

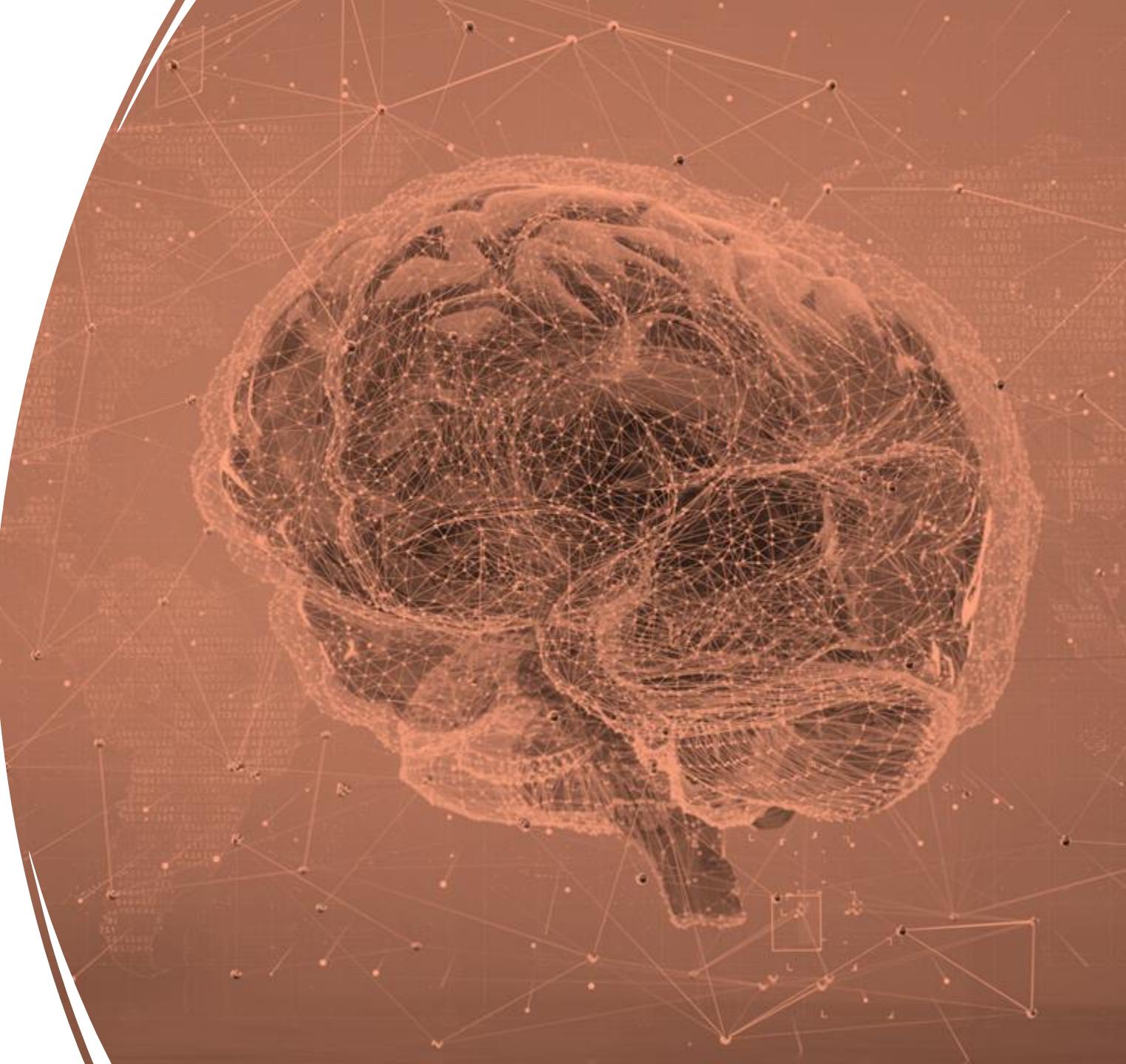
# Brain-immune relationships in asthma

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*Estelle Higgins, M.S.*

*Capstone Talk*

*5/5/2025*



# Gratitude



*Especially our participants!*



*Melissa Rosenkranz,  
PhD*



*Richard Davidson, PhD*



*William Busse, PhD*



*Corinna Frye*



*John Curtin, PhD*



*Danika Klaus, RN*



*Lyn Abramson, PhD*

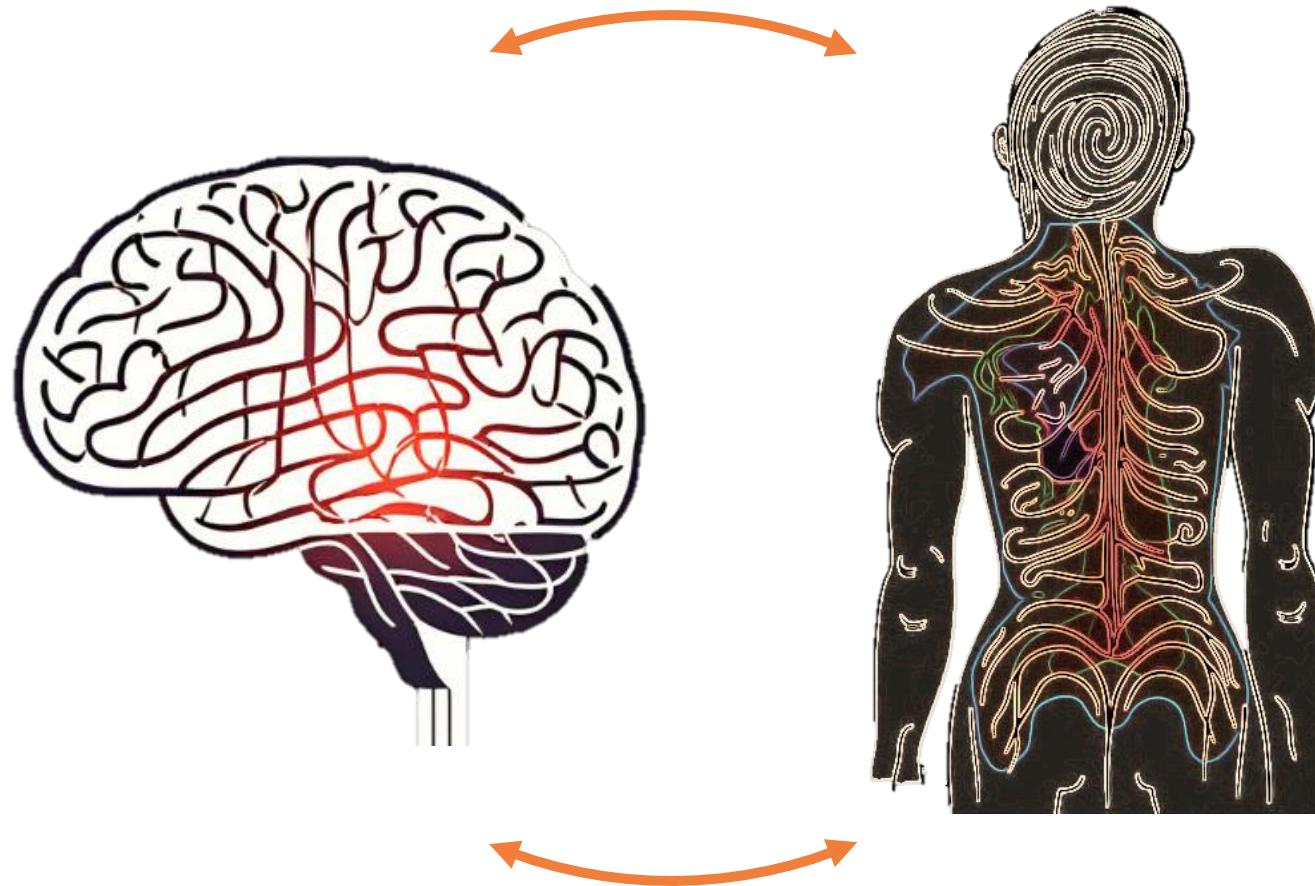


*Family*



*Penny (:*

1 in 4 Americans say most days, they are **too stressed to function**



**Chronic inflammation causes 3 in 5 deaths worldwide**

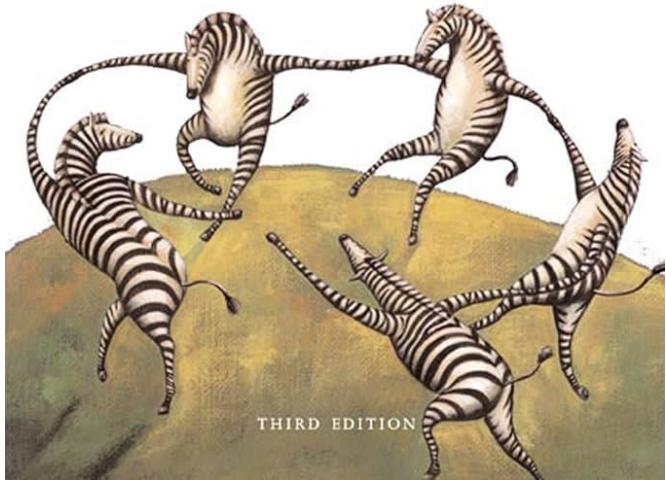
# Stress & Immune (Dys)function

ROBERT M. SAPOLSKY  
Author of *A Primate's Memoir*

## WHY ZEBRAS DON'T GET ULCERS

The Acclaimed Guide to Stress, Stress-Related Diseases, and Coping—Now Revised and Updated

"One of the best science writers of our time."  
—Oliver Sacks



Stress is a **dynamic, embodied** process

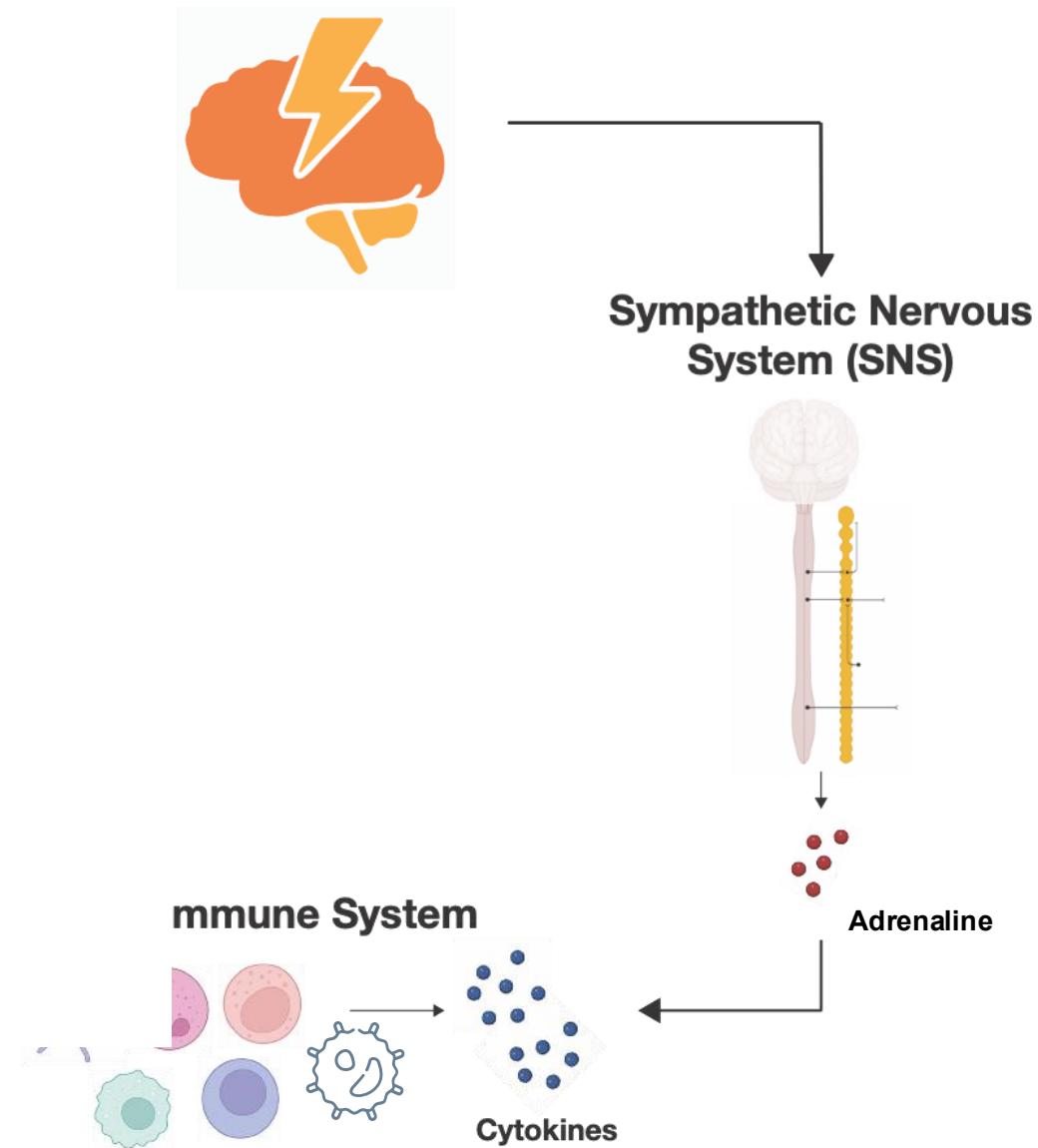


Immune system's role in **mental** and **physical health**

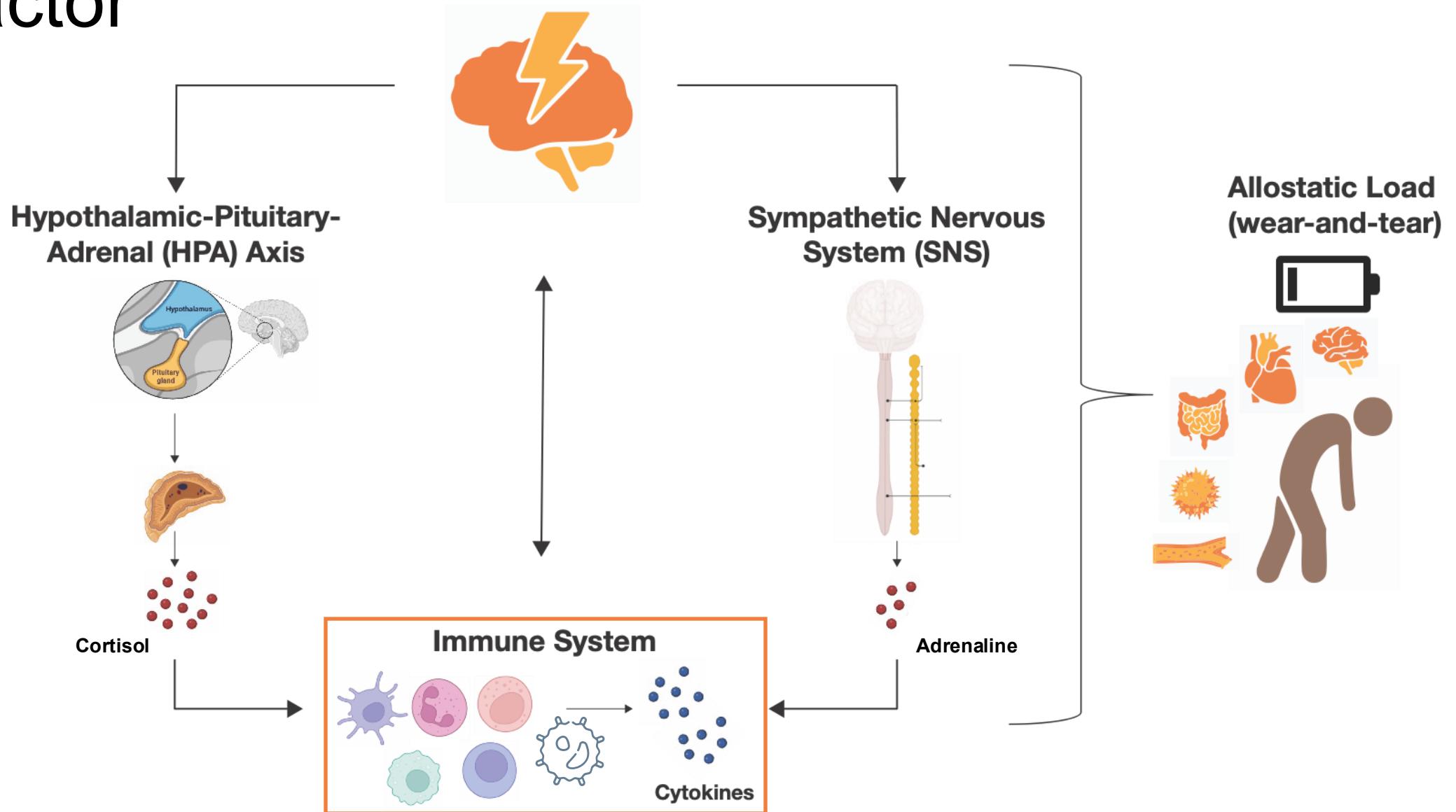


**Transdiagnostic risks...**  
**transdiagnostic resilience?**

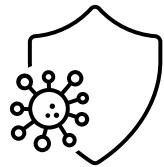
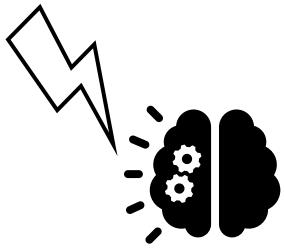
# Psychosocial stress responses involve multiple systems



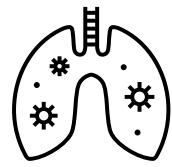
# Psychosocial stress is a transdiagnostic risk factor



# Overview & Roadmap



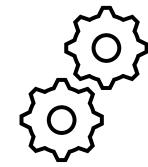
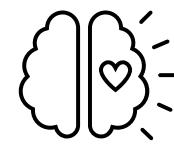
Emotion &  
Inflammation



Neuroimmune  
Mechanisms:  
Asthma

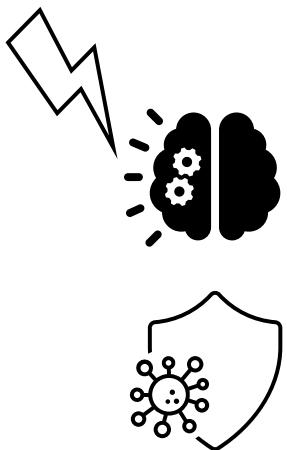


Mindfulness  
Intervention &  
Mechanisms in Asthma

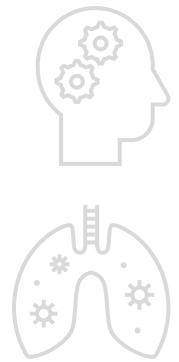


Recap & Future  
Directions

# Overview & Roadmap



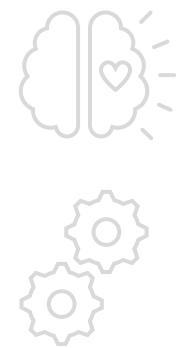
Emotion &  
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Neuroimmune  
Mechanisms:  
Asthma



