allies, and **social rejection**."



Seeley et al, 2007

iFC in BI Children

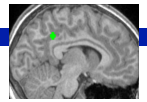
	N	Age	Gender	BIQ Total	BIQ Soc. Novelty	DISC Soc. Phobia Symptoms	SCARED Soc. Phobia
High BI	17	10.1 (0.8)	6M/11F	125.5 (16.1)	68.1 (10.2)	3.1 (3.3)	7.6 (3.2)
Low BI	25	10.2 (0.9)	12M/13F	75.6 (21.6)	38.2 (11.7)	0.6 (1.7)	2.2 (2.9)
All	42	10.4 (1.0)	18M/24F	95.8 (32)	50.3 (18.5)	1.6 (2.7)	4.9 (4.1)

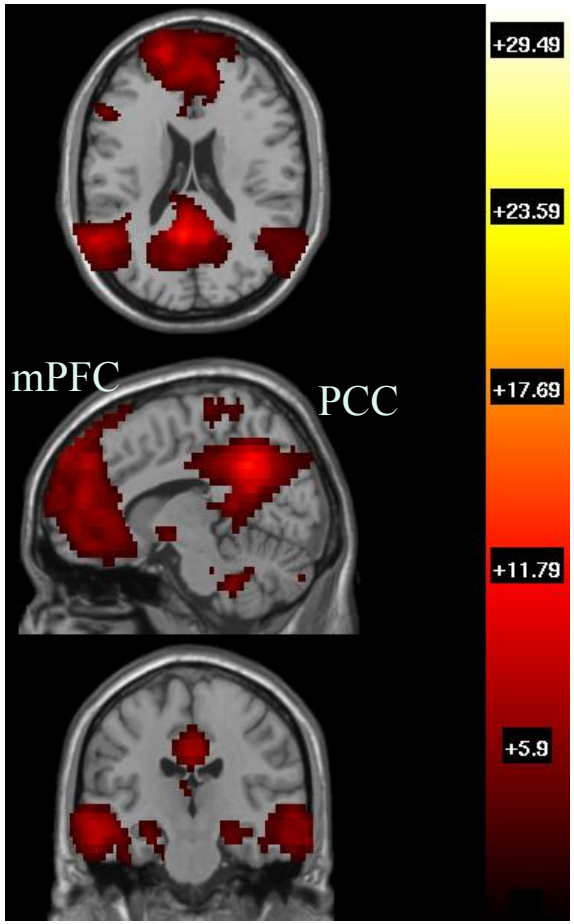
- Probed Salience and DMN iFC networks with seed-based analysis of resting state fMRI data
- 3T Siemens Magnetom Trio
- Analyses in SPM8/CONN toolbox

