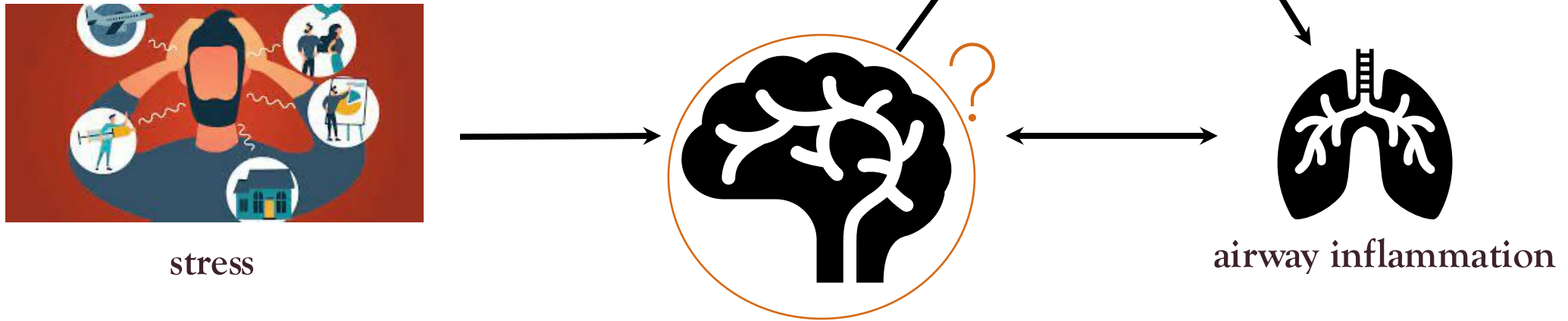


STRESS NEUROCIRCUITRY & AIRWAY INFLAMMATION IN ASTHMA

Estelle Higgins, William Busse, Stephane Esnault, Danika Klaus,
Melissa Rosenkranz
University of Wisconsin-Madison