Mindfulness  
Intervention &  
Mechanisms in Asthma

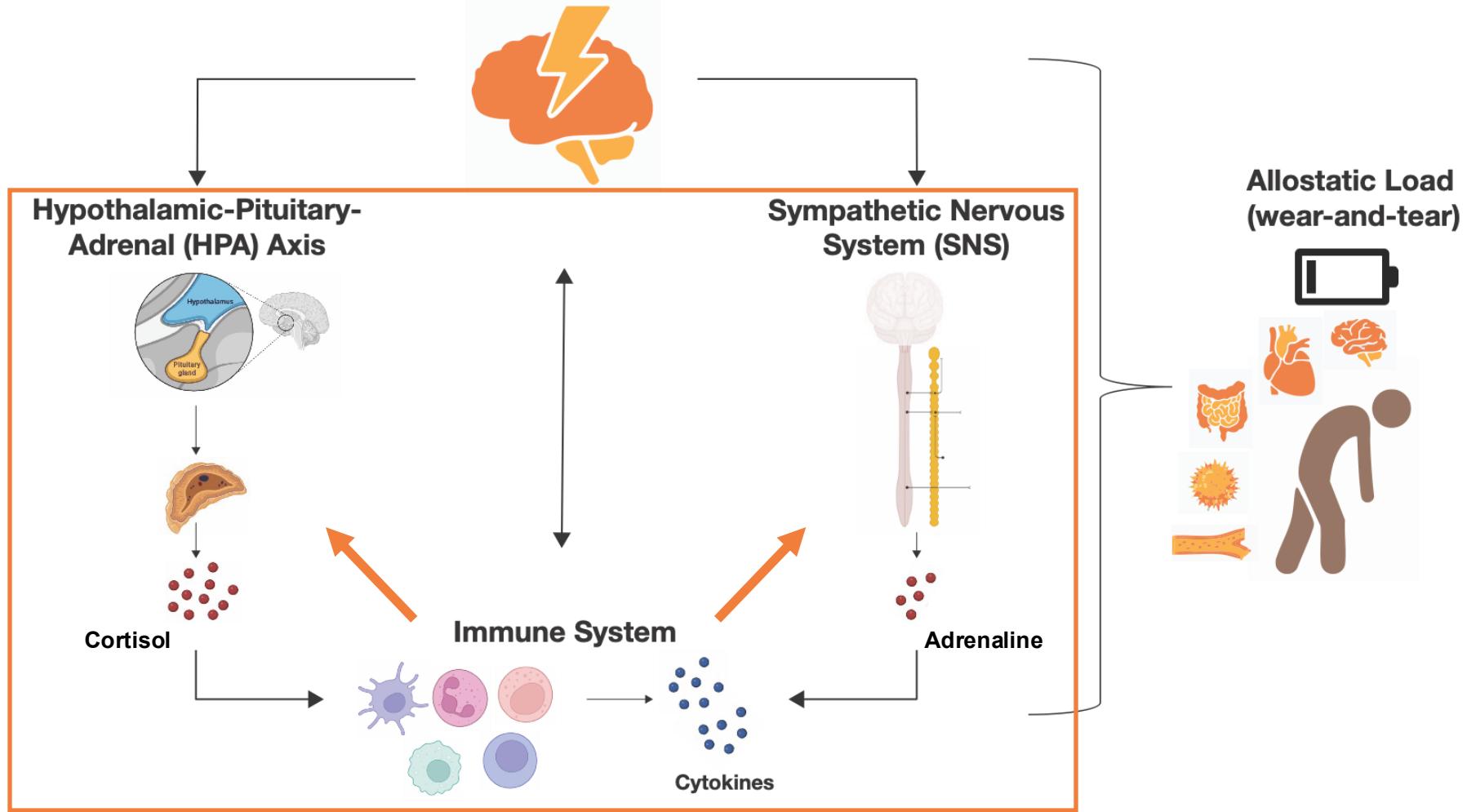


Recap & Future  
Directions

*Are inflammation and lifetime stress associated with acute stress responses in healthy adults?*

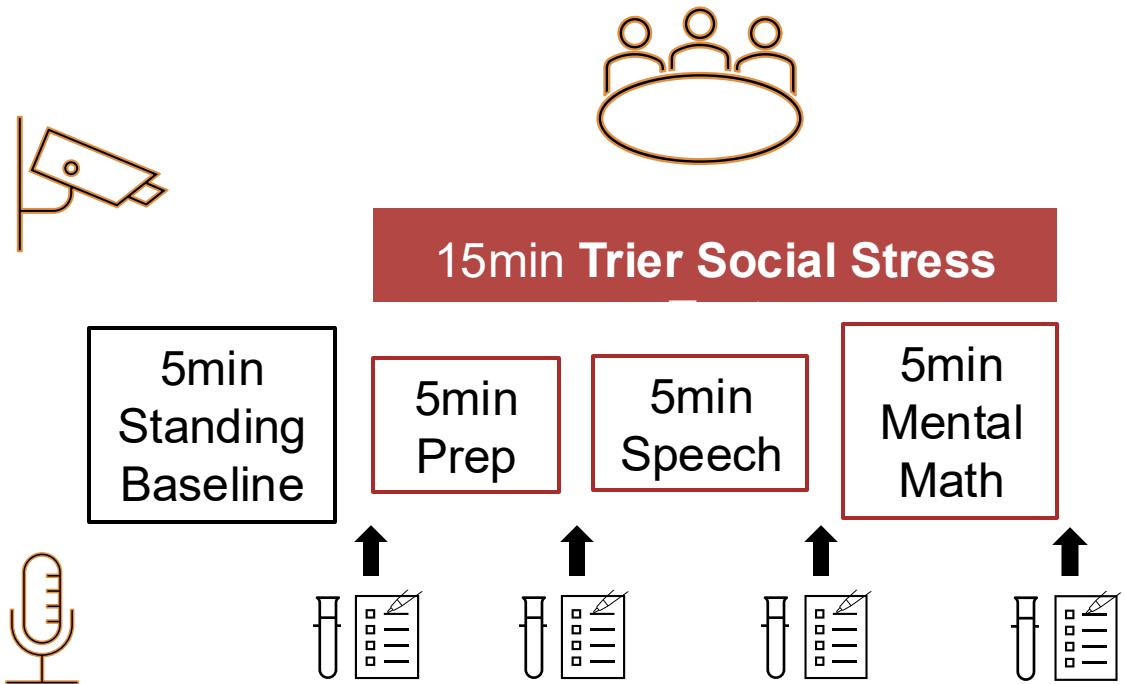
Are inflammation and lifetime stress associated with acute stress responses in healthy adults?

# How does baseline inflammation impact acute stress responses in different systems?



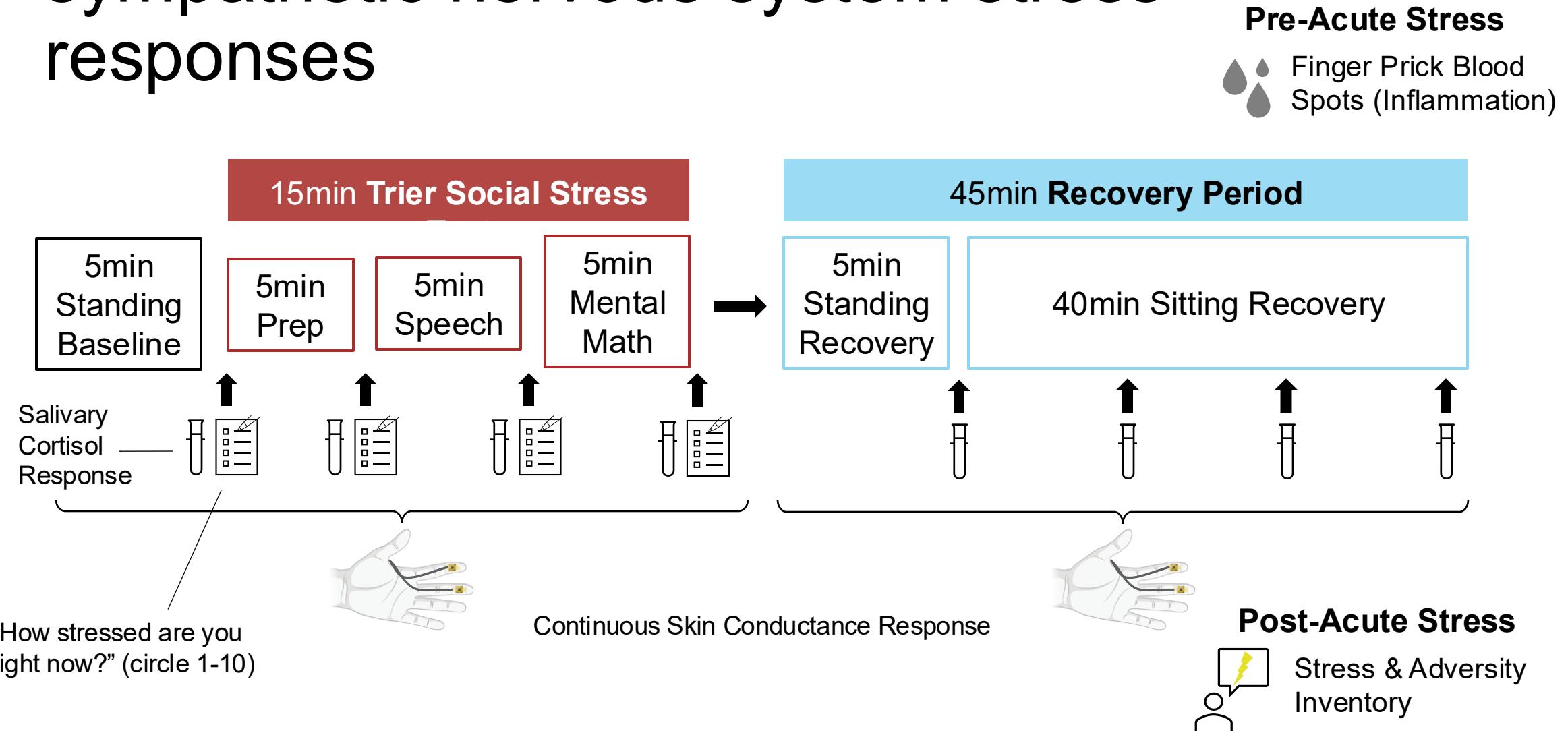
*Are inflammation and lifetime stress associated with acute stress responses in healthy adults?*

# Inducing acute stress responses in the lab with the TSST



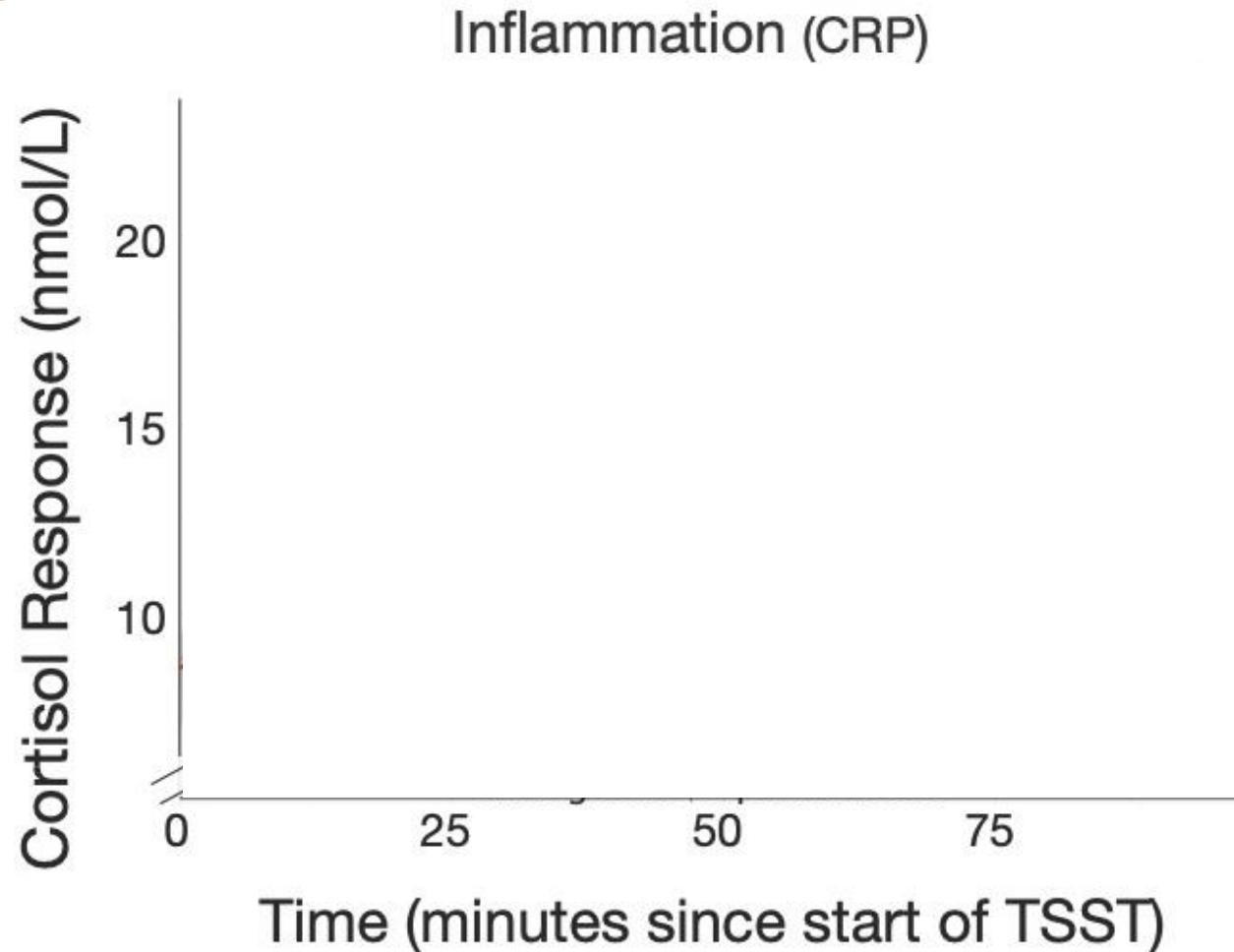
Are inflammation and lifetime stress associated with acute stress responses in healthy adults?

# We measured inflammation, HPA axis, and sympathetic nervous system stress responses



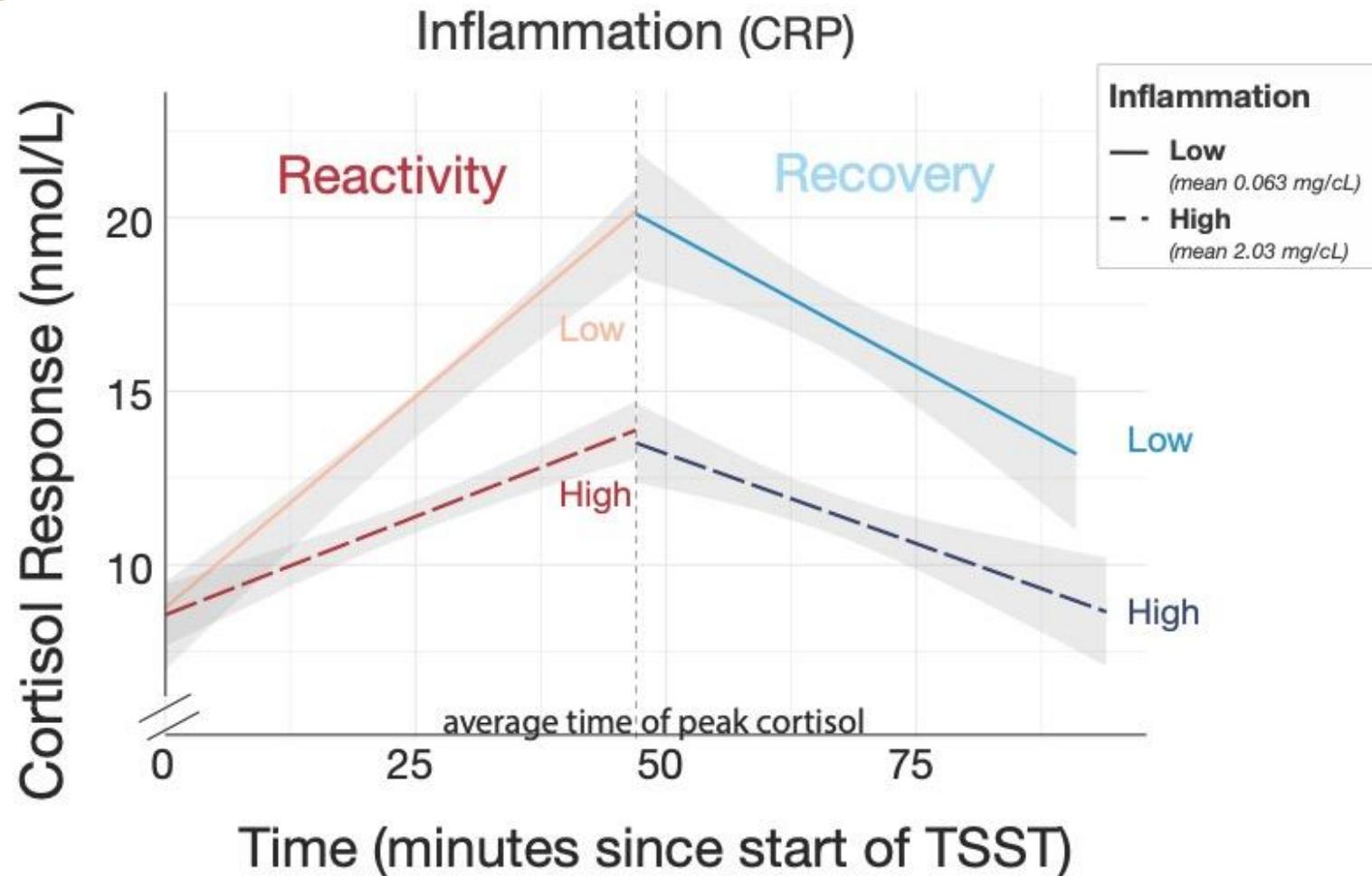
*Are inflammation and lifetime stress associated with acute stress responses in healthy adults?*

Higher inflammation and lifetime stressor severity were associated with blunted cortisol response



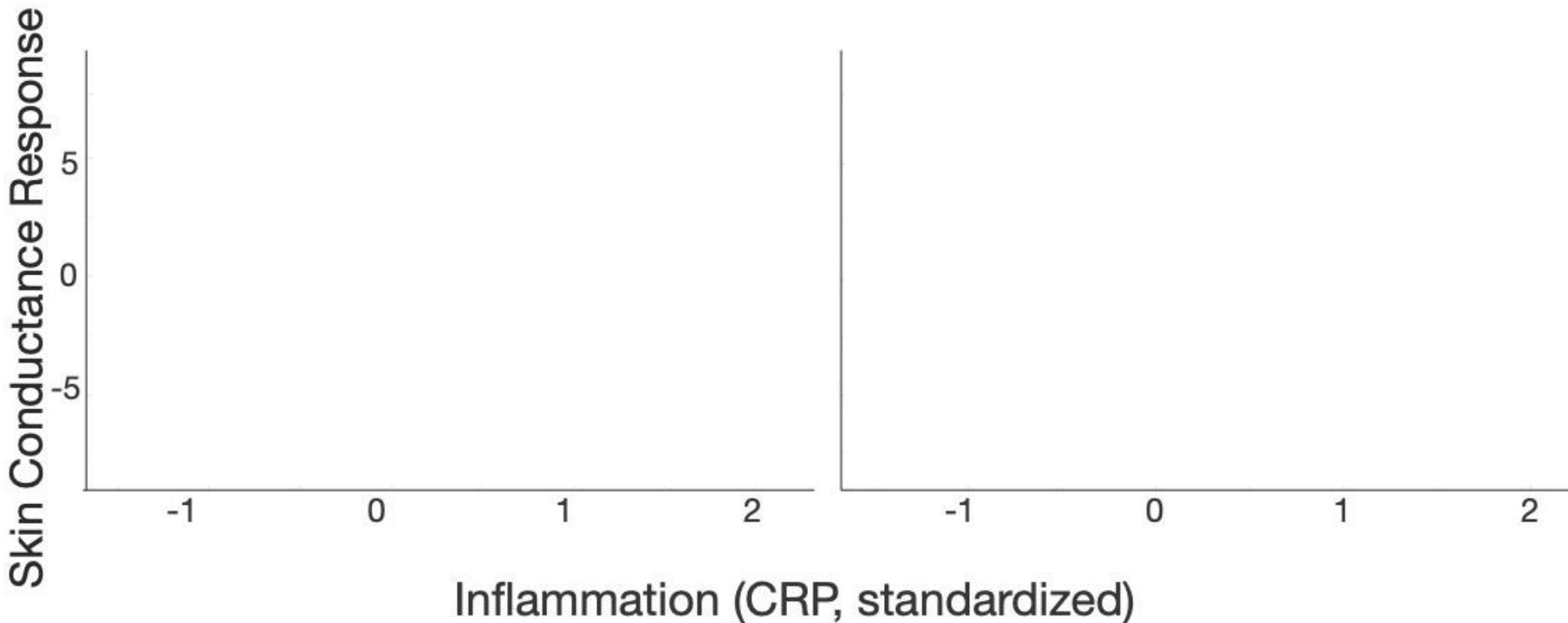
Are inflammation and lifetime stress associated with acute stress responses in healthy adults?