Taber-Thomas et al, in prep

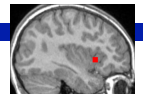
iFC networks

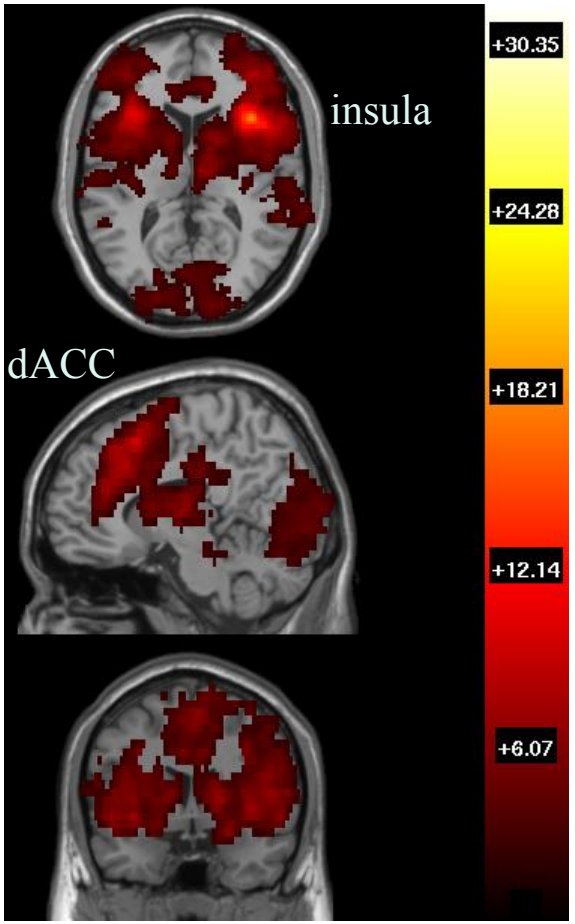
DMN





Salience



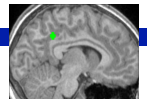


height p(FDR)<0.0001, cluster(FDR) p<0.001

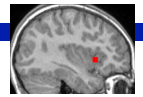
Taber-Thomas et al, in prep

iFC related to BI

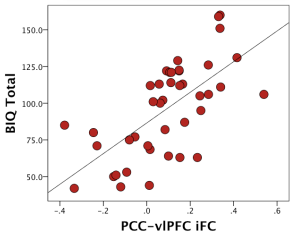
DMN



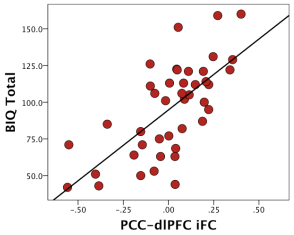
Salience