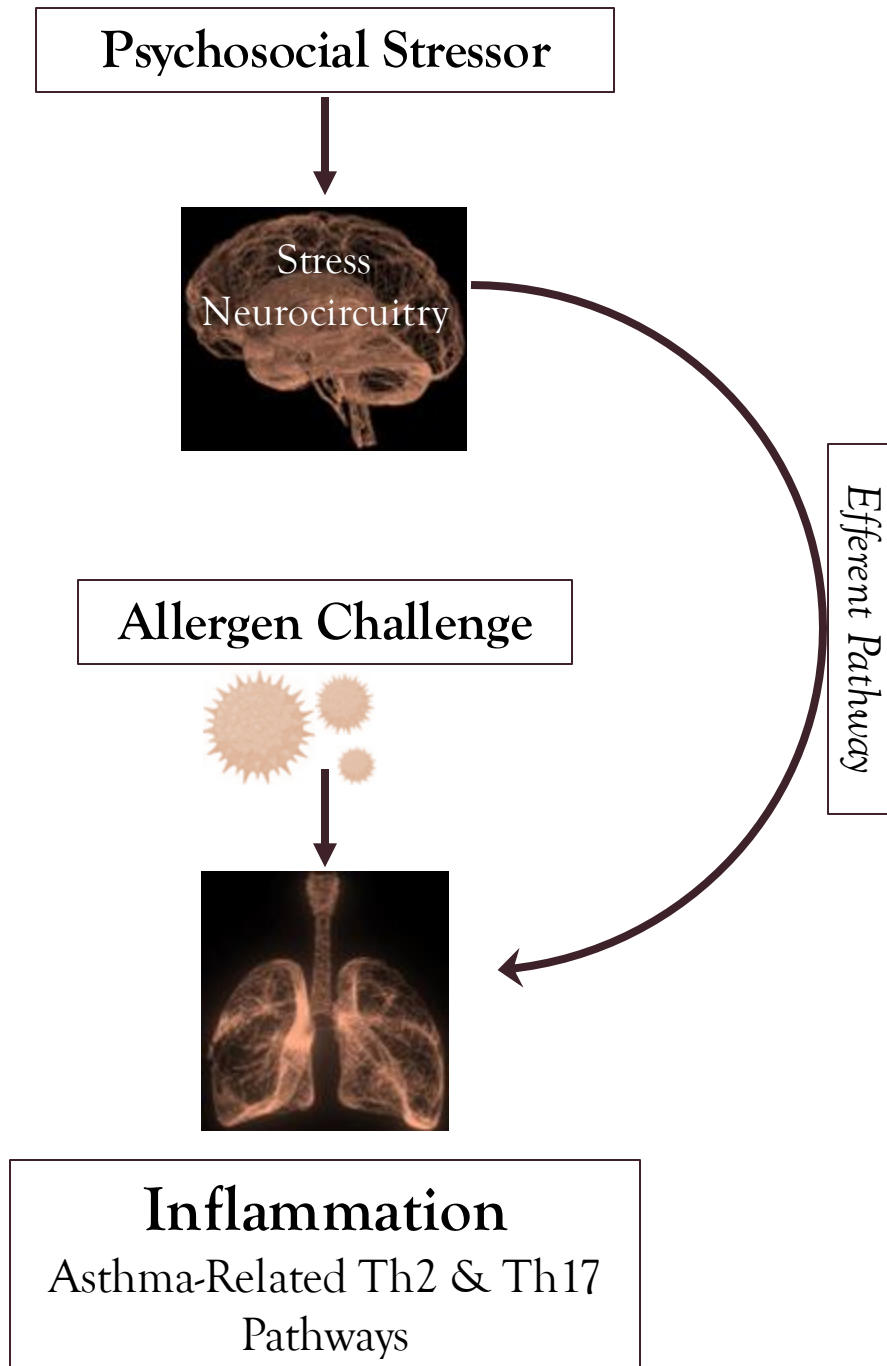
BACKGROUND

BACKGROUND



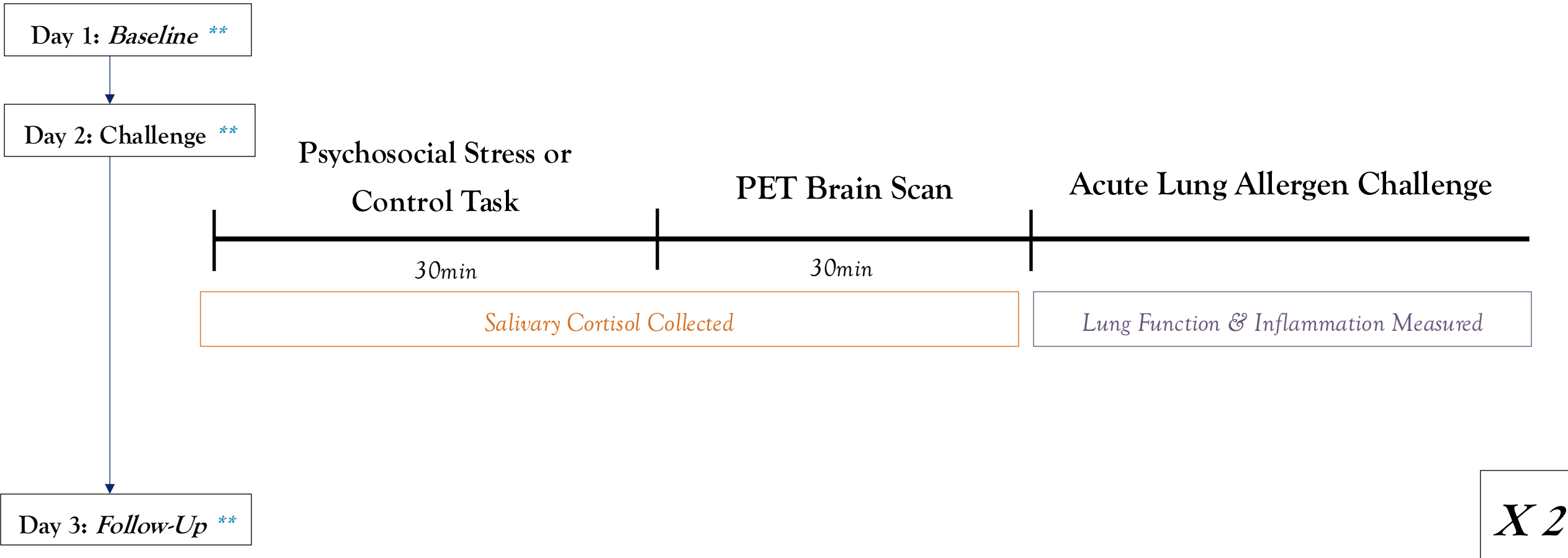
- Initial evidence:
 - Emotion neurocircuitry & inflammation
 - Th17 cells ($IL-1\beta/IL-17$ pathways), asthma, & psychological distress