# Higher inflammation and lifetime stressor severity were associated with blunted cortisol response



*Are inflammation and lifetime stress associated with acute stress responses in healthy adults?*

Inflammation and lifetime stressor severity  
were *not* associated with skin conductance  
response



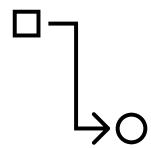
# Key Takeaways

- Individuals with higher **lifetime stressor exposure** and **baseline inflammation** had **reduced cortisol**, but not skin conductance response to acute stress
- Response profiles may predict future risk, inform intervention

# Limitations



Healthy sample, low inflammation



No immune manipulation

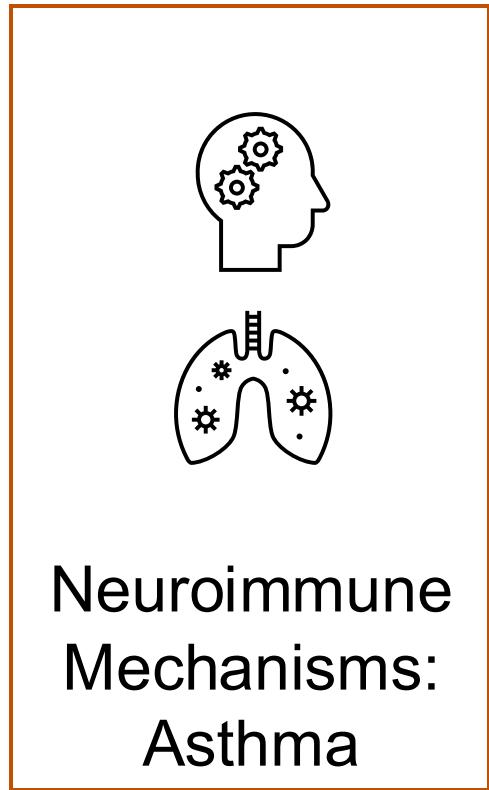


Neural mechanisms?

# Overview & Roadmap

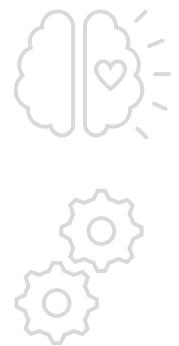


Emotion &  
Inflammation



*What neural mechanisms link asthma-related inflammation to chronic and acute distress?*

Mindfulness  
Intervention &  
Mechanisms in Asthma



Recap & Future  
Directions

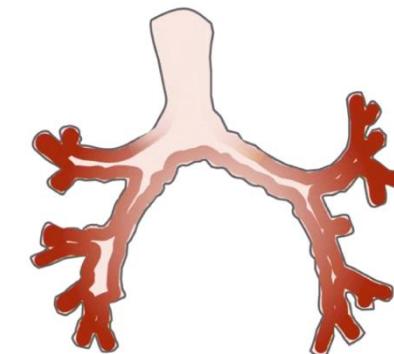
What neural mechanisms link asthma-related inflammation to chronic and acute distress?

# Asthma model of neuroimmune-emotion interactions

Depression & anxiety rates 2x  
the general population

Global Asthma  
Prevalence:  
262 million

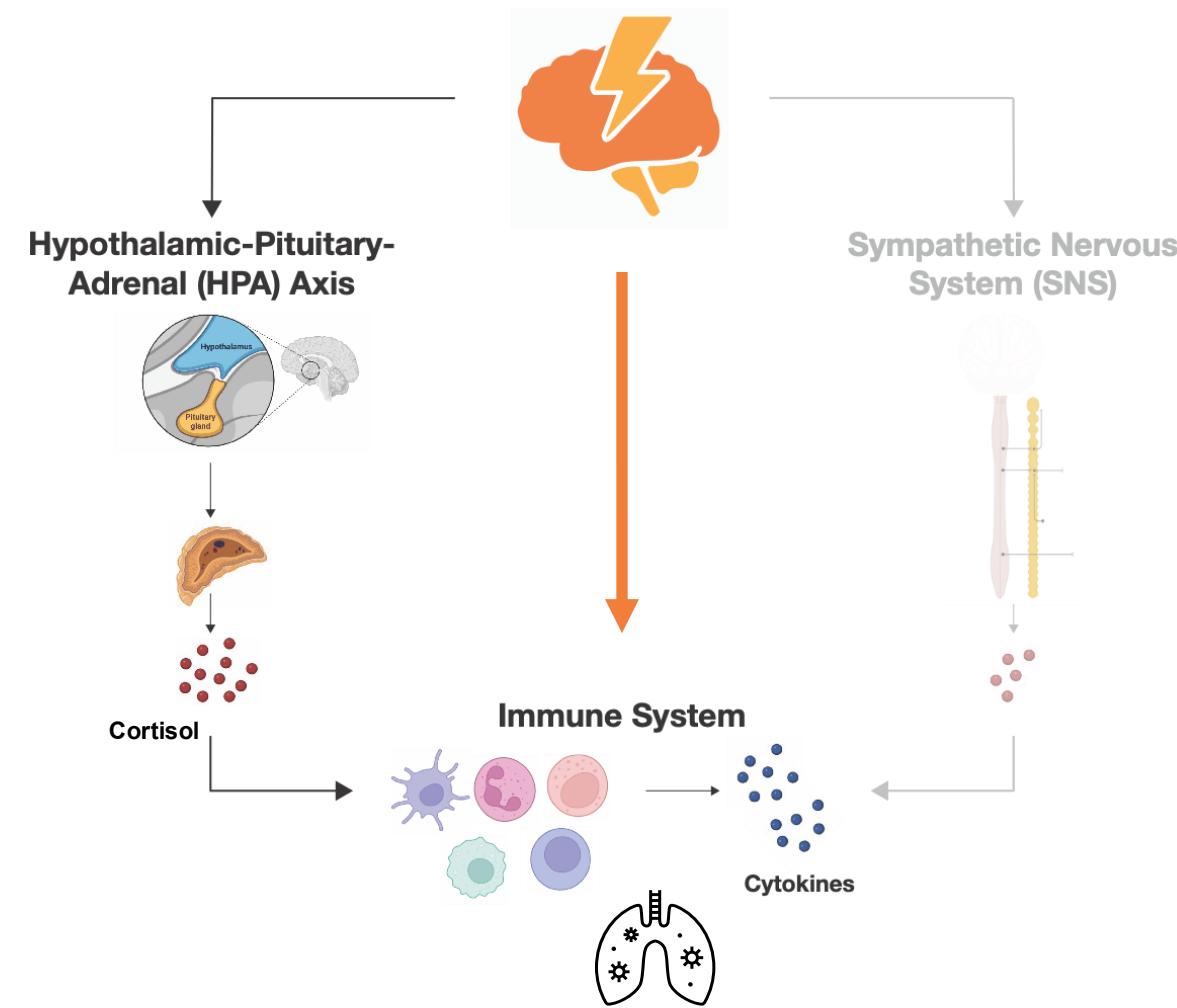
~1200 deaths/day



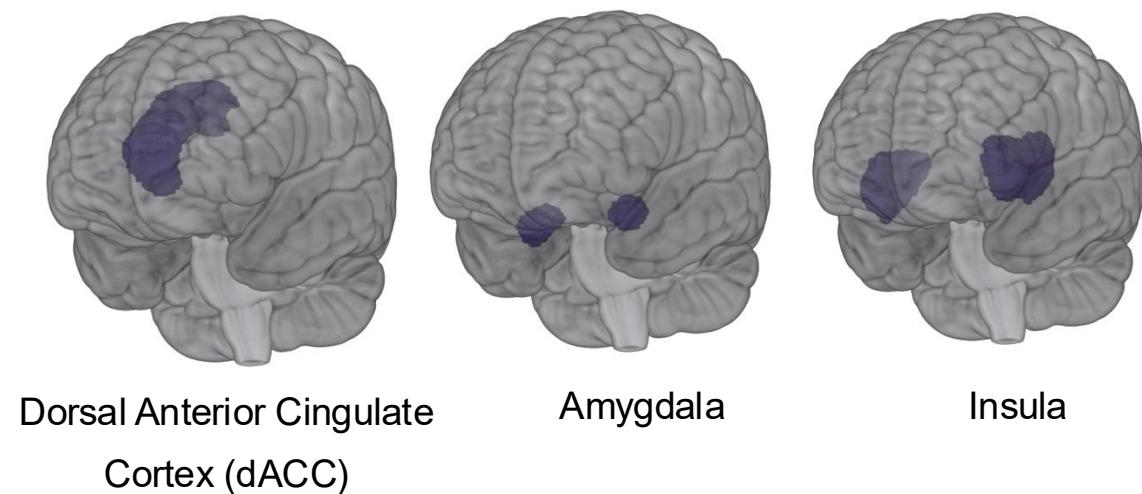
Higher Stress: more severe, poorly-controlled, treatment-resistant asthma

What neural mechanisms link asthma-related inflammation to chronic and acute distress?

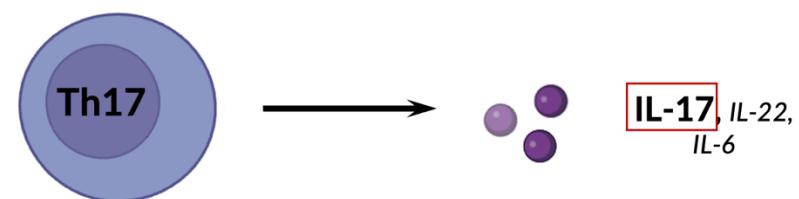
# Brain and immune pathways remain unknown



Stress/emotion neurocircuitry: **salience network**



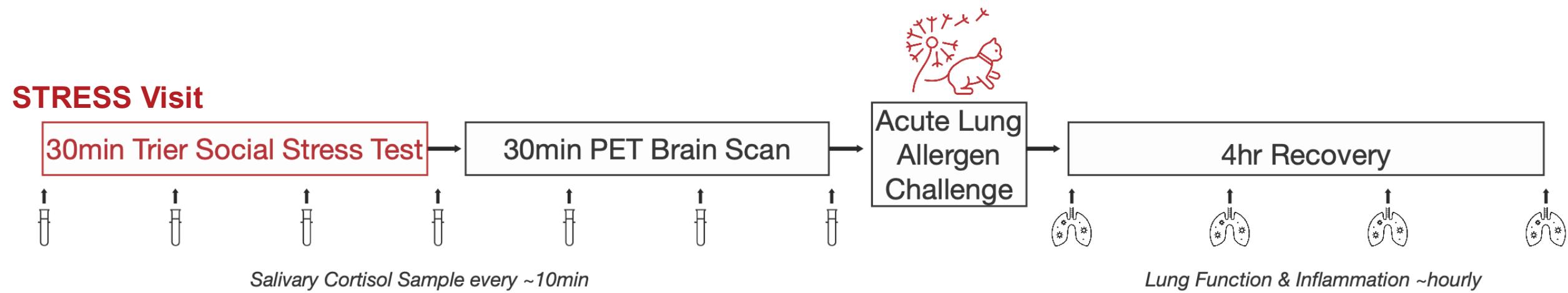
Immune pathways: asthma, stress, depression



(Beurel et al., 2013; Menon, 2015)

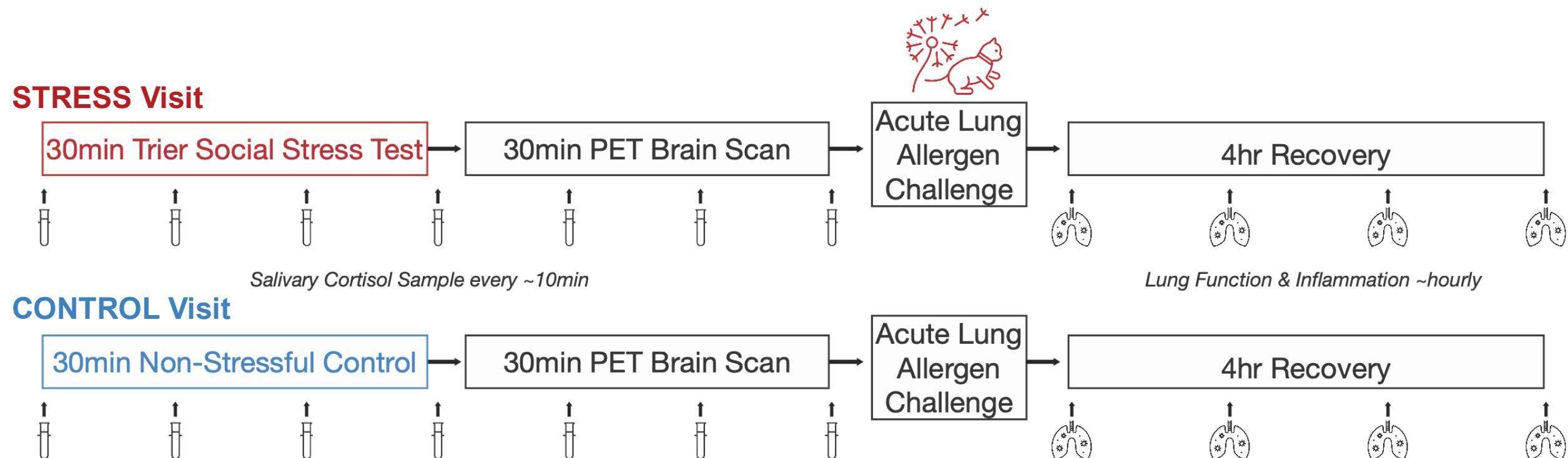
What neural mechanisms link asthma-related inflammation to chronic and acute distress?

# Within-subjects design manipulated acute stress *and* inflammation: brain-to-lung

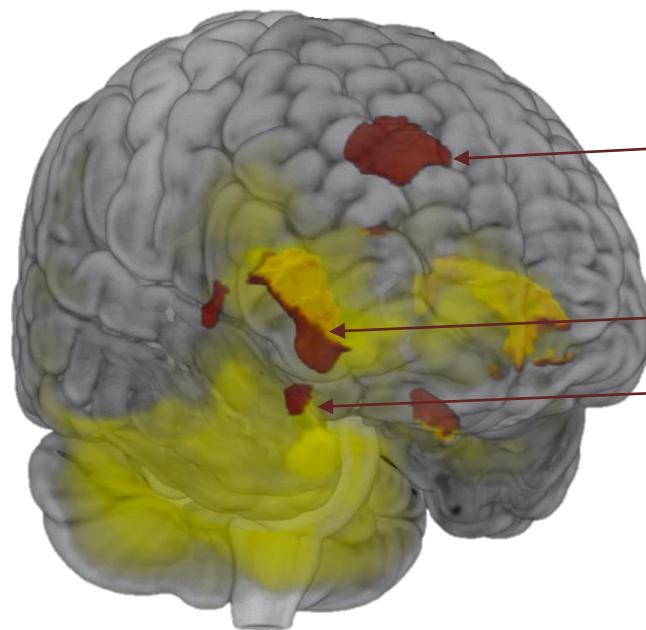


What neural mechanisms link asthma-related inflammation to chronic and acute distress?

# Within-subjects design manipulated acute stress and inflammation: brain-to-lung



# Cortisol response to acute stress was associated with brain response to acute stress



Dorsal Anterior Cingulate Cortex  
(dACC)

Insula  
Amygdala



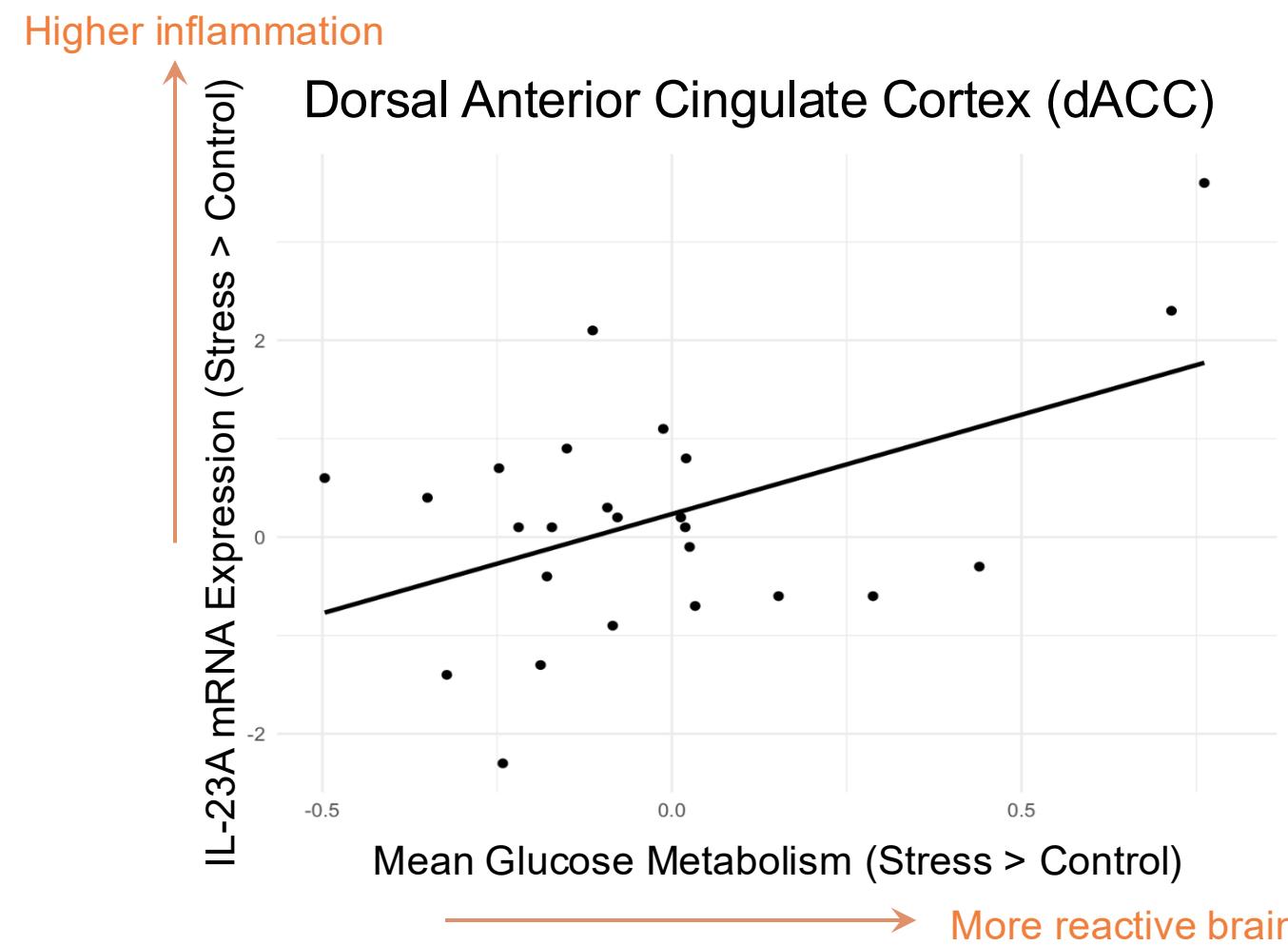
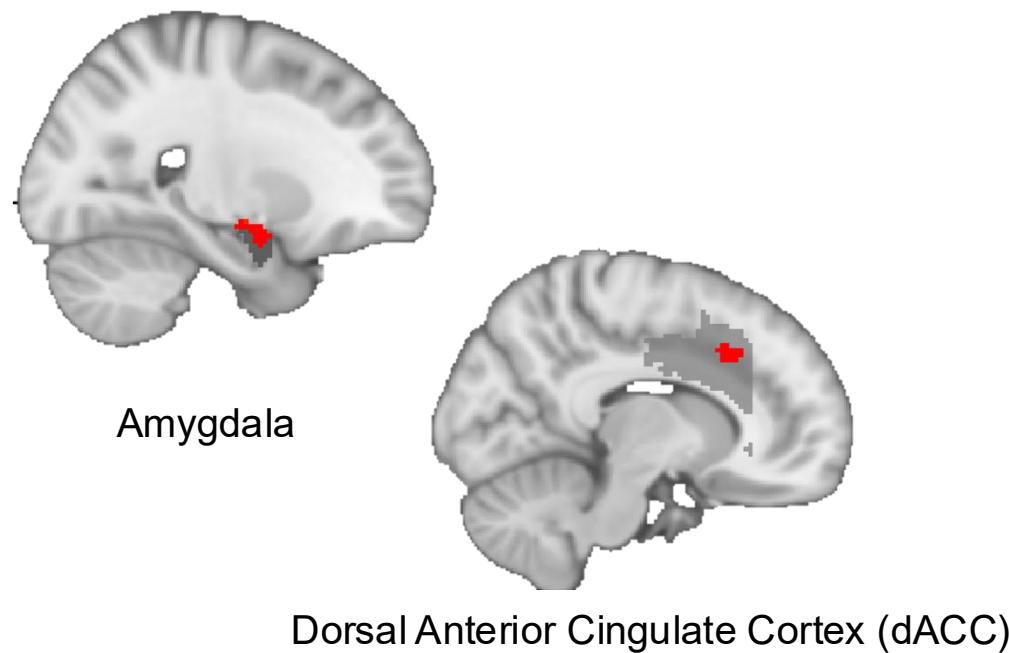
*stress > control & greater cortisol response*



*local Salience Network peaks*

What neural mechanisms link asthma-related inflammation to chronic and acute distress?