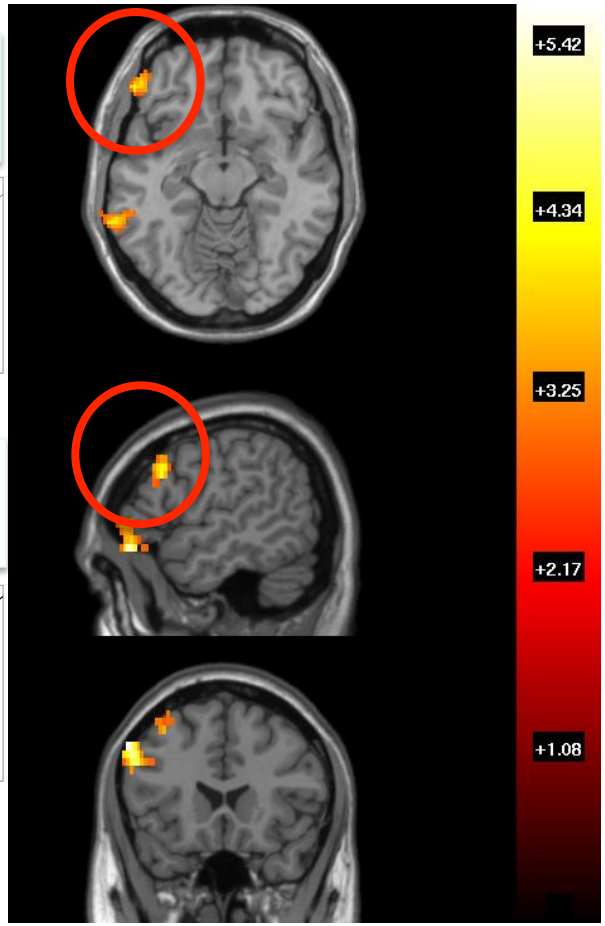


vlPFC

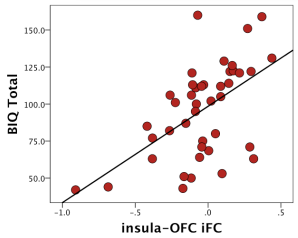


dlPFC

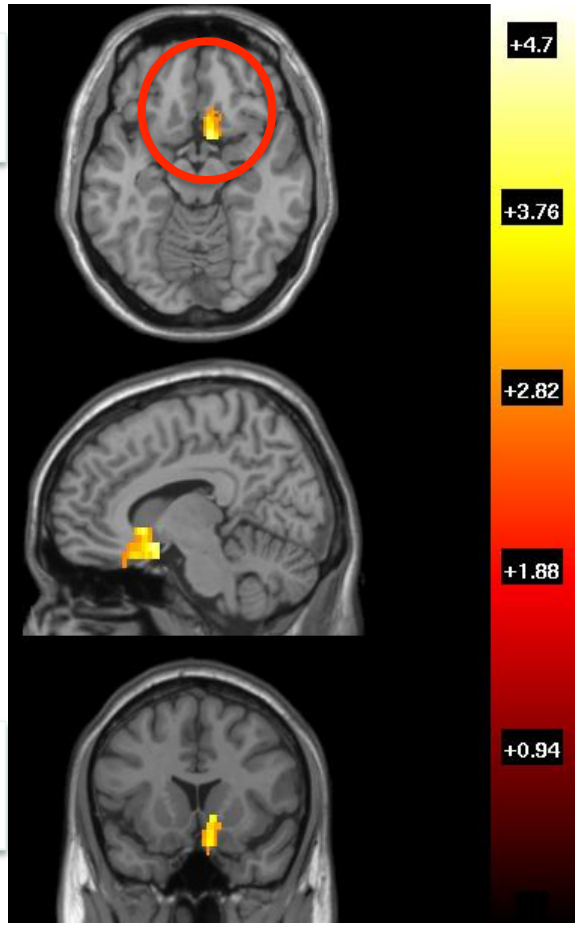




mOFC



N. Acc.

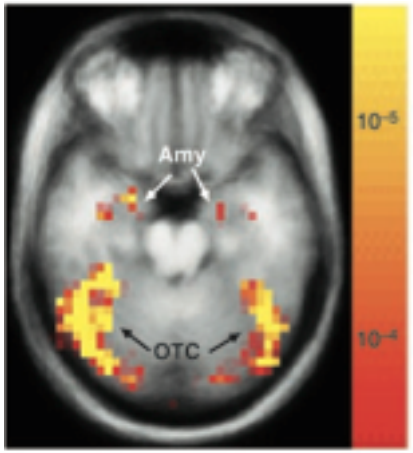


height p(unc)<0.005, cluster(FDR) p<0.05

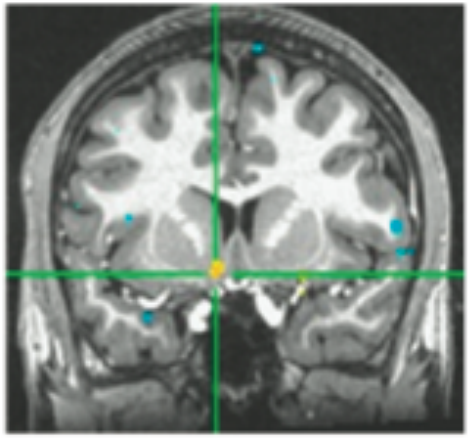
Taber-Thomas et al, in prep

Neural Perturbations in BI

- How do we reconcile these emerging storylines?

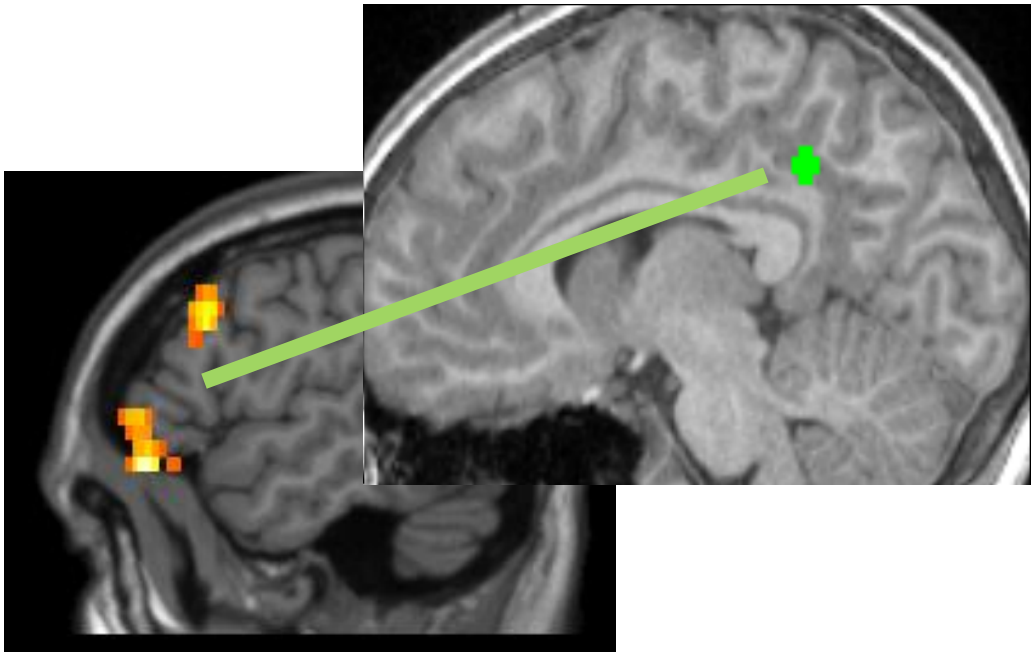


?