HYPOTHESES



STUDY DESIGN

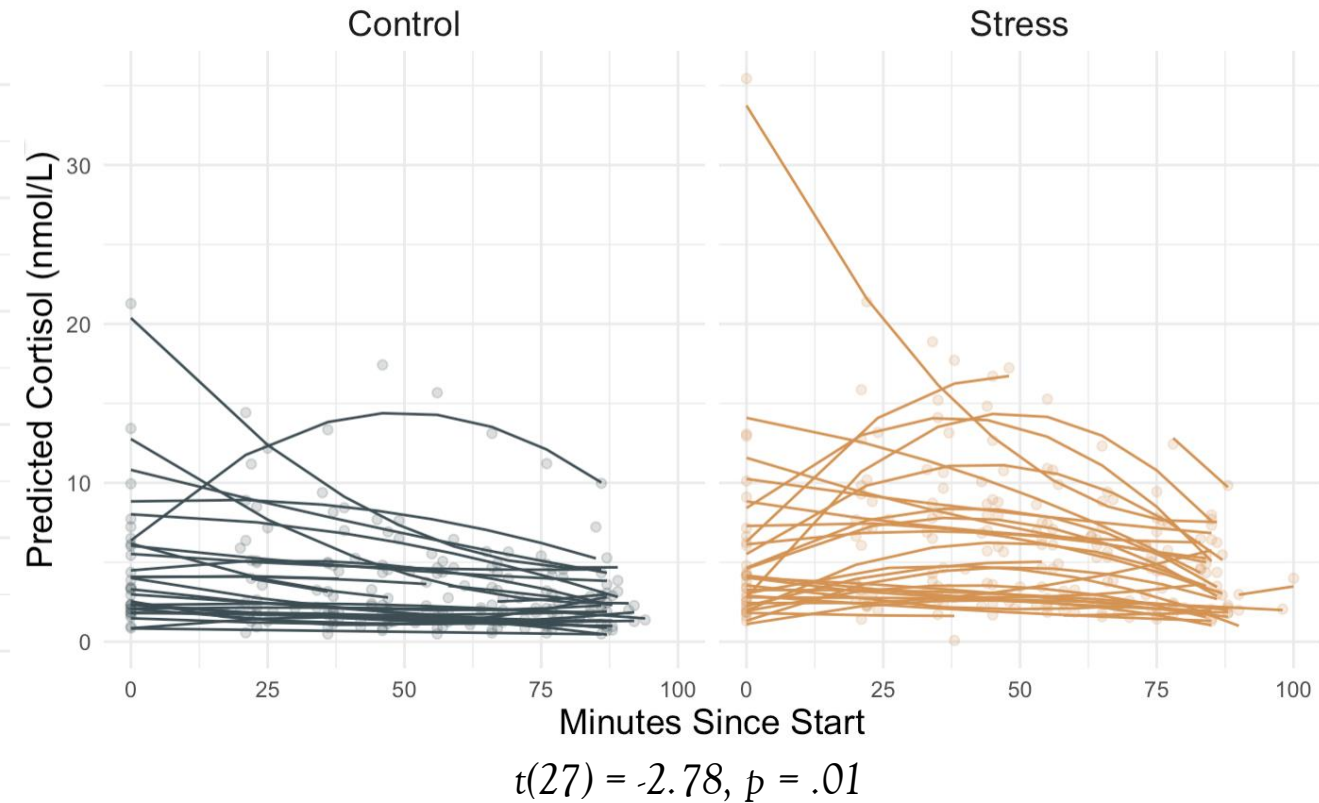
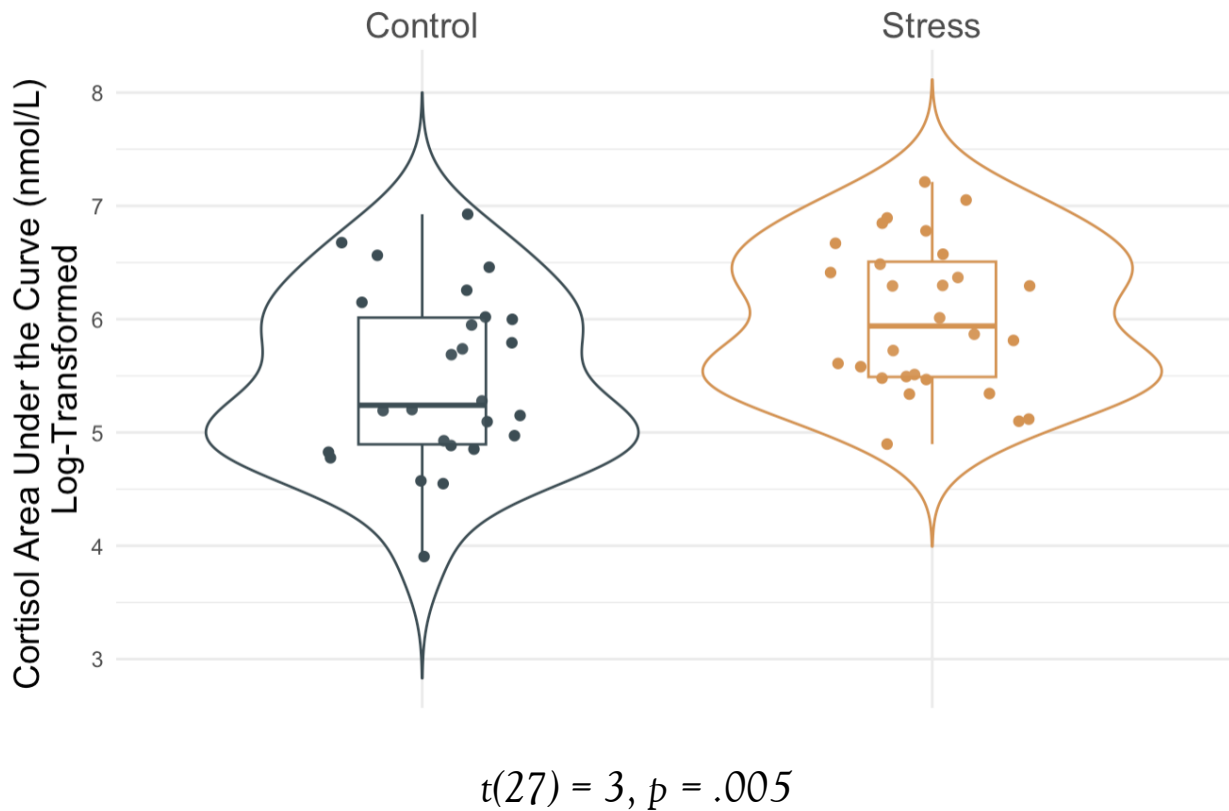
STUDY DESIGN