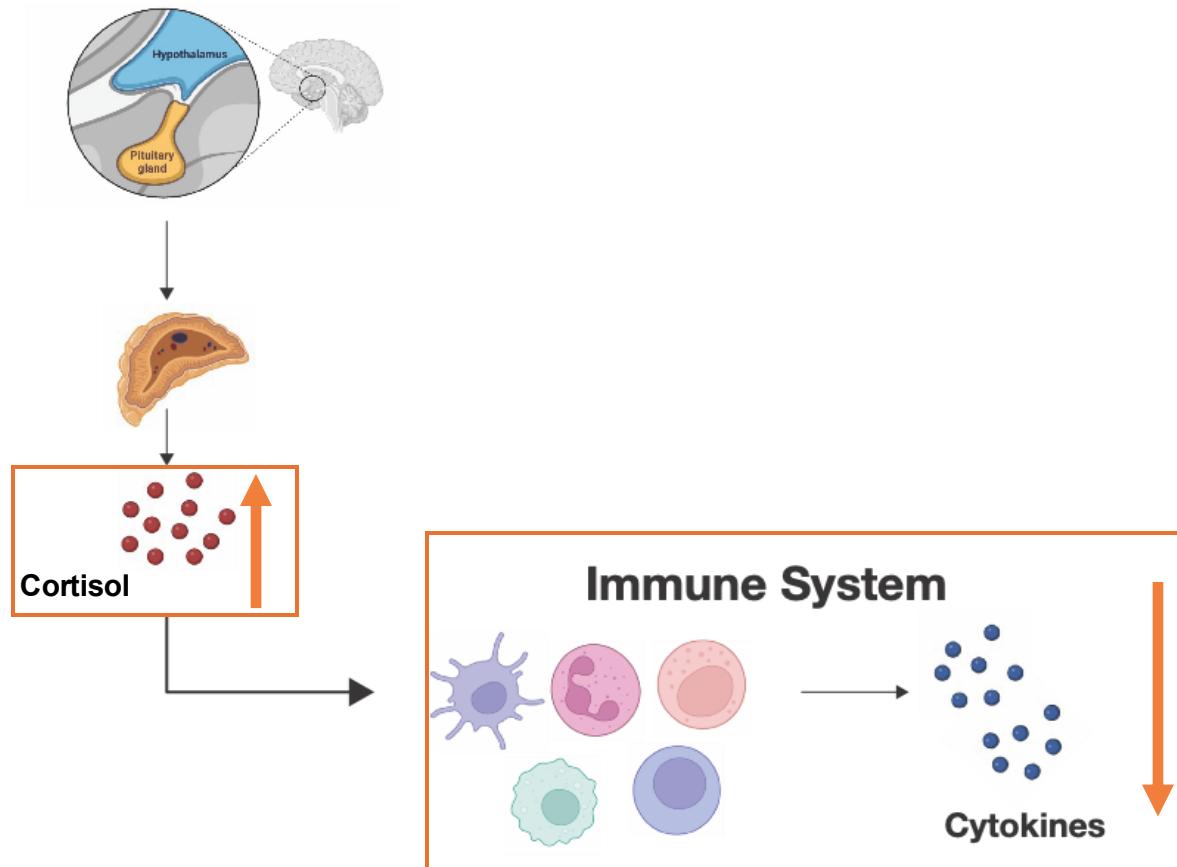
# Salience network reactivity to acute stress predicted airway inflammation



*What neural mechanisms link asthma-related inflammation to chronic and acute distress?*

# Acute cortisol suppresses inflammation, but chronic stress amplifies inflammation

Hypothalamic-Pituitary-  
Adrenal (HPA) Axis

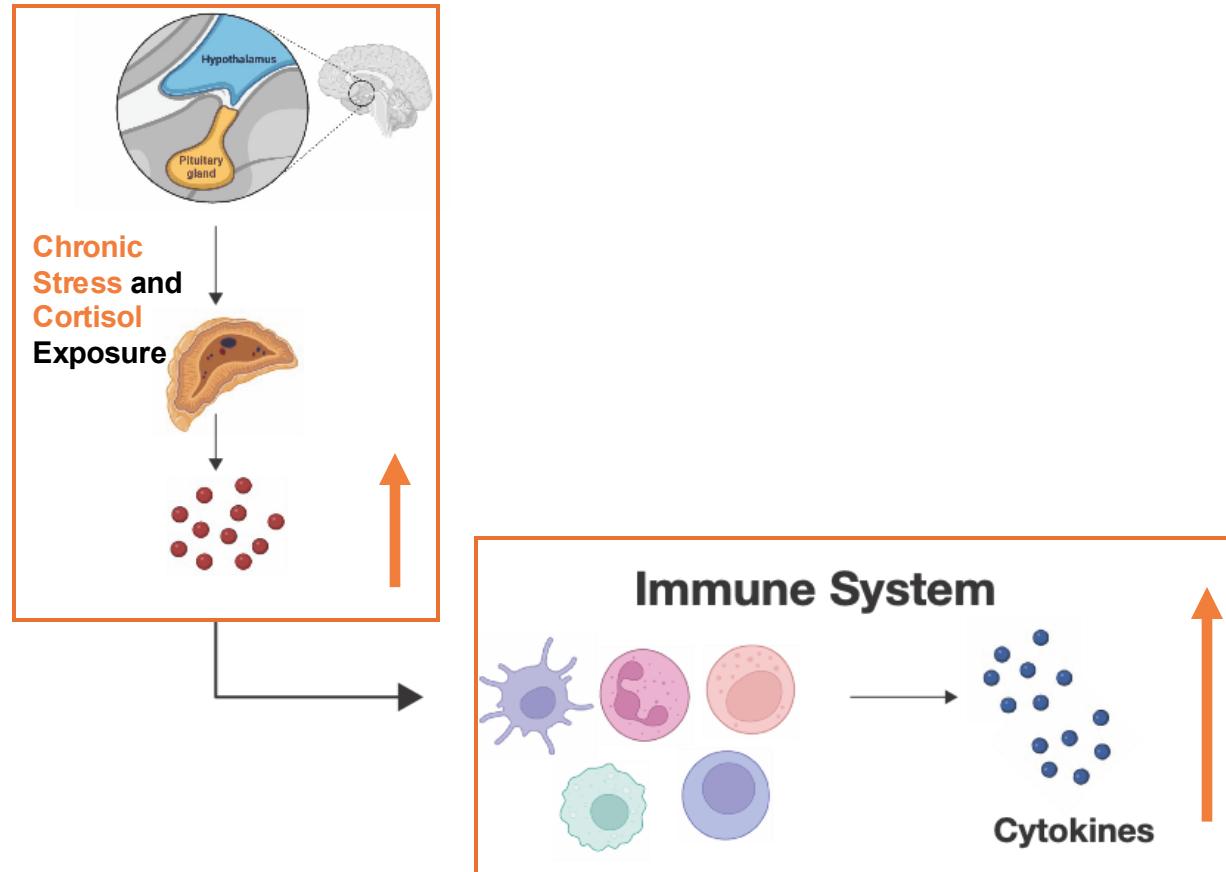


(Chen et al., 2006)

*What neural mechanisms link asthma-related inflammation to chronic and acute distress?*

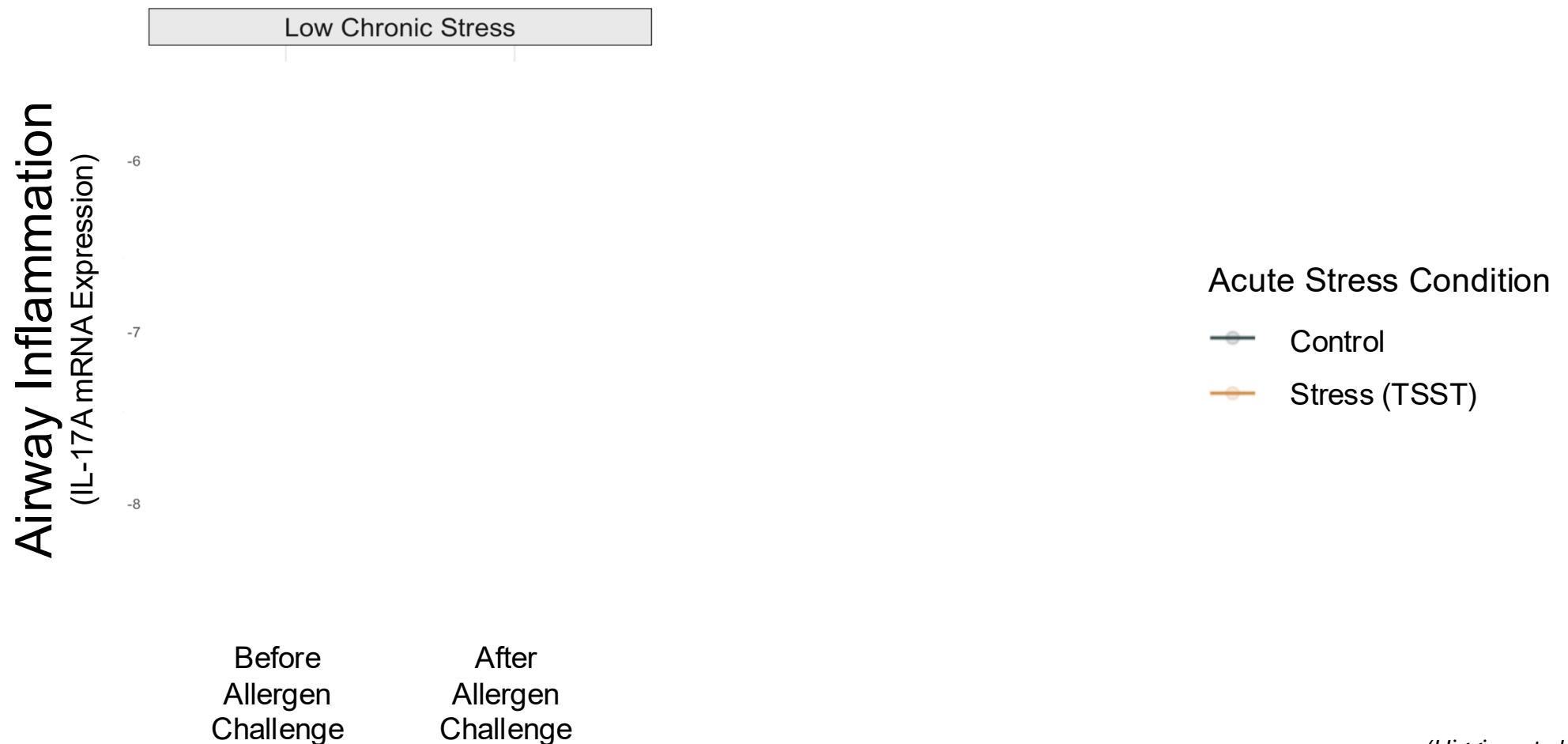
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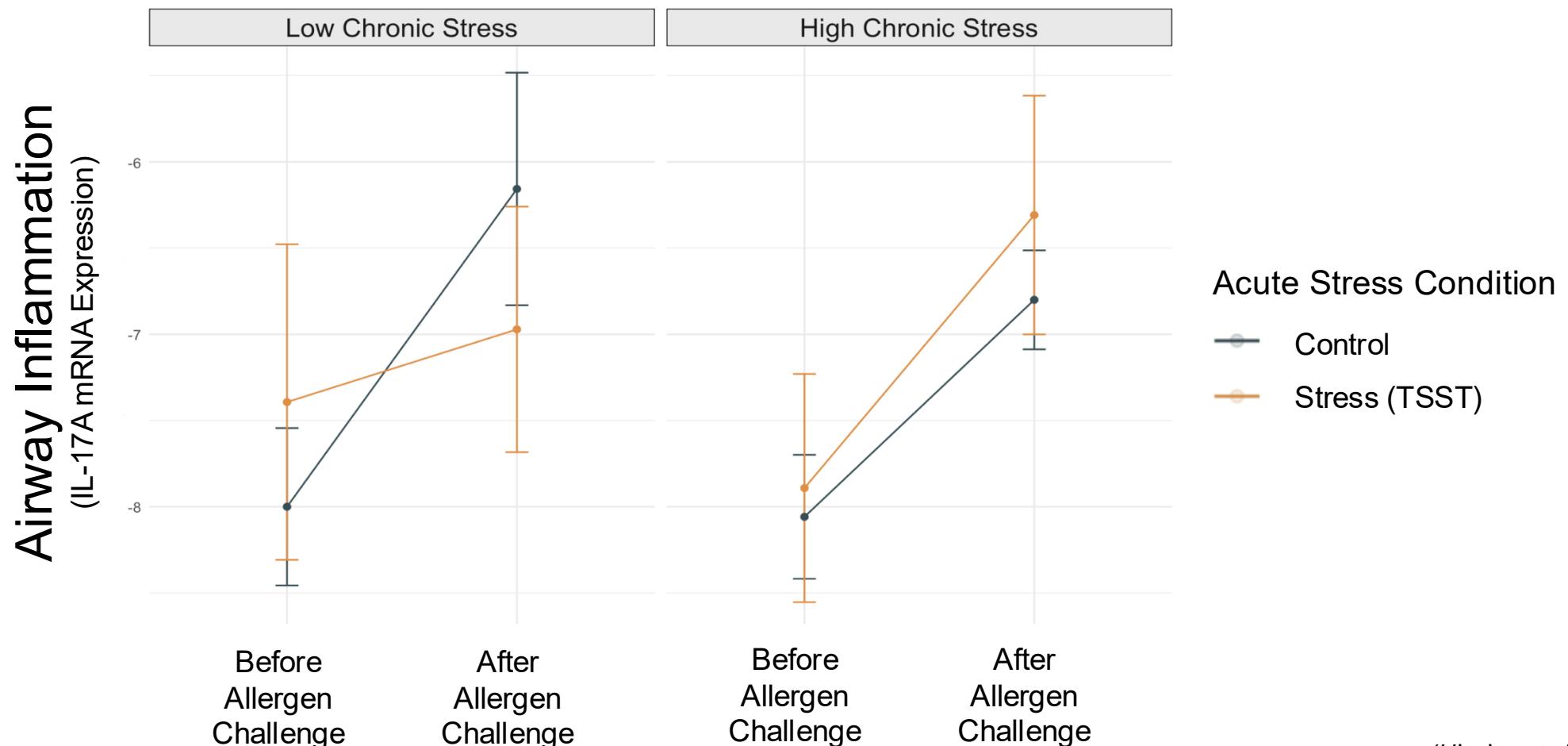


(Chen et al., 2006)

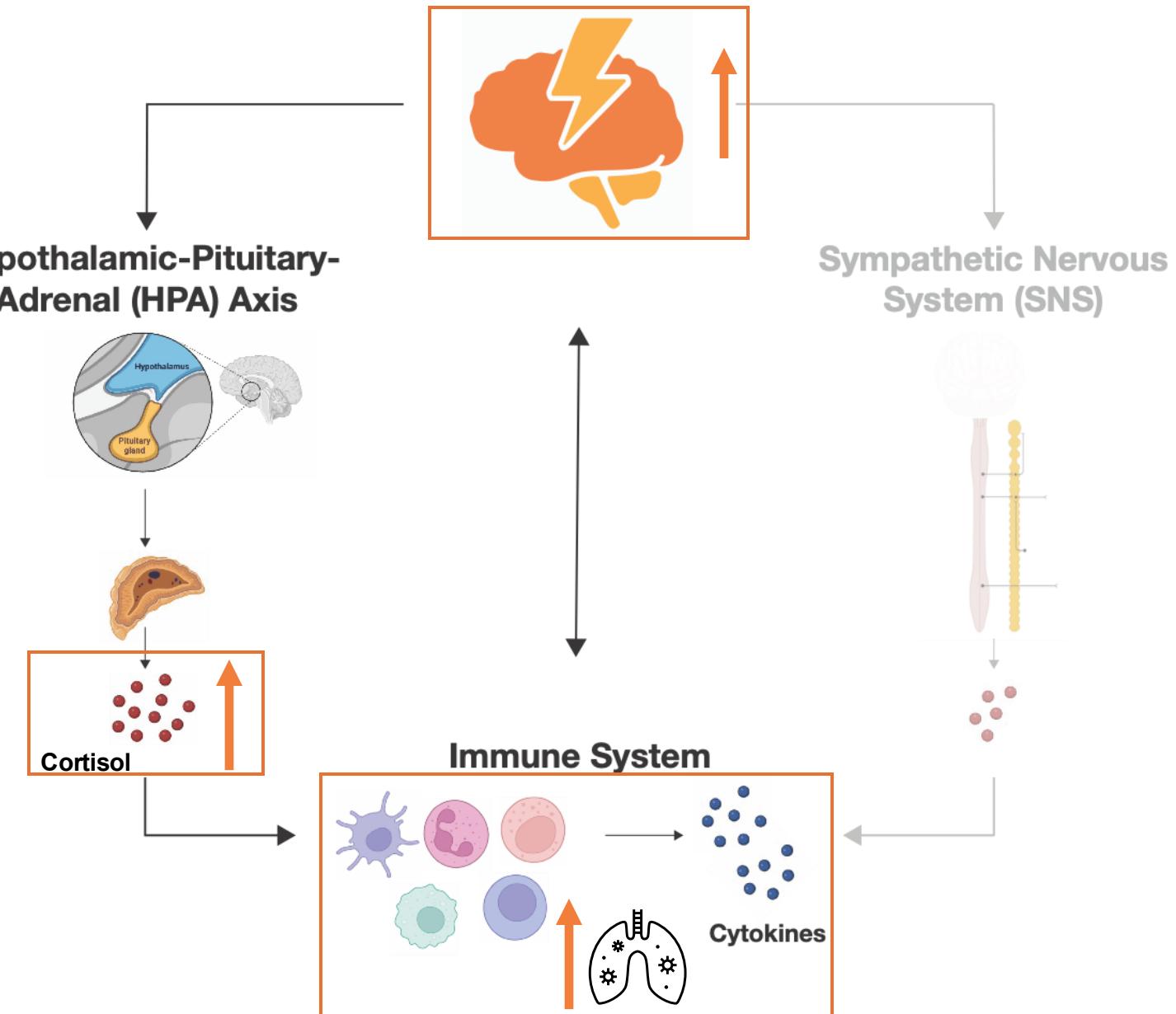
# Chronic stress amplified effects of acute stress on airway inflammation