“Heightened State of Readiness”

Default



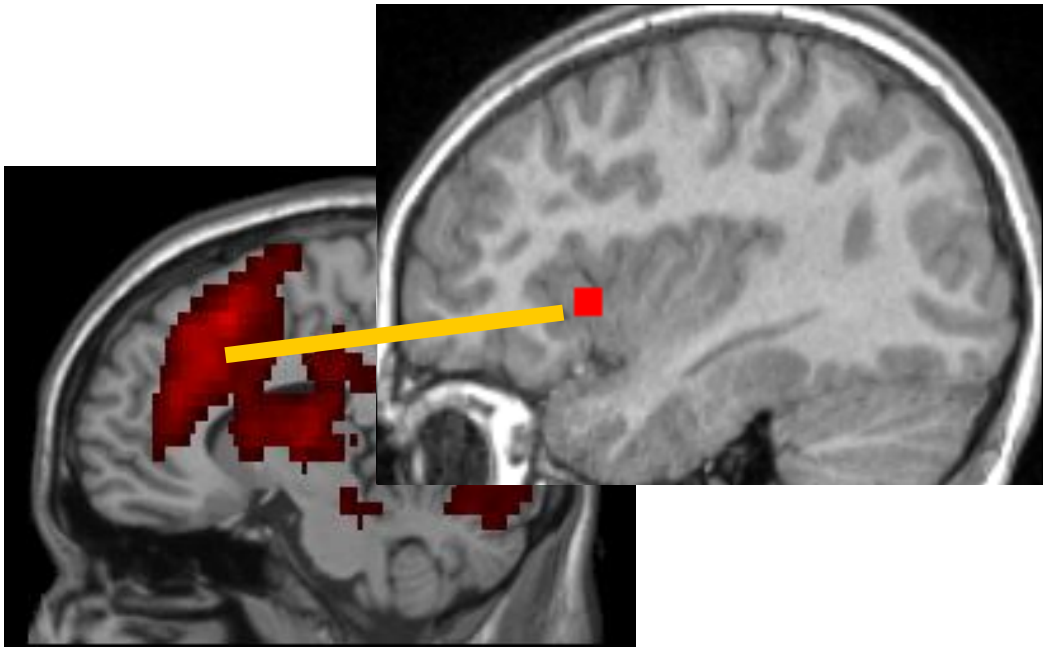
Increased intrinsic functional integration of DMN with lateral PFC/executive control network

Taber-Thomas et al, in prep

“Processing motivationally salient information”