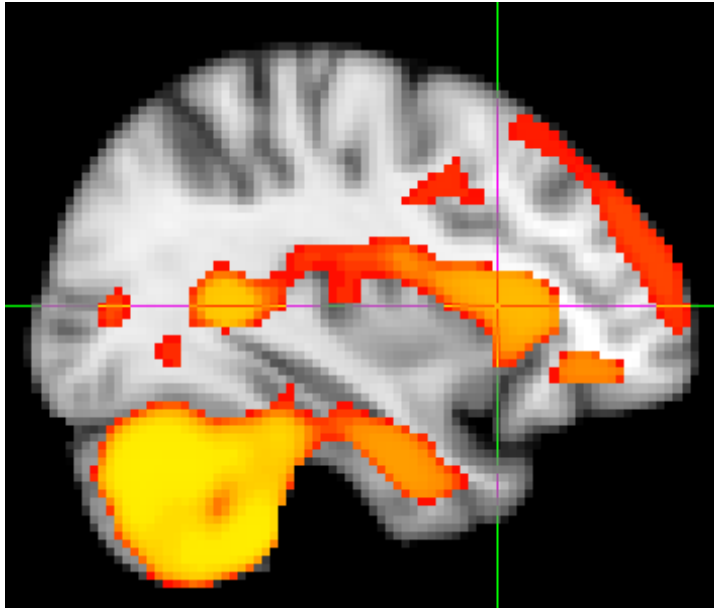
** *Airway inflammation measured (daily)*