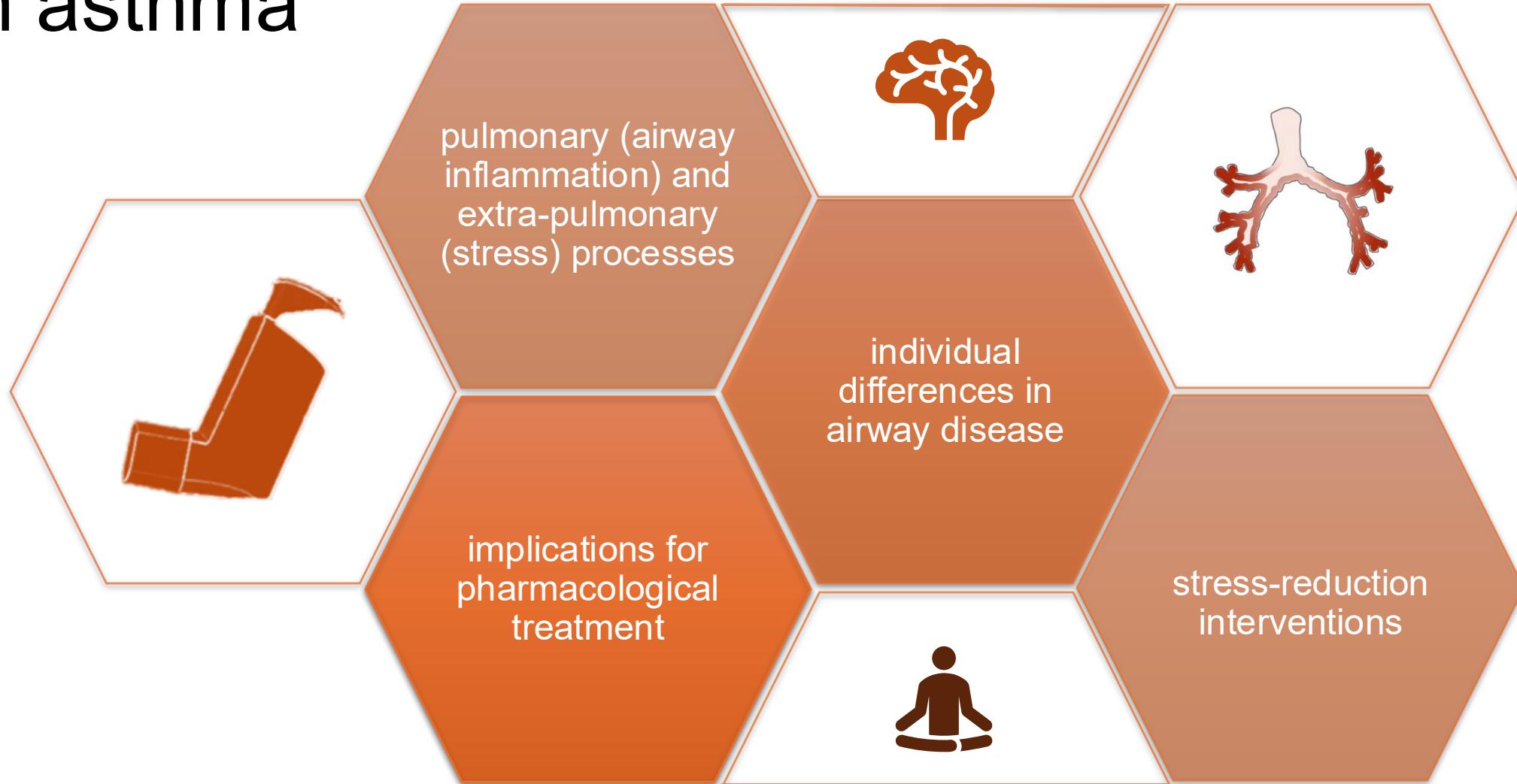
# Chronic stress amplified effects of acute stress on airway inflammation



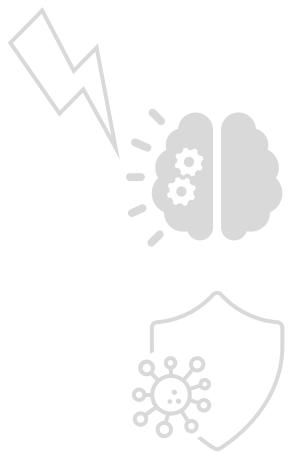
**Main Takeaway:**  
Individual differences  
in neural and cortisol  
responses to acute  
stress impacted  
airway inflammation  
responses to  
allergen challenge



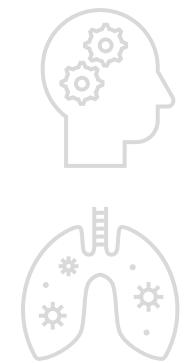
# Integrative treatment and prevention are needed in asthma



# Overview & Roadmap



Emotion &  
Inflammation



Neuroimmune  
Mechanisms:  
Asthma



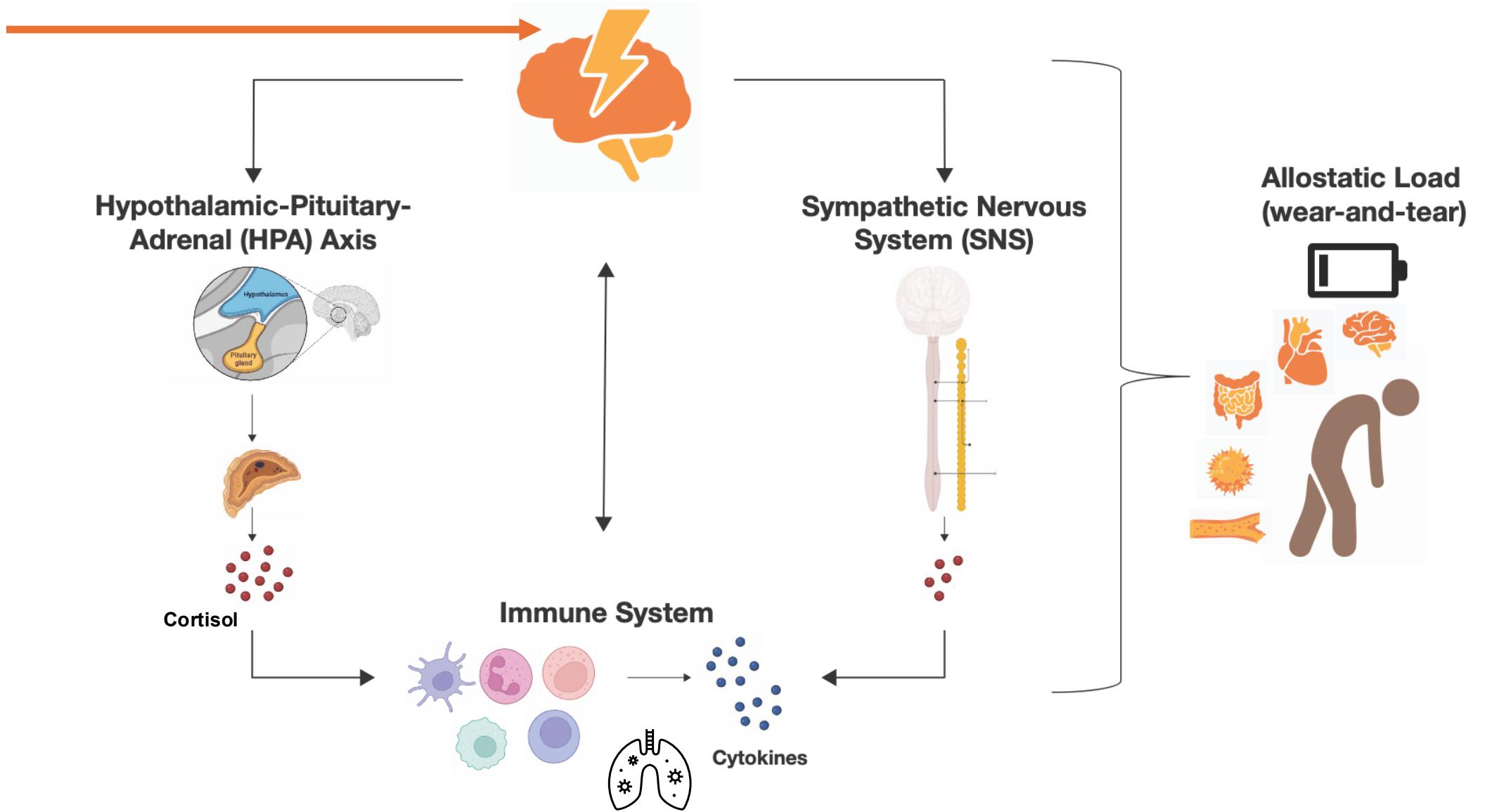
Mindfulness  
Intervention &  
Mechanisms in Asthma



Recap & Future  
Directions

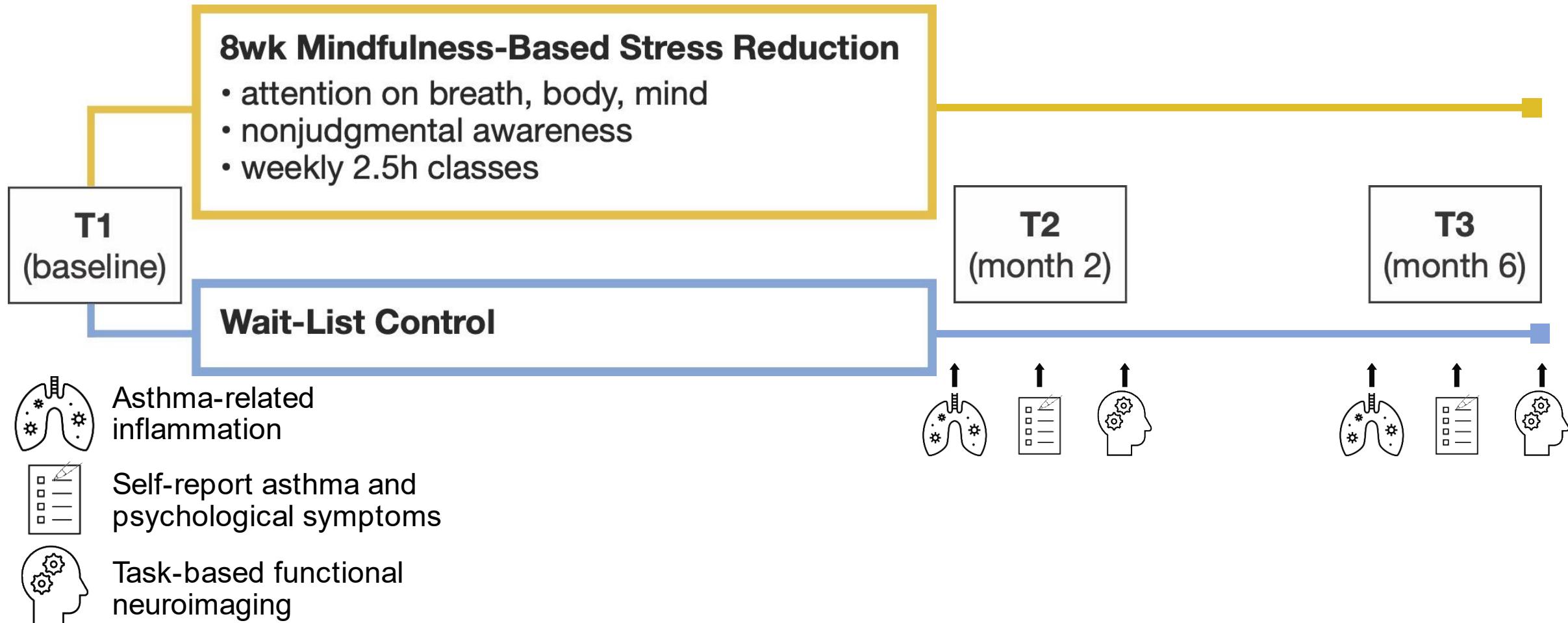
*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

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*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

# Mindfulness-Based Stress Reduction (MBSR) in Asthma



*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

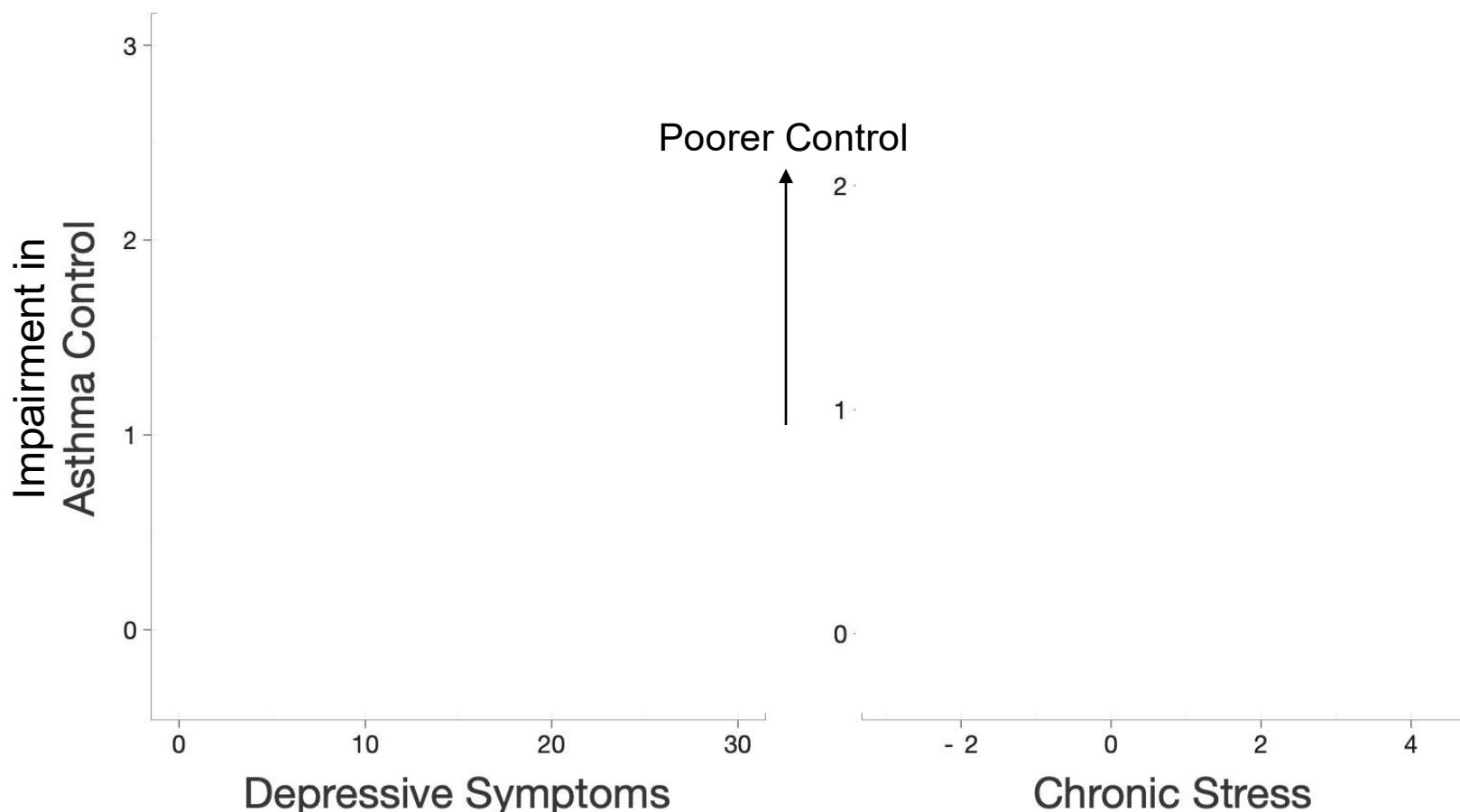
# Asthma Control measures daily asthma management

-  Nighttime awakenings
-  Activity limitations
-  Shortness of breath/wheezing
-  Inhaler use