Salience

Typical insula-dACC network

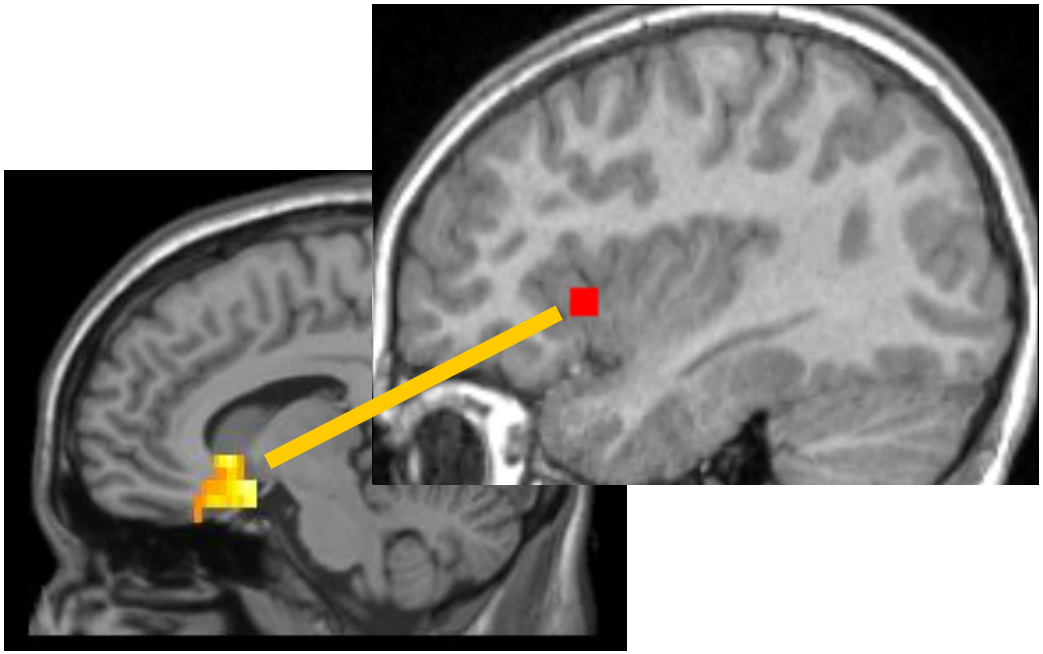


Taber-Thomas et al, in prep

Altered network—Altered Sensitivity to Feedback

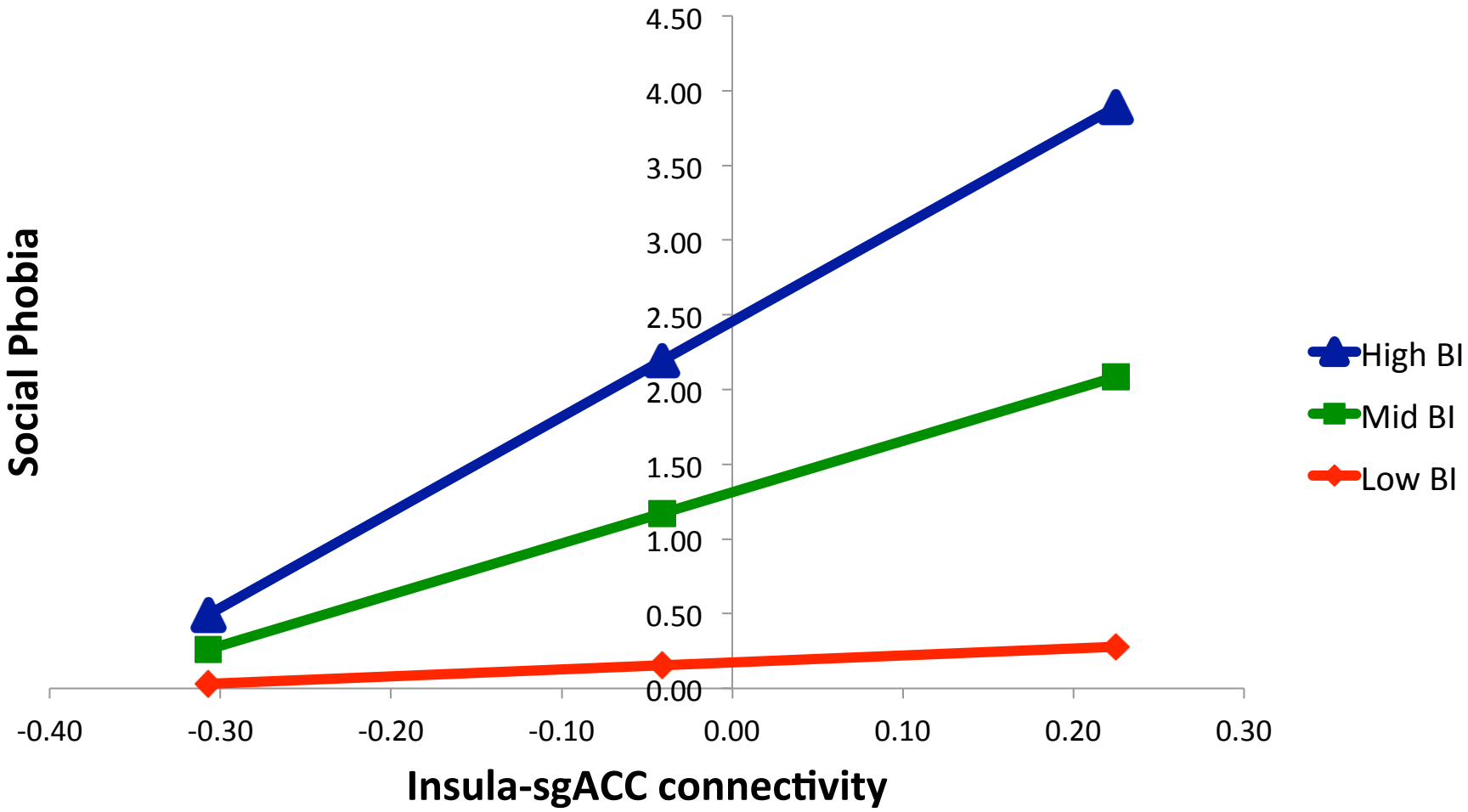
Salience

Altered insula-OFC network



Taber-Thomas et al, in prep

Reflecting Risk for Anxiety?