RESULTS

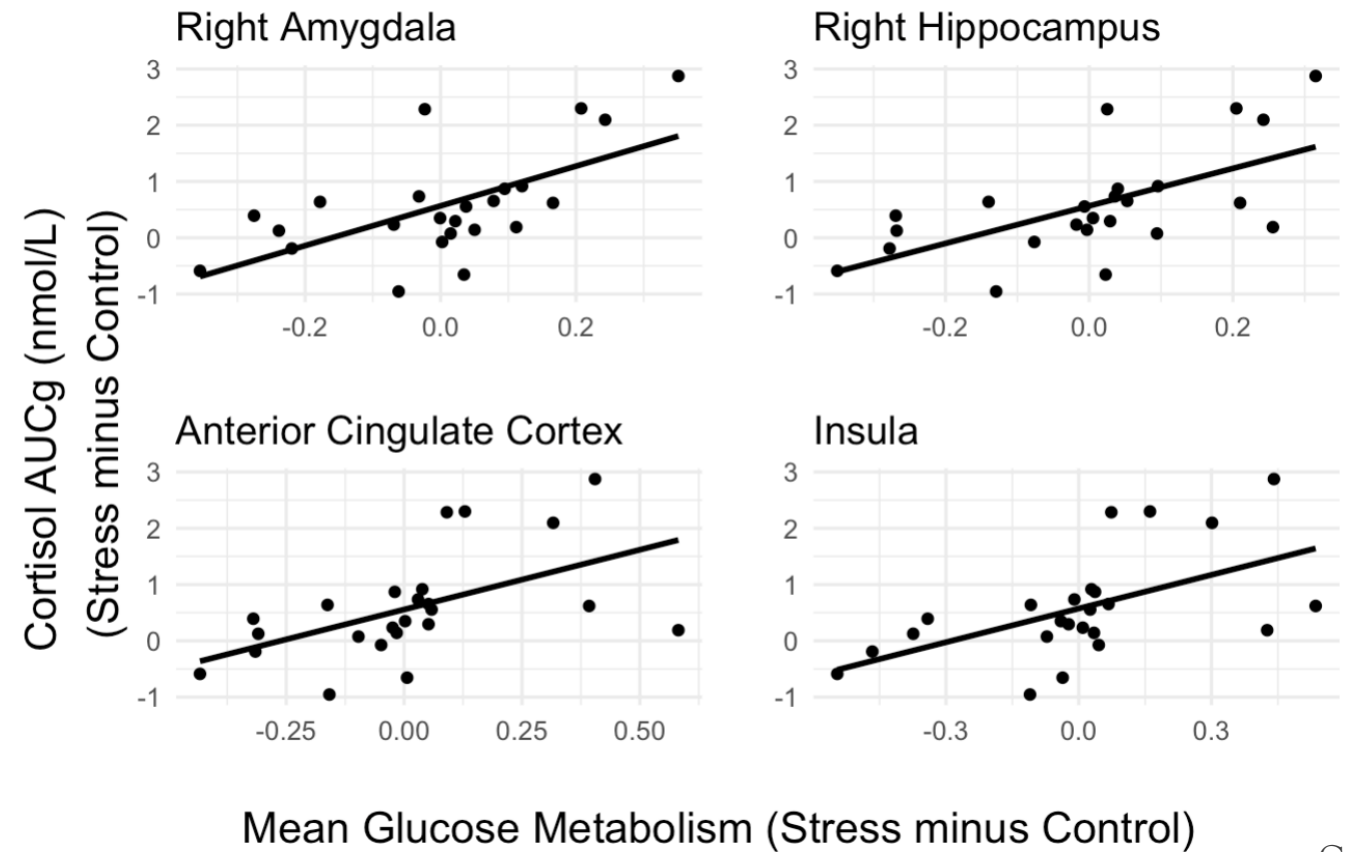
ACUTE STRESS INCREASES CORTISOL



CORTISOL RESPONSE TO STRESS IS ASSOCIATED WITH STRESS NEUROCIRCUITRY ACTIVATION



$p < .05$ corrected