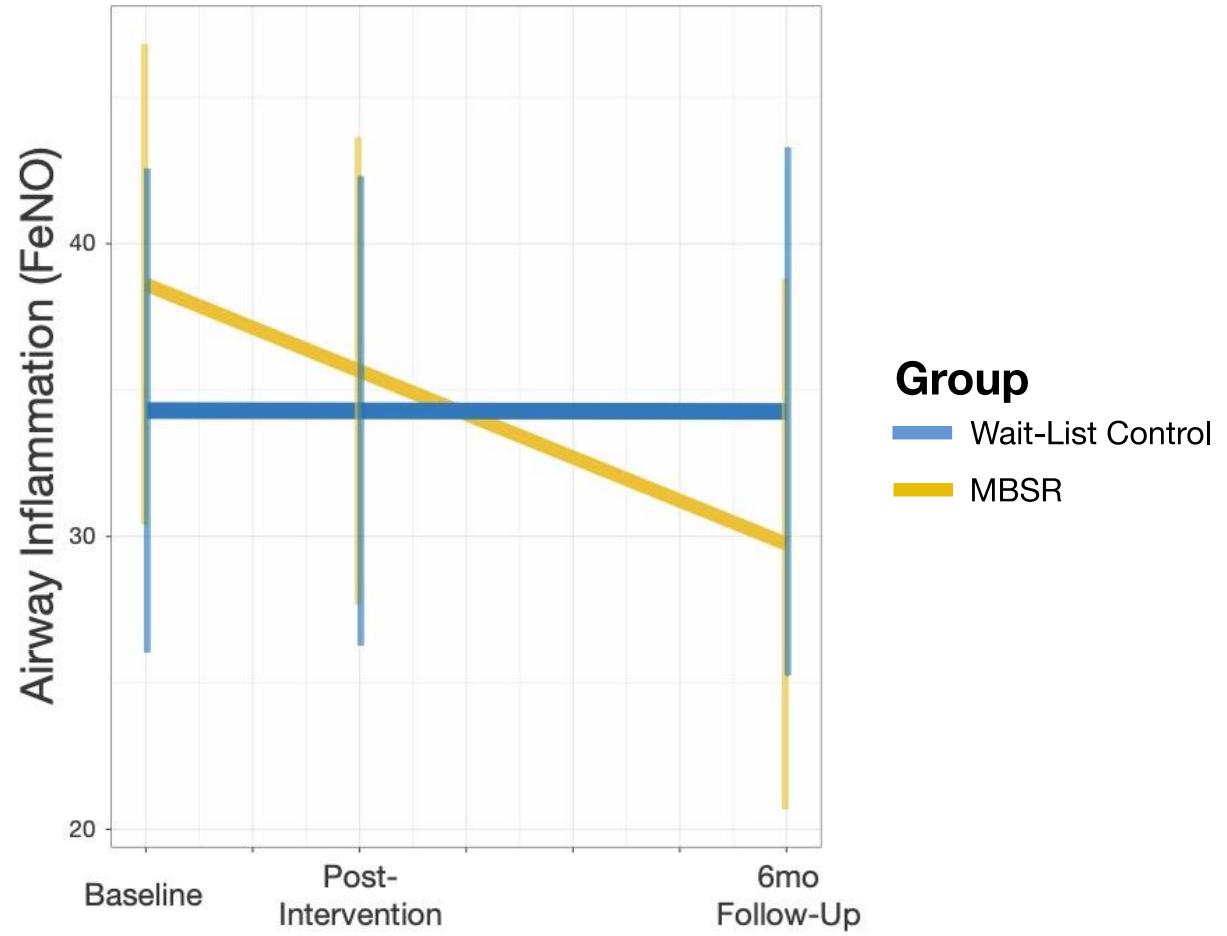
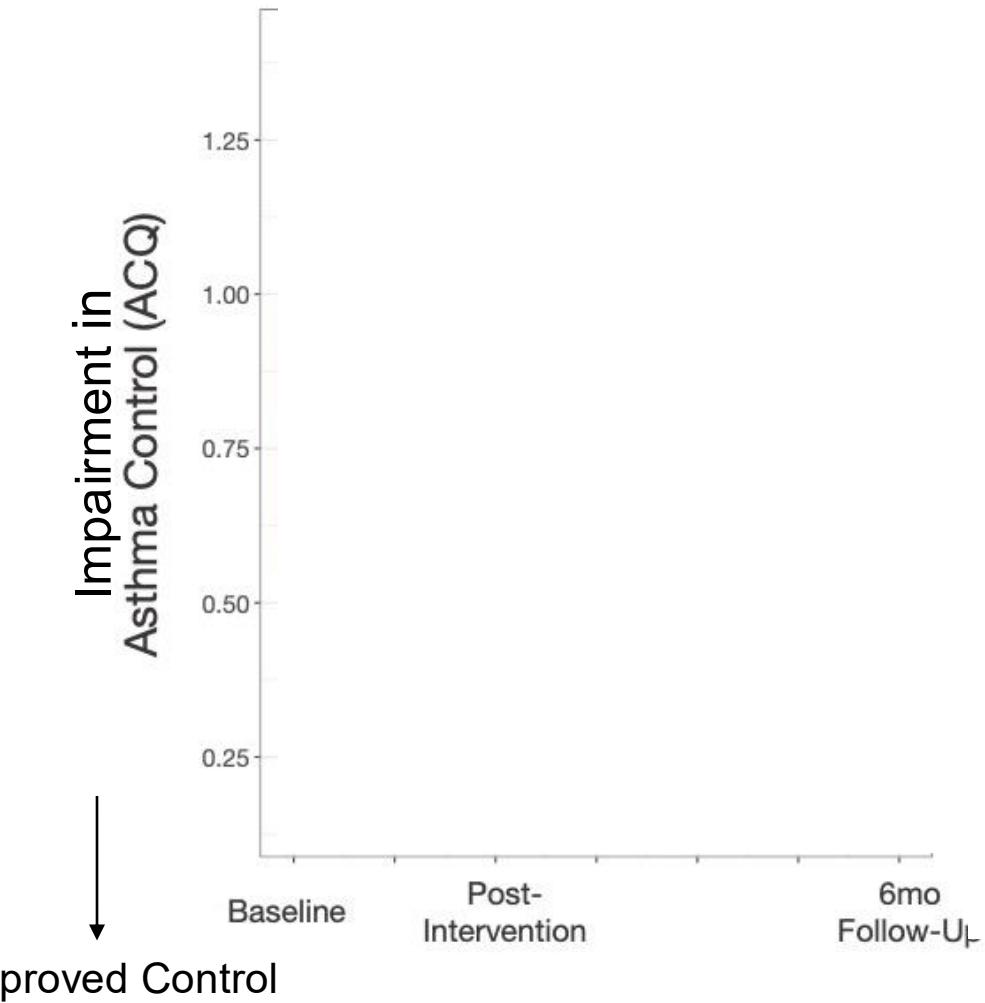
## *What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

Poorer asthma control was associated with depressive symptoms & chronic stress at baseline



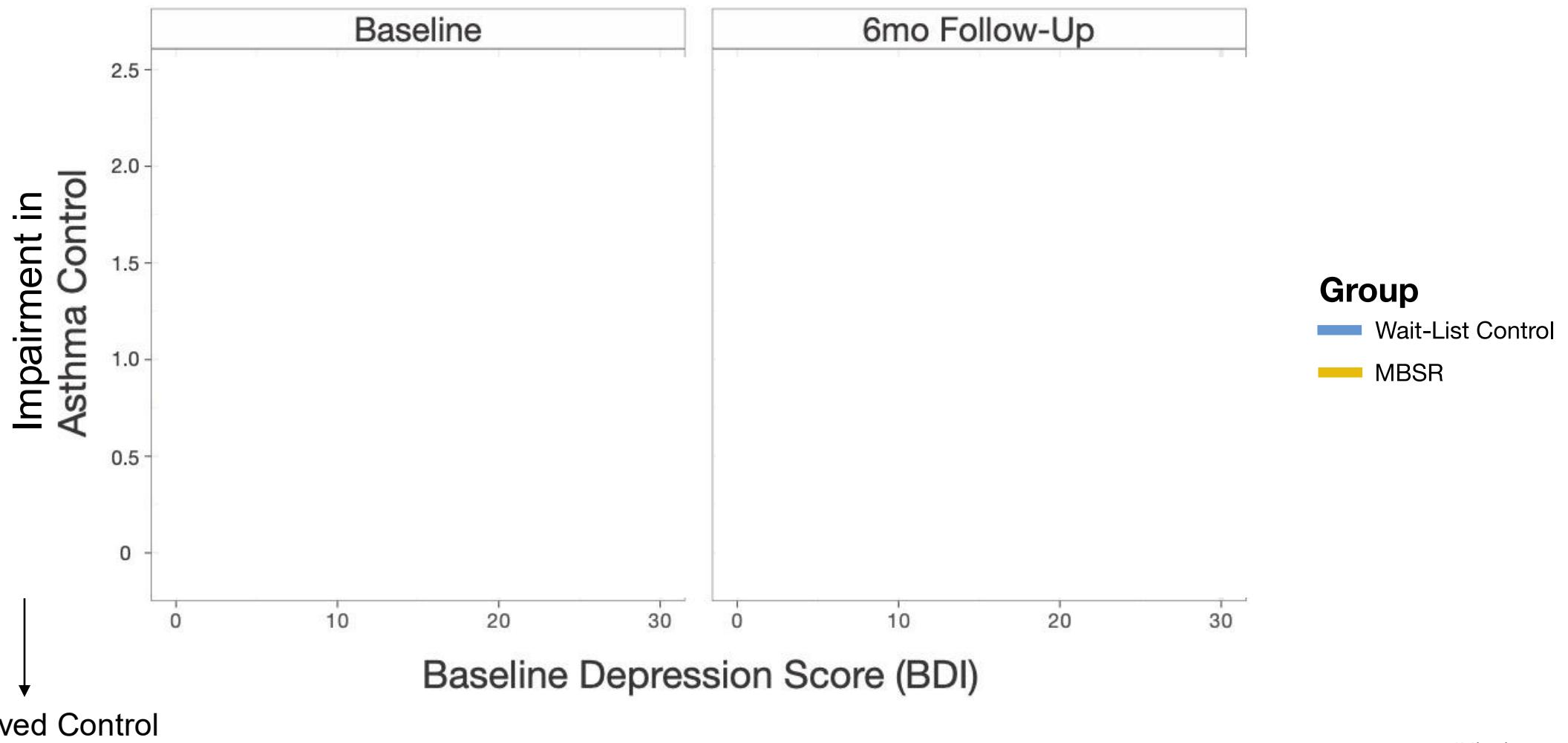
*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

# MBSR improved asthma control & reduced airway inflammation



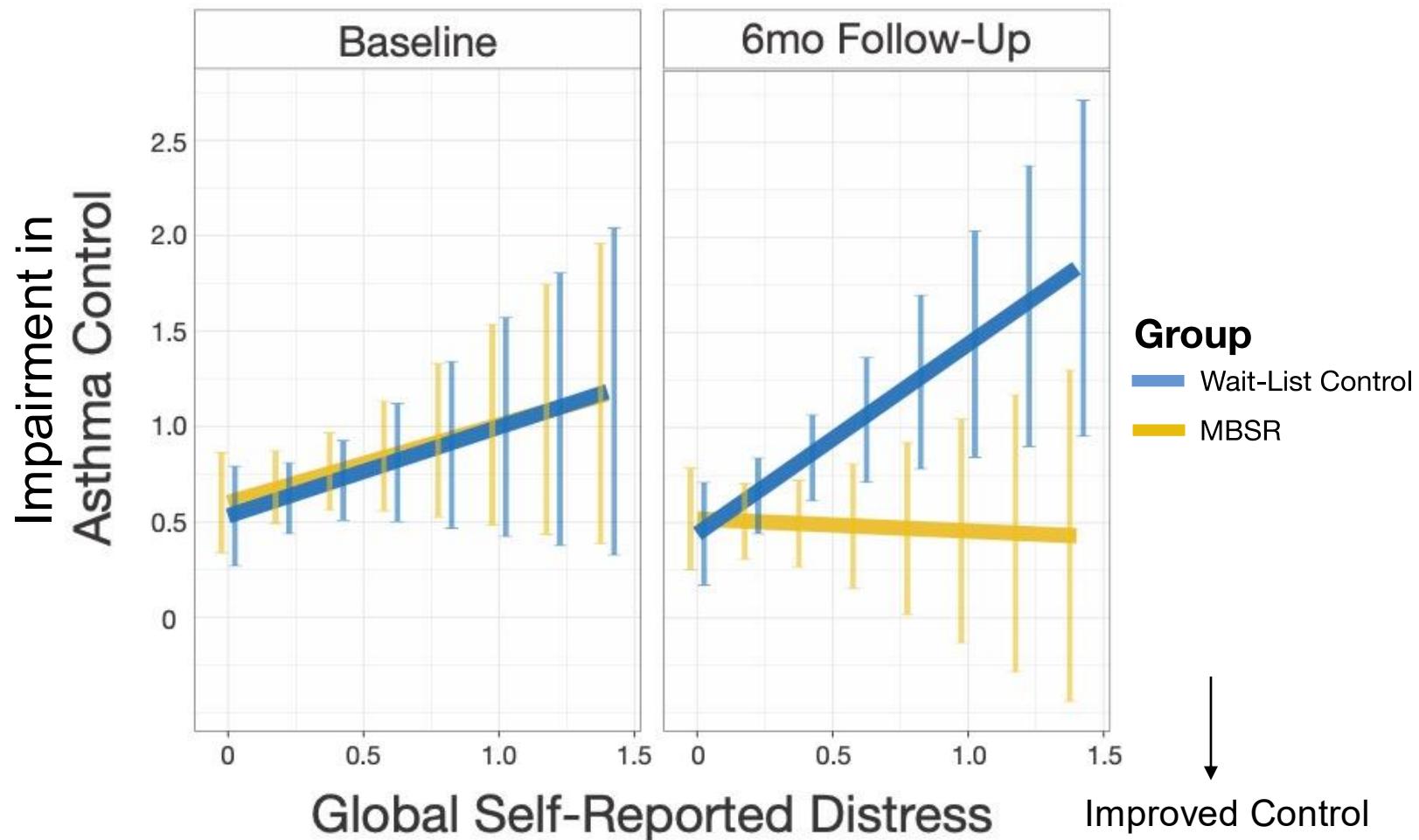
*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

MBSR improved asthma control most for those with highest baseline depression

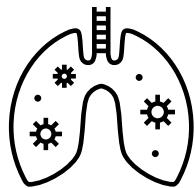


*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

# MBSR improved asthma control, associated with reduced distress



# Main Takeaways



Asthma Control ↑ & Airway Inflammation ↓



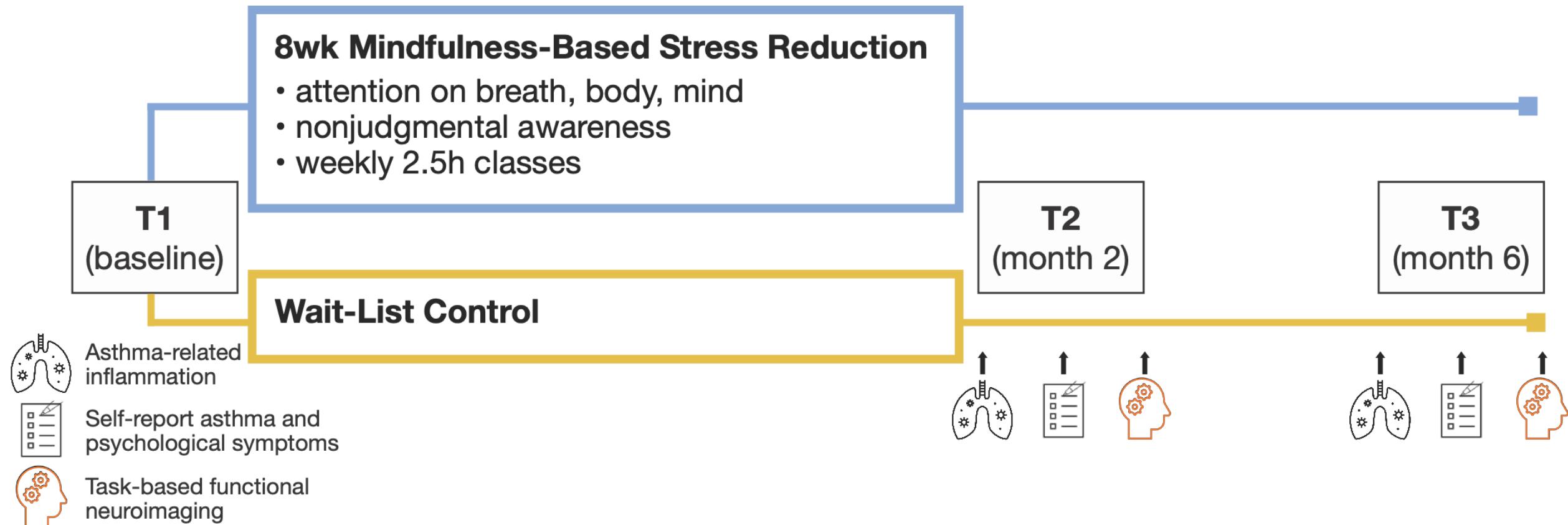
Psychological Distress ↓



Mindfulness ↑

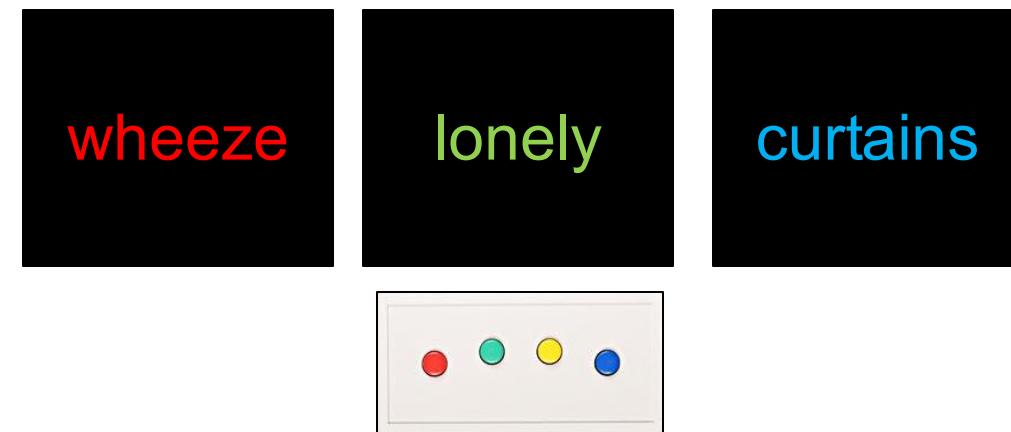
*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

# Mindfulness-Based Stress Reduction (MBSR) in Asthma



*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

# Task-based functional neuroimaging



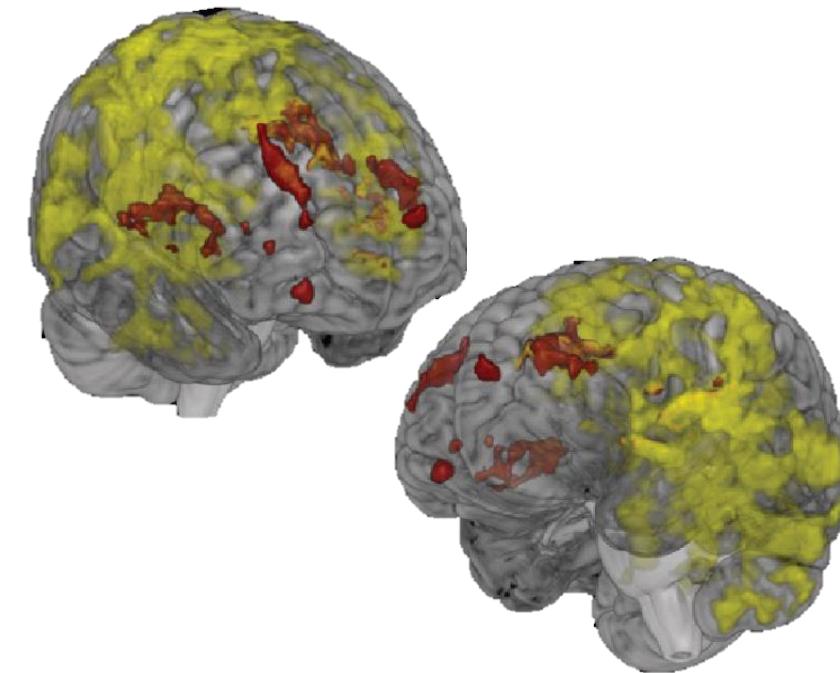
wheeze

*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

MBSR decreased prefrontal and amygdala reactivity  
post-intervention

*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

MBSR **decreased prefrontal** and **amygdala reactivity** post-intervention, associated with increased **mindfulness**



Increased Mindfulness  
(from T1 to T2)

Five Facet Mindfulness  
Questionnaire Change

20  
10  
0  
-10  
-20

-100

0

100

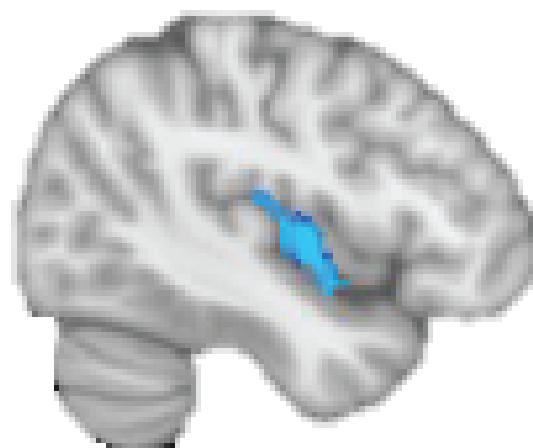
Decreased Brain Reactivity  
(from T1 to T2)

Increased Brain Reactivity  
(from T1 to T2)