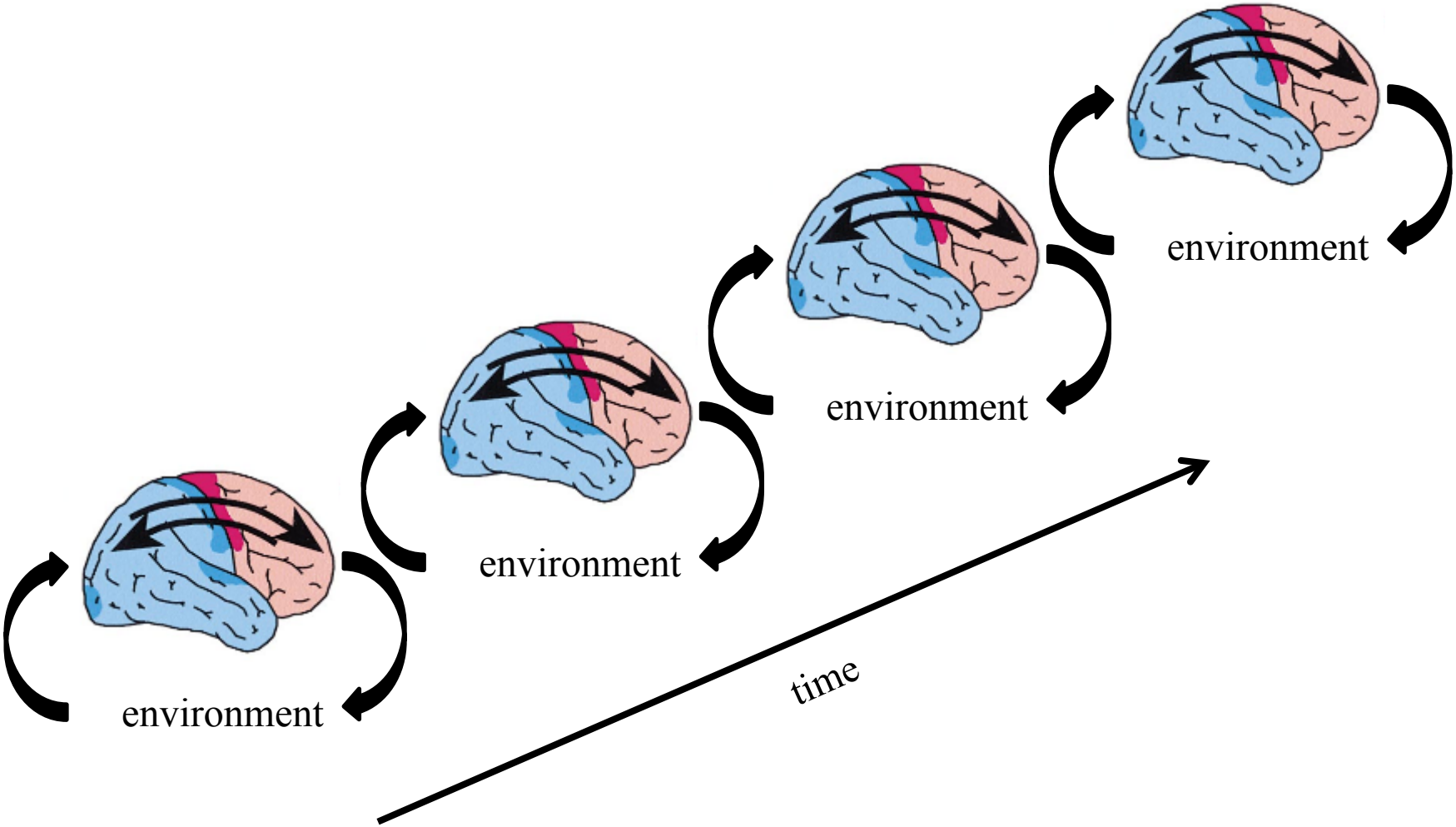
p=0.01

Taber-Thomas et al, in prep

Summary

- BI is associated with altered salience and DMN network connectivity.
- BI moderated neurobehavioral association—high BI children with the strongest insula-OFC may be at greatest risk for anxiety
- Supports the broader notion that a shift in salience network connectivity from more dorsal (dACC) to more ventral (mOFC/ N.Acc.) system may be a mechanism of early risk for anxiety.

Attention and Socioemotional Development



Empirical Strategy

- Manipulating Attention Biases to Threat
  - Children ages 9-12 years at increased risk due to BI
- Examining the First emergence of the Attention-Temperament Link
  - Infants ages 4 mos to 24 mos
- Visual Attention Patterns during Social Interactions





Perez-Edgar COIL RIG

Developmental Tethers