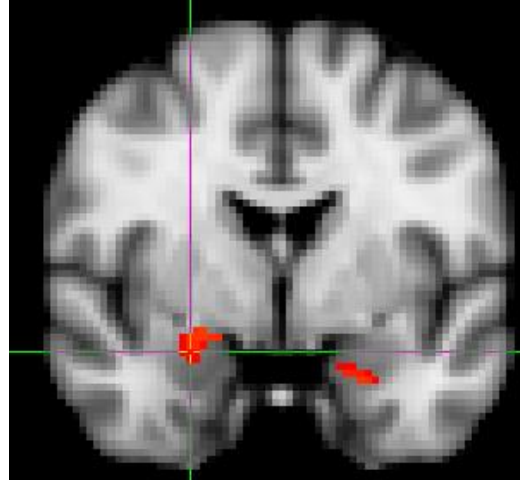
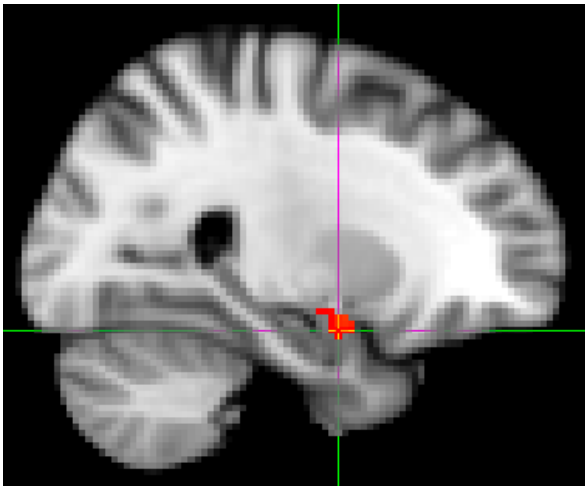


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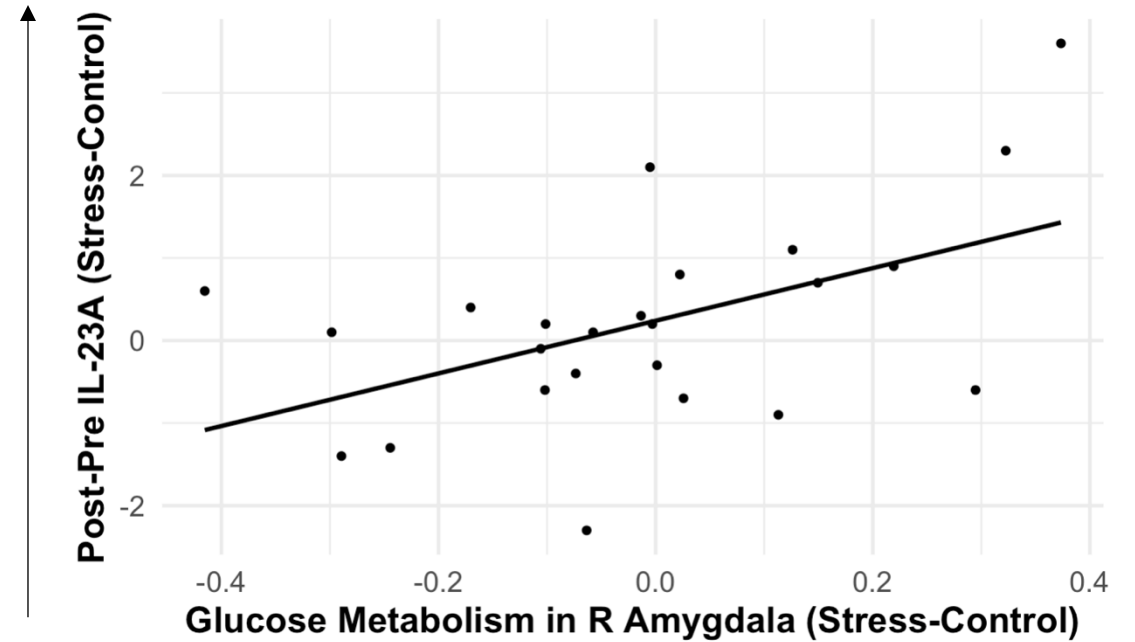
Greater glucose
metabolism, in
stress vs control