- Whole-brain widespread clusters
- Local Salience Network and prefrontal peaks

*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

# Decreased inflammation was associated with decreased insula reactivity



Increased Inflammation

(from T1 to T2)

Sputum % Eosinophils Change

7.5  
5.0  
2.5  
0.0  
-2.5

Decreased Brain Reactivity  
(from T1 to T2)

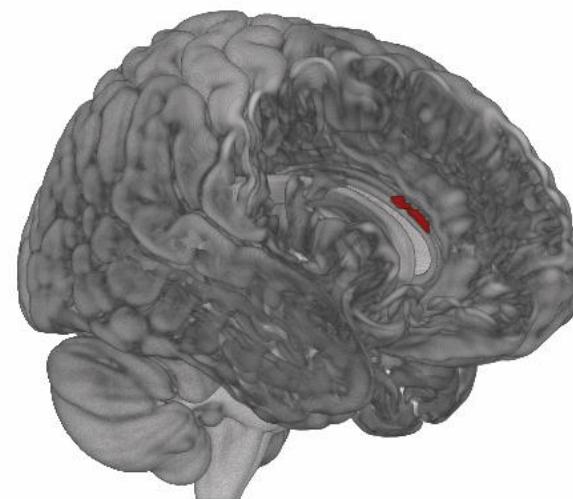
-100 0 100

Increased Brain Reactivity  
(from T1 to T2)

(Higgins et al., in prep)

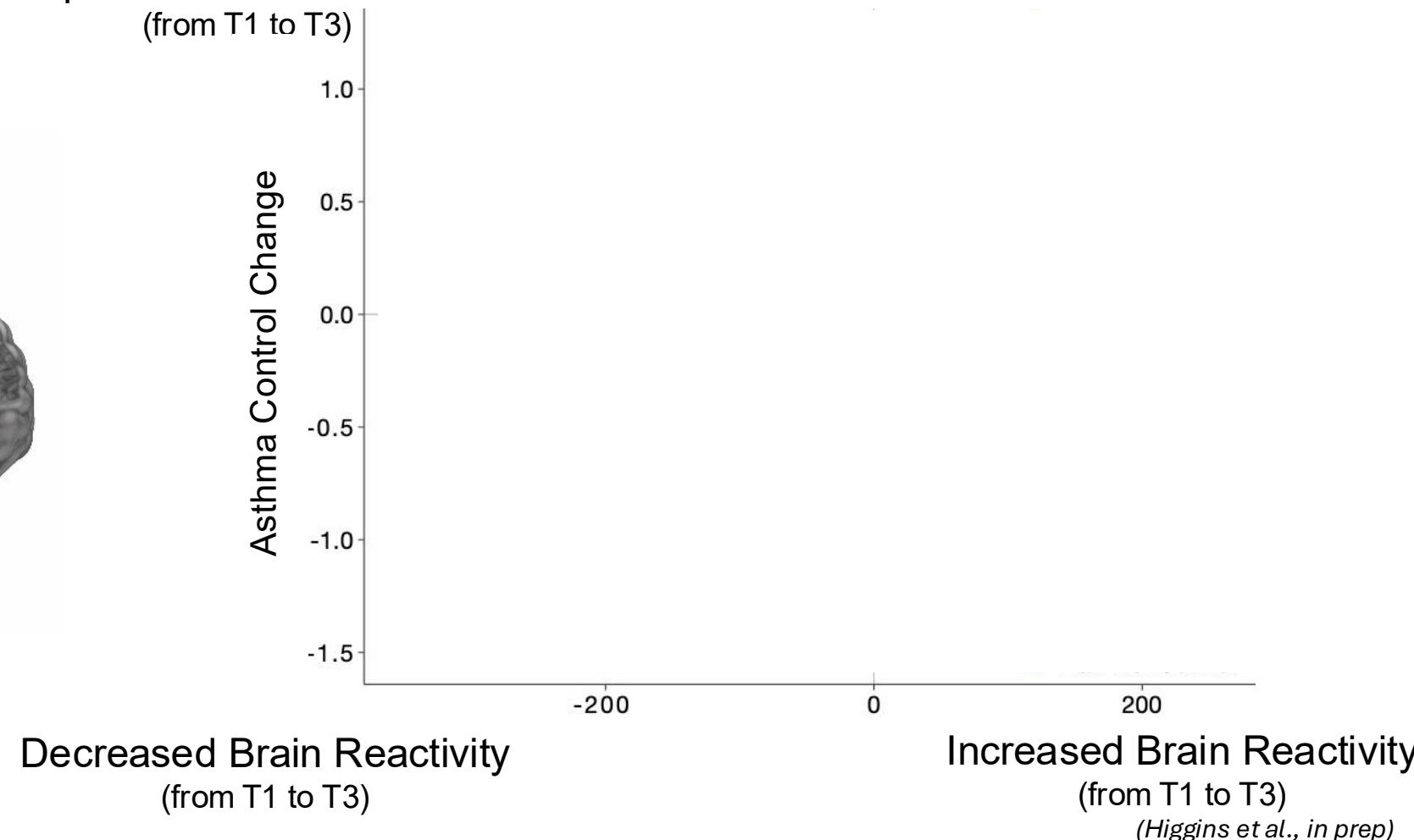
*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

**Improved asthma control was associated with increased dACC reactivity at 6mo follow-up**



Improved Asthma Control

(from T1 to T3)



Decreased Brain Reactivity  
(from T1 to T3)

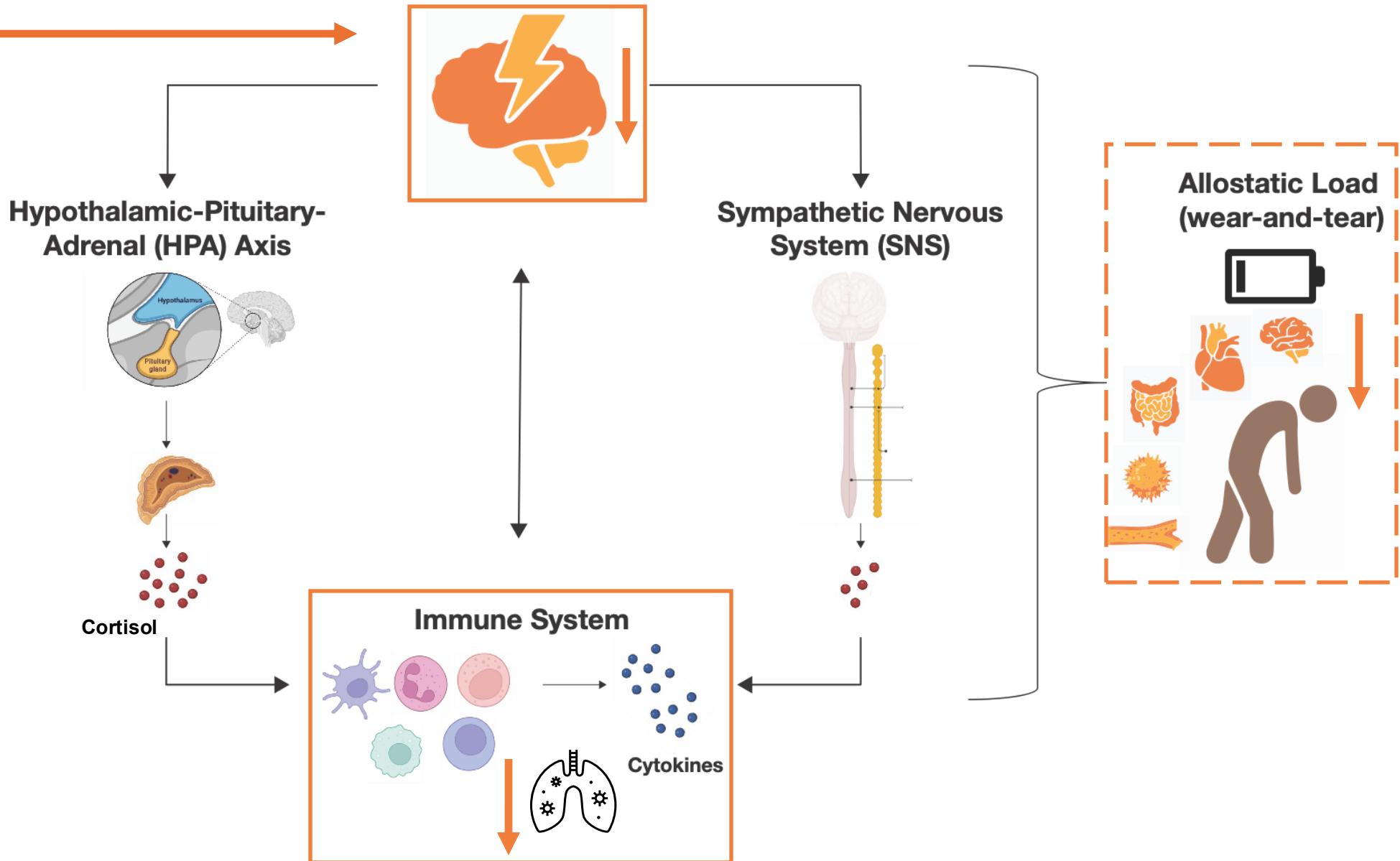
Increased Brain Reactivity  
(from T1 to T3)  
(Higgins et al., in prep)

*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*

# Key Takeaways

- MBSR alters neural processing of aversive cues: decreased reactivity + enhanced regulation
  - associated with positive disease outcomes
- Importance of targeting mind-body relationships in asthma treatment

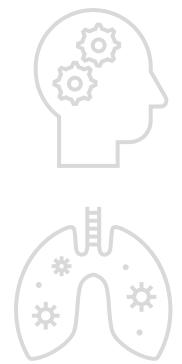
*What are the psychological, biological, and neural mechanisms of mindfulness benefits in asthma?*



# Overview & Roadmap



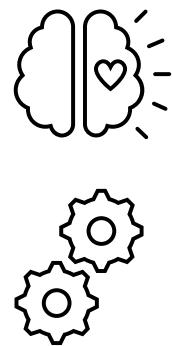
Emotion &  
Inflammation



Neuroimmune  
Mechanisms:  
Asthma



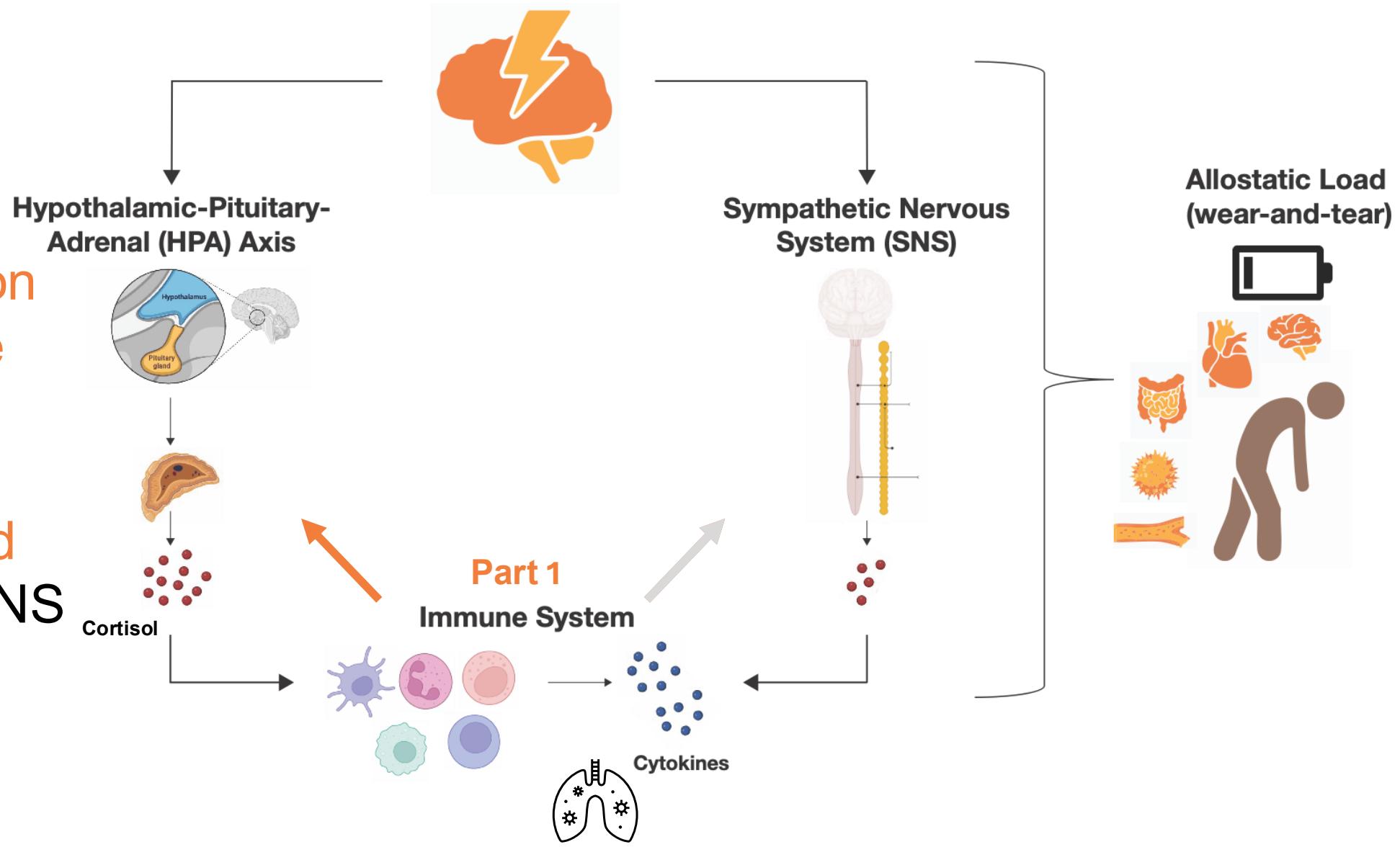
Mindfulness  
Intervention &  
Mechanisms in Asthma



**Recap & Future  
Directions**

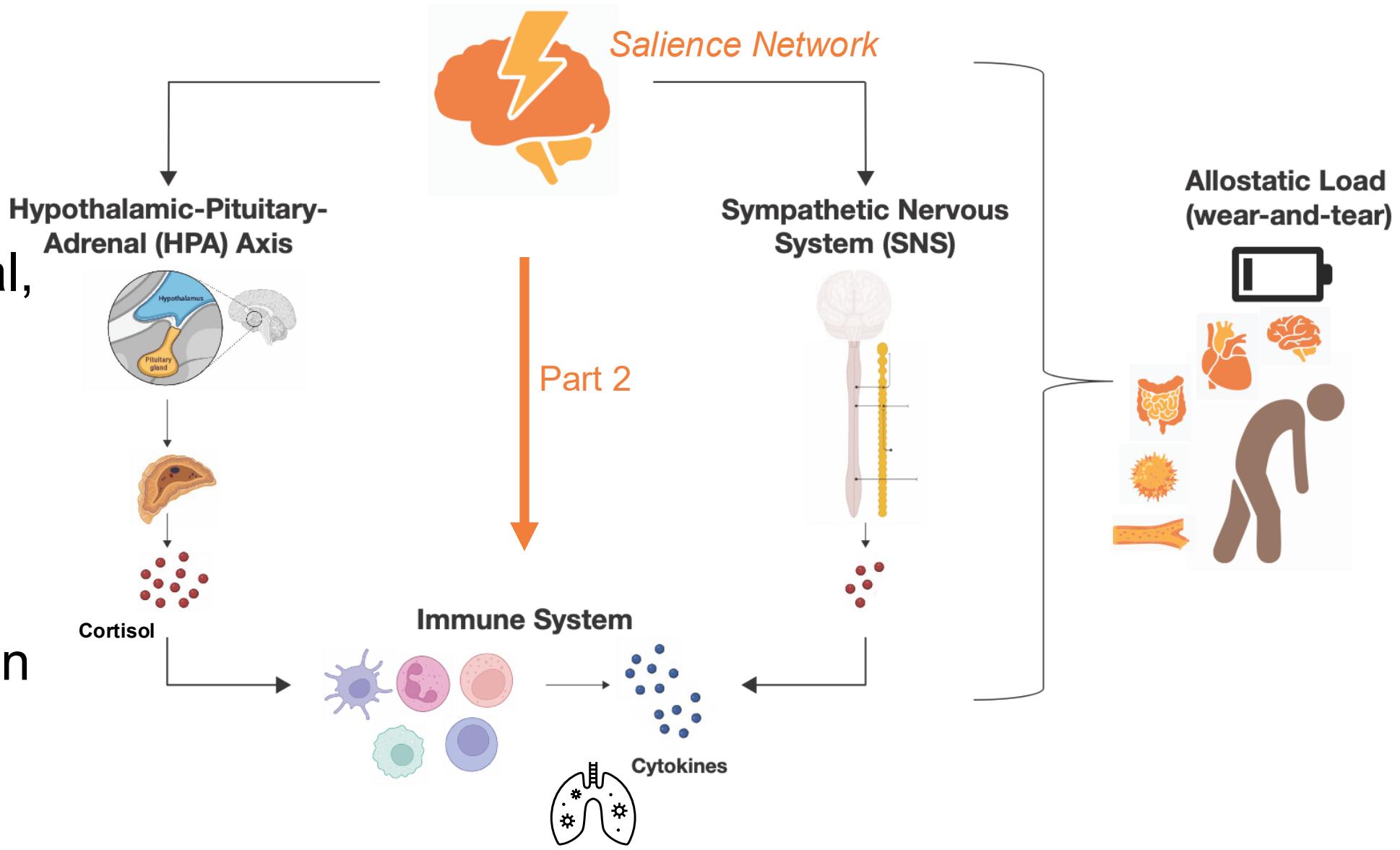
# What we learned, why it matters, & what's next

Inflammation  
and lifetime  
stress  
associated  
with blunted  
HPA, not SNS



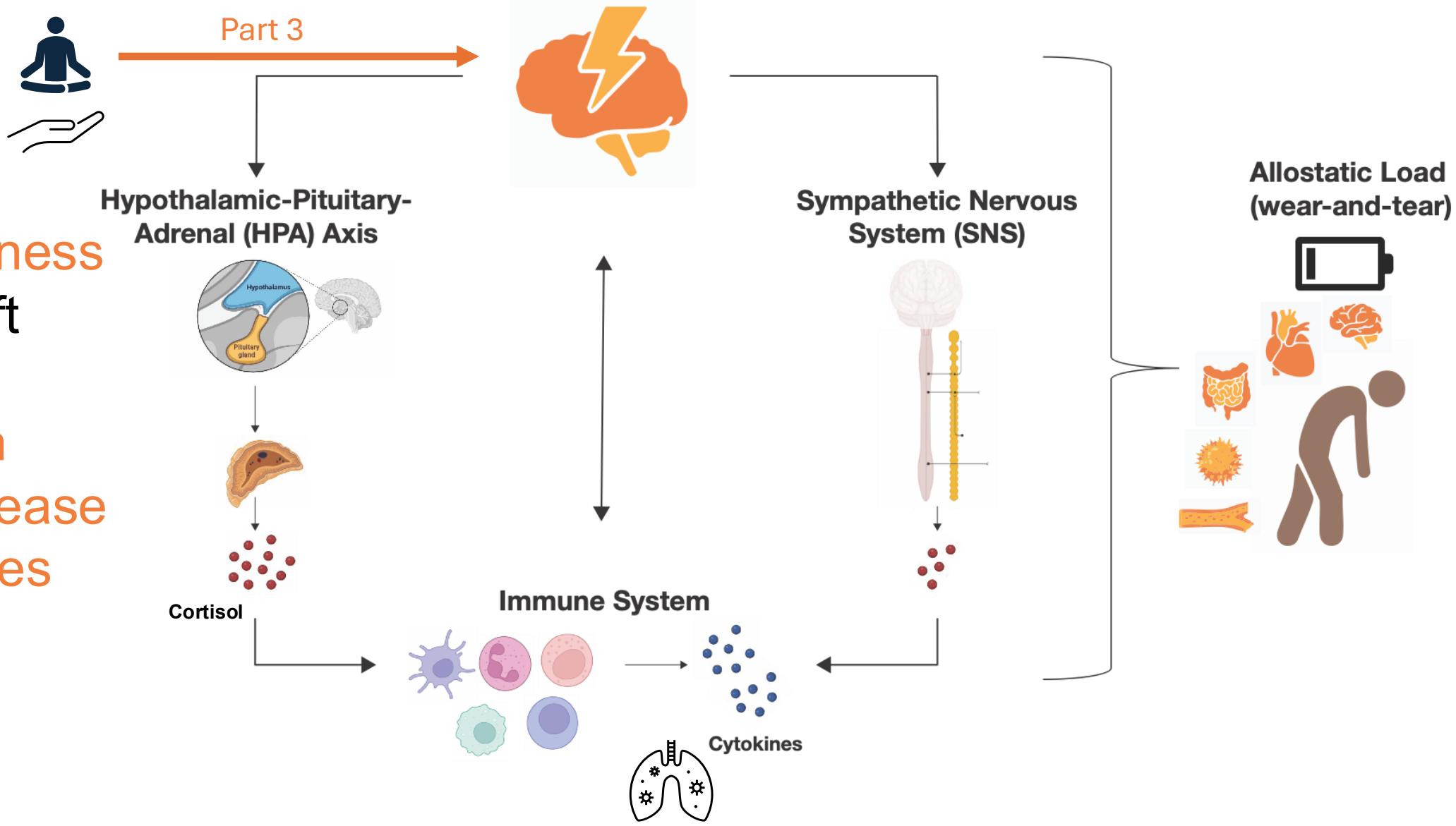
# What we learned, why it matters, & what's next

