Understanding the Science **of Wellness**

Divide No More: The Brain-Body Connection

<Speaker Name>
<Credentials>

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Overview

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Overlap Between Rheumatology and Wellness

Chapter One

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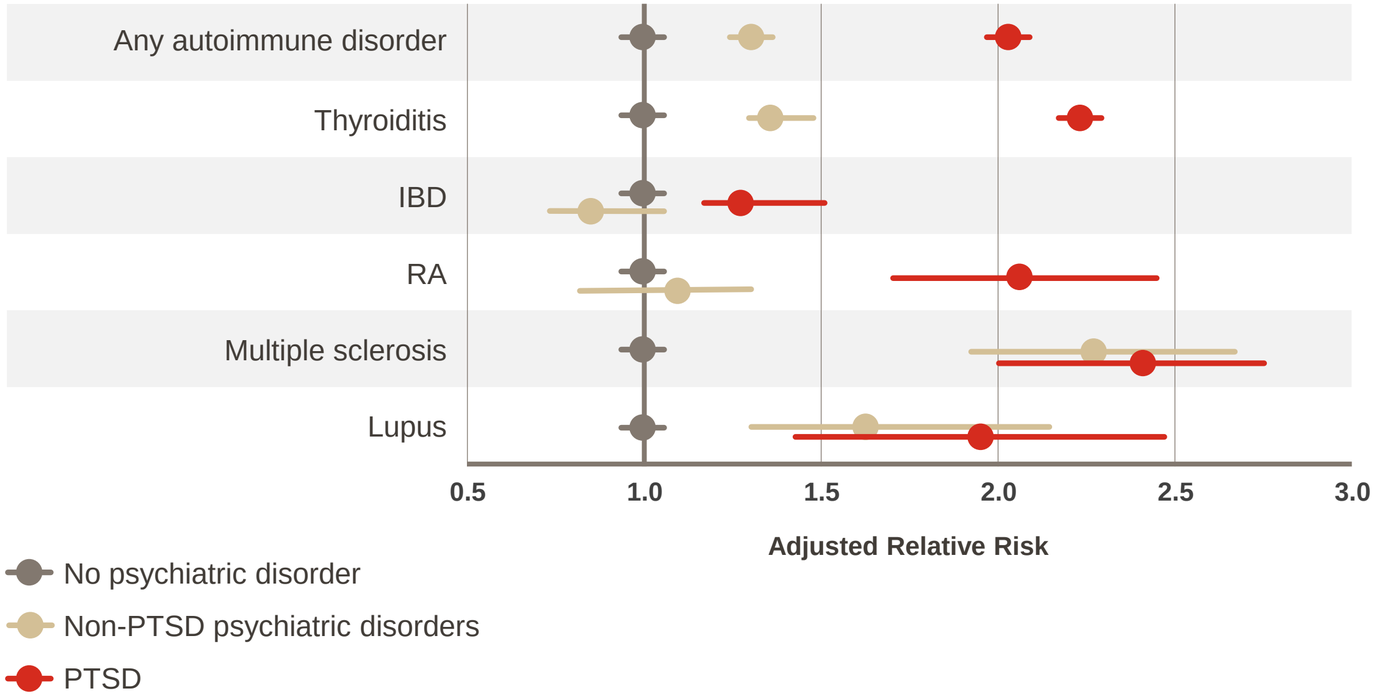
Exposure to Stress As an Adult Can Increase Risk for Inflammatory Disorders

Risk for Autoimmune Disorders in Iraq and Afghan War Veterans

N=666,269



Compared to veterans with no psychiatric disorders, veterans with **PTSD and/or other psychiatric disorders had significantly higher risk**[*†] for inflammatory disorders

*P<.001 veterans with PTSD vs veterans without any psychiatric disorder; †P<.05 veterans with non-PTSD psychiatric disorders vs veterans without any psychiatric disorder.
IBD = inflammatory bowel disease; PTSD = posttraumatic stress disorder; RA = rheumatoid arthritis.
O'Donovan A, et al. *Biol Psychiatry.* 2015;77(4):365-374.