IL-23A EXPRESSION POST-AIRWAY CHALLENGE INCREASE IS ASSOCIATED WITH STRESS-RELATED AMYGDALA ACTIVATION

*Greater increase in
inflammation,
in stress vs control*



$p < .05$ corrected



*Greater glucose
metabolism, in
stress vs control*

CONCLUSIONS

CONCLUSIONS

- Psychosocial stress-evoked **cortisol** associated with **brain activity** (*amygdala, hippocampus, ACC, insula*)
- Greater **Th17-related** (*IL-23A mRNA*) inflammatory response to allergen associated with increased **stress-related amygdala activity**
- **Stress-related brain activity** predicts increased **inflammatory signaling capacity**
 - Efferent pathway
 - Targeted treatments

THANK YOU!



Work supported by NHLBI (R01 HL123284)



Melissa Rosenkranz, PhD



Richard Davidson, PhD



William Busse, PhD



Danika Klaus, RN



Stephane Esnault, PhD

...and many more!

QUESTIONS

QUESTIONS

QUESTIONS

TH17 CELLS

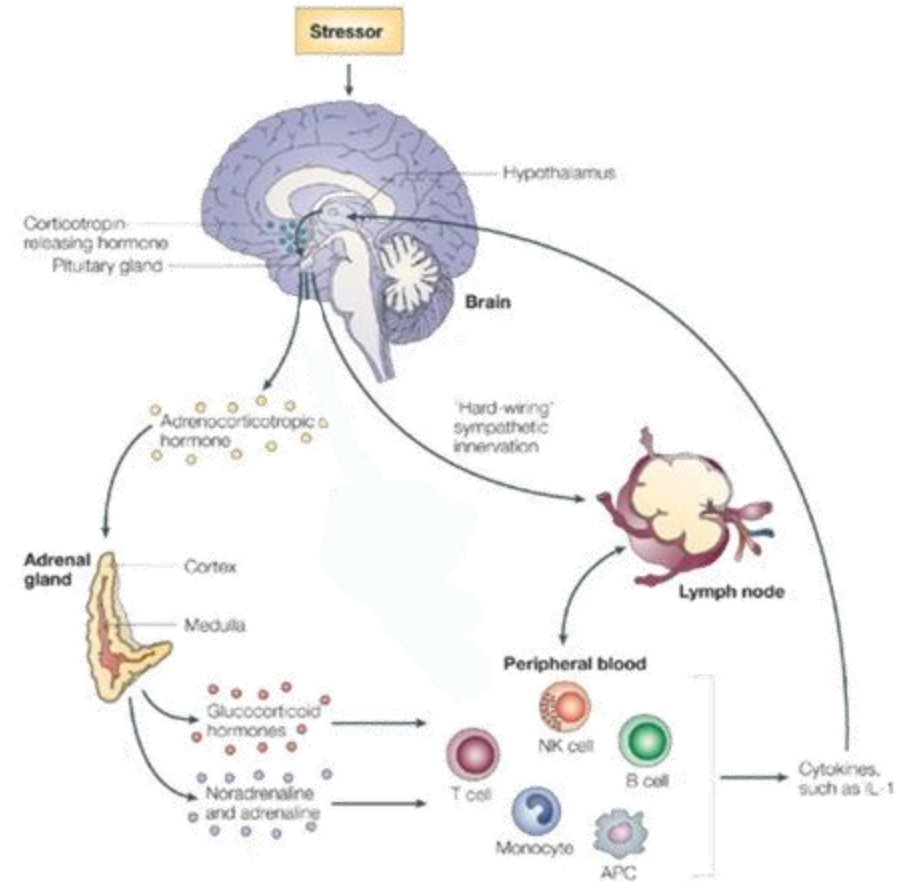
- Adaptive Immune System → IL-17 (*neutrophils*)
- Differentiation promoted by IL-23, TNF- α , IL-1 β , IL-21 (requires IL-6 and TGF β)
- Psychological Stress → ↑ IL-23A, IL-1 β , IL-6

Asthma:

- IL-17 in severe asthma; modulates Th2 responses in mild asthma
- EOS (Th2 cells) release IL-1 β → IL-17 expression

HOW DOES THE BRAIN INFLUENCE THE AIRWAY?