Bidirectional,  
brain-mediated  
interactions  
between  
stress and  
inflammation



# What we learned, why it matters, & what's next

Mindfulness  
can shift  
brain  
function  
and disease  
outcomes



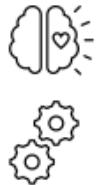
# What we learned, **why it matters**, & what's next

 Who, how, & what – integrative treatment

# What we learned, why it matters, & **what's next**



Who, how, & what – integrative treatment

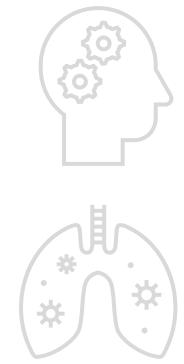


Scalable digital interventions & predictive, personalized modeling in asthma

# Overview & Roadmap



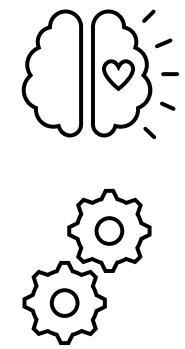
Emotion &  
Inflammation



Neuroimmune  
Mechanisms:  
Asthma



Mindfulness  
Intervention &  
Mechanisms in Asthma



**Recap & Future  
Directions**

*How do psychological, neural, and biological risk factors predict responses to MBSR in asthma?*

# Who benefits most and why?

- Linear models are limited in modeling complexity → *machine learning*

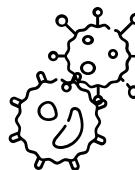


- Random Forest/XGBoost + Feature Selection
  - **Predictors:** neuroimaging, immune, psychological symptoms, demographics
  - **Outcomes:** MBSR responder/non-responder; asthma control, psychological symptoms

# Who benefits most and why?



Precision mind-body health: tailor intervention based on underlying (psycho)biological processes

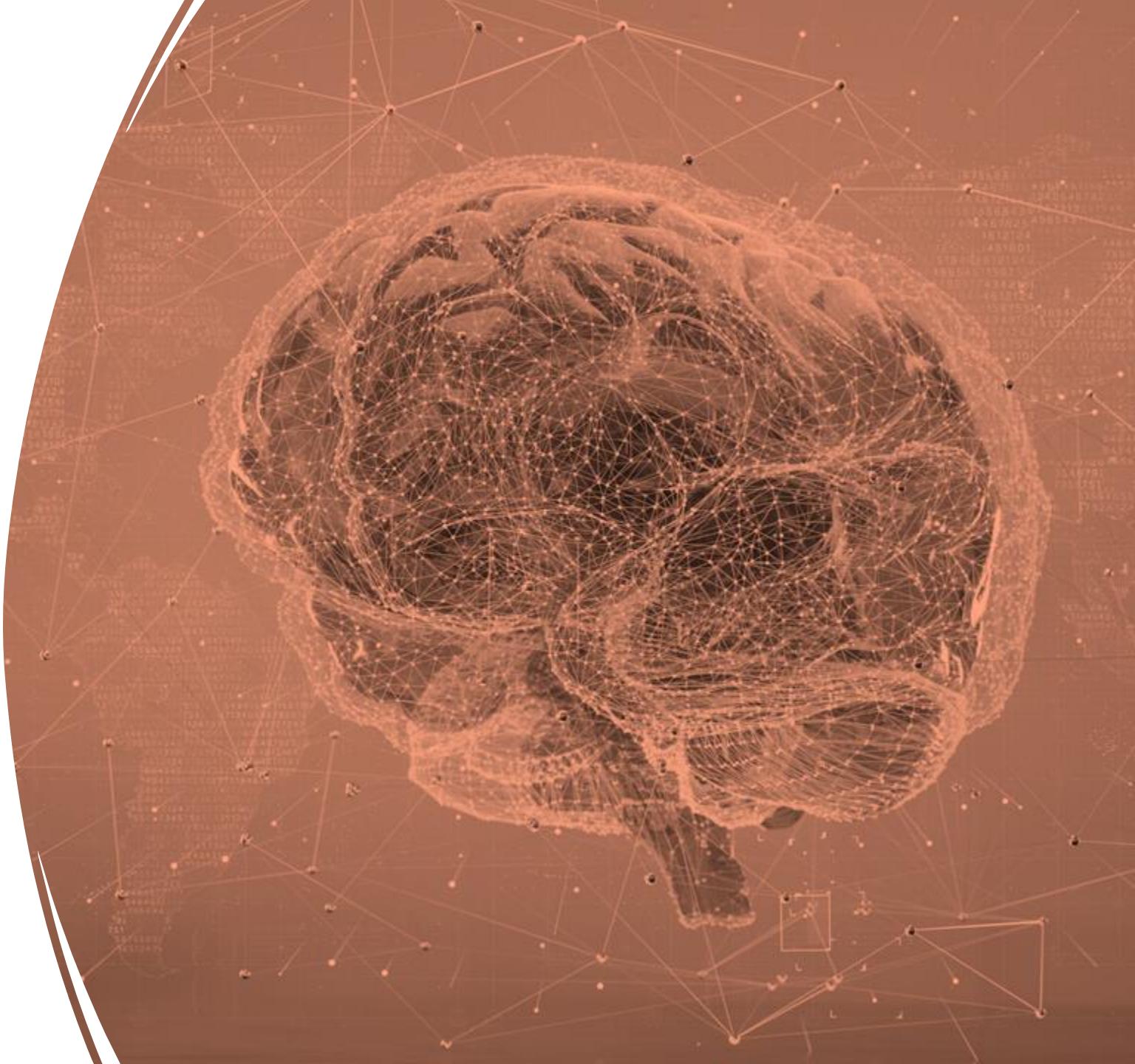


Long-term vision: beyond asthma to other chronic inflammatory diseases

# Thank You!

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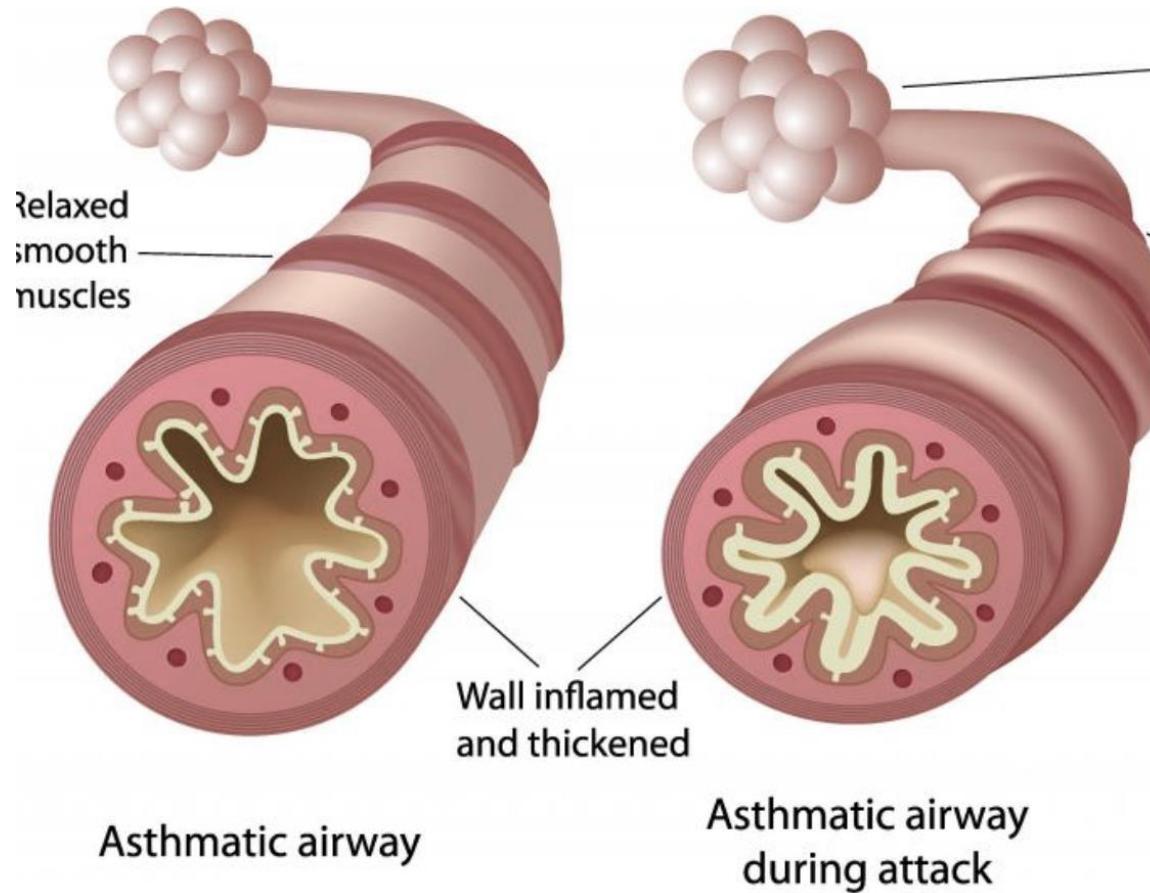
## *Questions?*



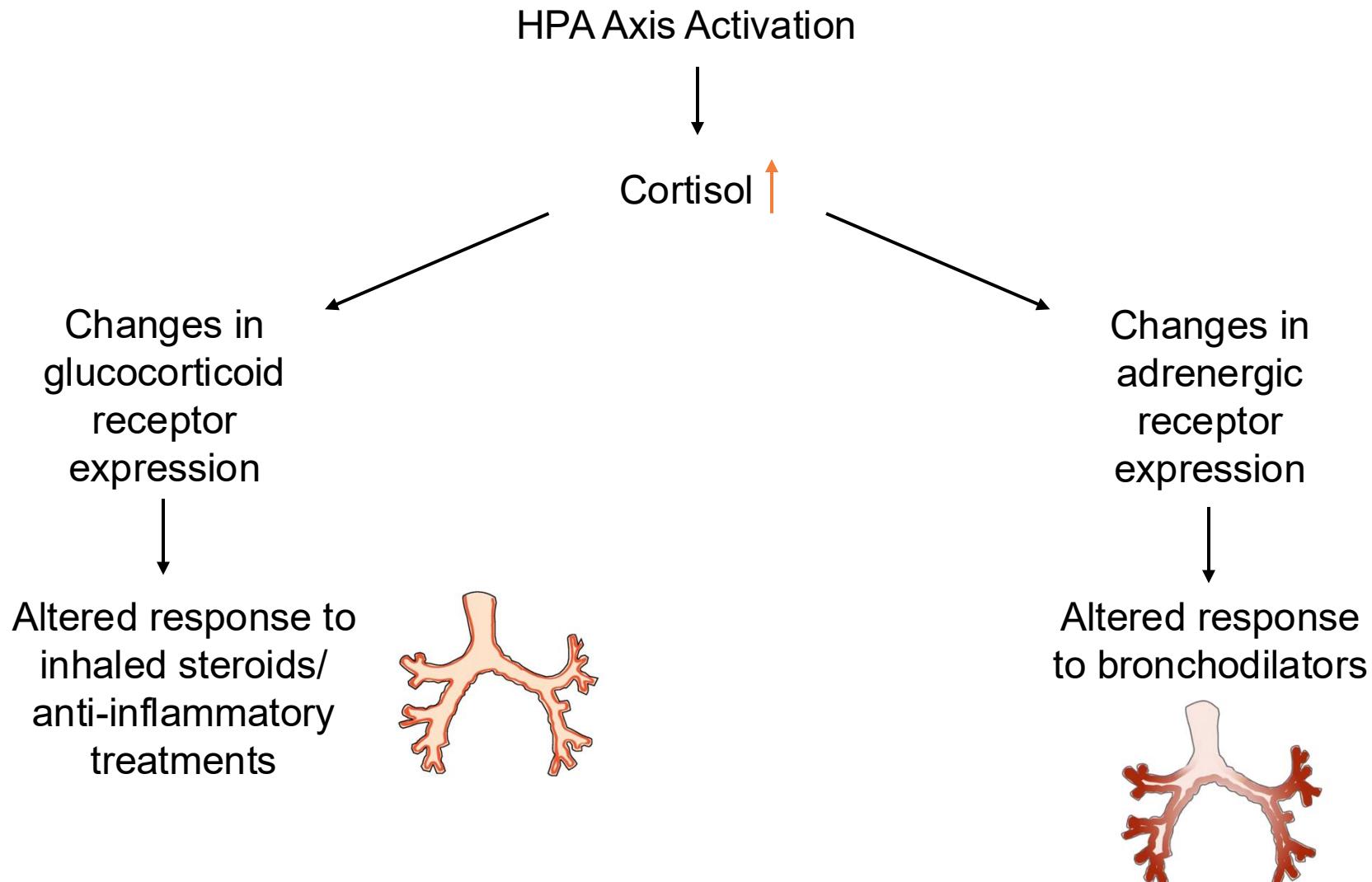
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# Airways narrow during asthmatic response

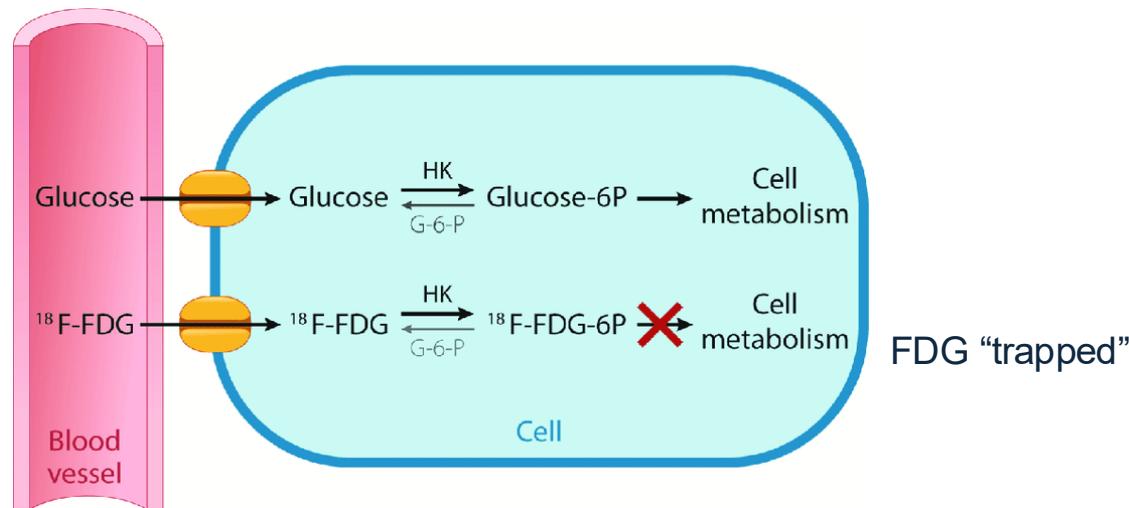


# Stress & response to medications



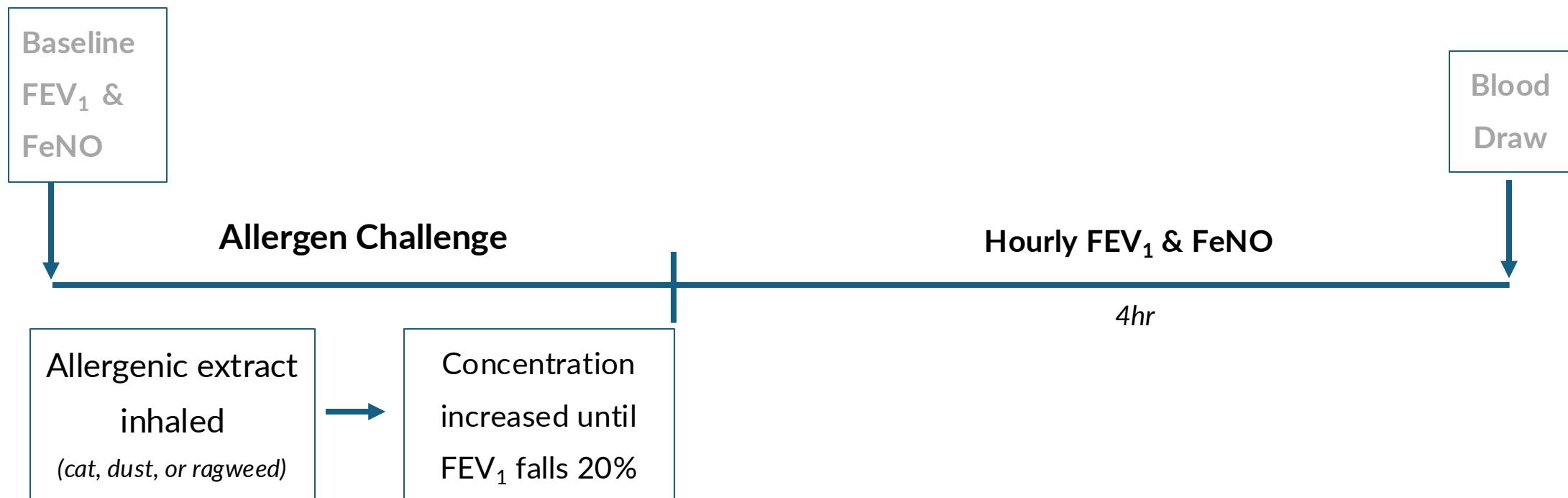
# PET

- Brain Glucose Metabolism: fluoro-18-deoxyglucose (FDG)-Positron Emission Tomography (PET)
  - Venous FDG injection → [uptake time: TSST] → Scan



(Rahman et al., 2019)

# Allergen challenge



FEV<sub>1</sub>: Forced Expiratory Volume (1s) = Lung Function

FeNO: Fraction of Exhaled Nitric Oxide = Airway Inflammation

# Whole-Brain Regressions + a priori ROIs

- Amygdala
- Anterior Cingulate Cortex
- Insula / Operculum / lateral OFC