- **Distal Mechanism:** brain (sub/cortical)
 - *In-Between Mechanisms:* brainstem
- **Proximal Mechanisms:**
 - *HPA Axis*
 - *Sympathetic Nervous System*
 - *Neurogenic Inflammation (Sensory Neuropeptides)*

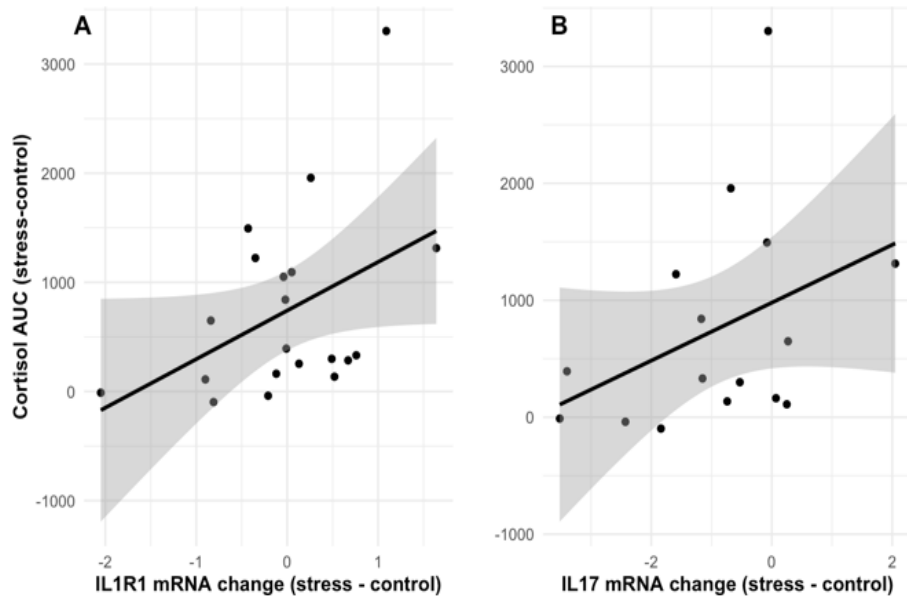


PRIOR EVIDENCE

- Psychosocial Stressor → Increased Cortisol, associated with Airway Inflammation

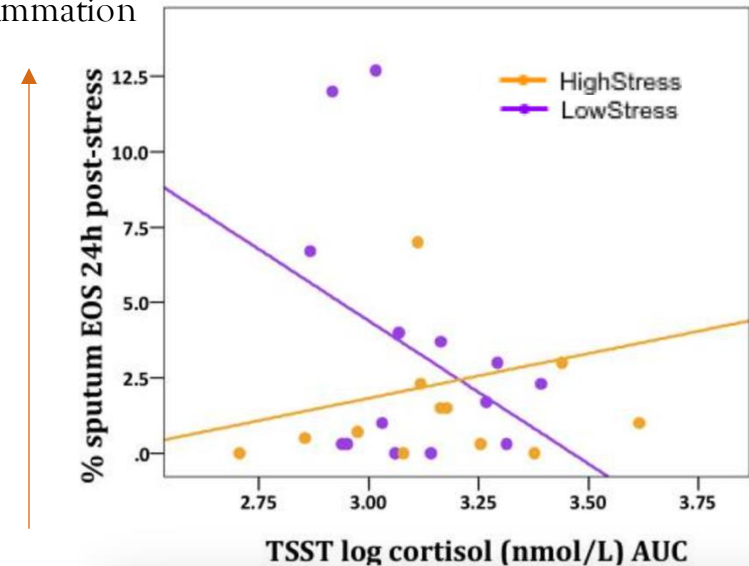
Biomarkers

- Th17 path (IL-17A, IL-1R1)



- Th2 path (EOS) moderated by chronic stress

greater airway
inflammation



(Rosenkranz et al., 2016)

greater cortisol

PRIOR EVIDENCE

- Psychosocial Stressor → Stress Neurocircuitry Activation associated with Airway Inflammation Biomarkers
 - *Th2 pathway (FeNO) & Th17 cell mRNA (IL23A, IL1R1)*