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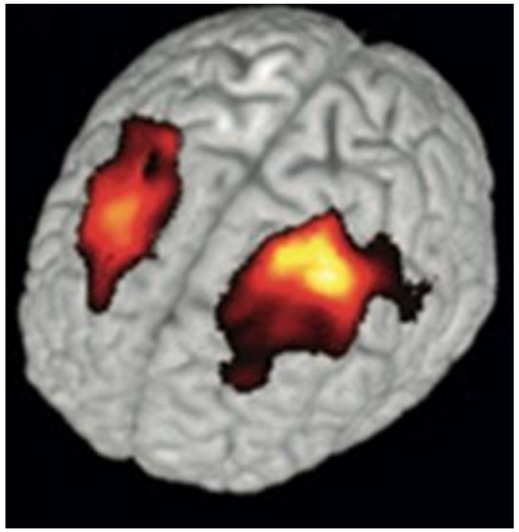
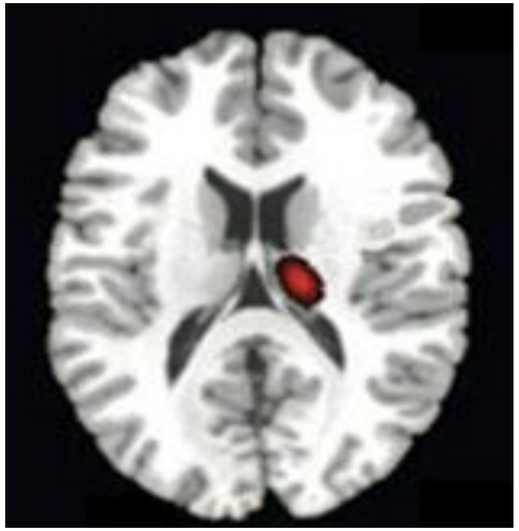
Chronic Back Pain Is Associated With Gray-Matter Atrophy in Areas Involved With Cognition and Emotional Regulation

Decreased Regional Gray-Matter Density Decreases in Patients With Chronic Back Pain (n=26)



Areas in red indicate decreased **gray-matter density in the dorsal prefrontal cortex**



Right anterior thalamus is shown at the **peak of decreased thalamic gray matter**

Patients with chronic back pain had **5%-11% less neocortical gray matter**

The magnitude of this decrease is equivalent to **10-20 years of normal aging**

Apkarian AV, et al. *J Neurosci*. 2004;24(46):10410-10415.

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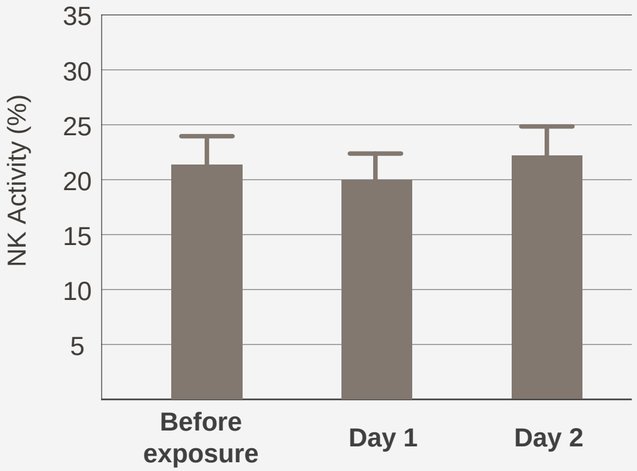
Change in Psychosocial Environment Can Positively Effect Immune Functioning

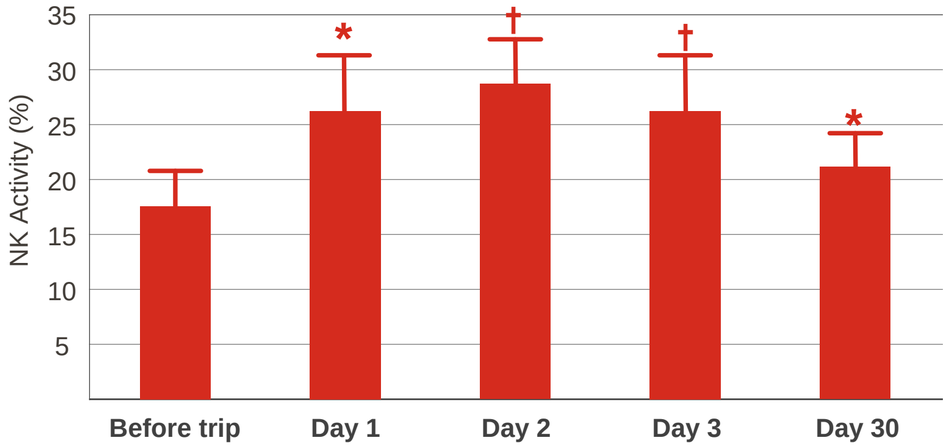
Effects of Forest Bathing Trip on NK Cell Activity

Urban Exposure



No change in NK cell activity for urban exposure

Forest Bathing



Forest bathing **increased NK cell activity, which lasted for 30 days** after the trip

Data are presented as the mean ± SE. *P<.05 vs before trip; †P<.01 vs before trip.
NK = natural killer; SE = standard error.
Li Q. *Environ Health Prev Med.* 2010;15(1):9-17.

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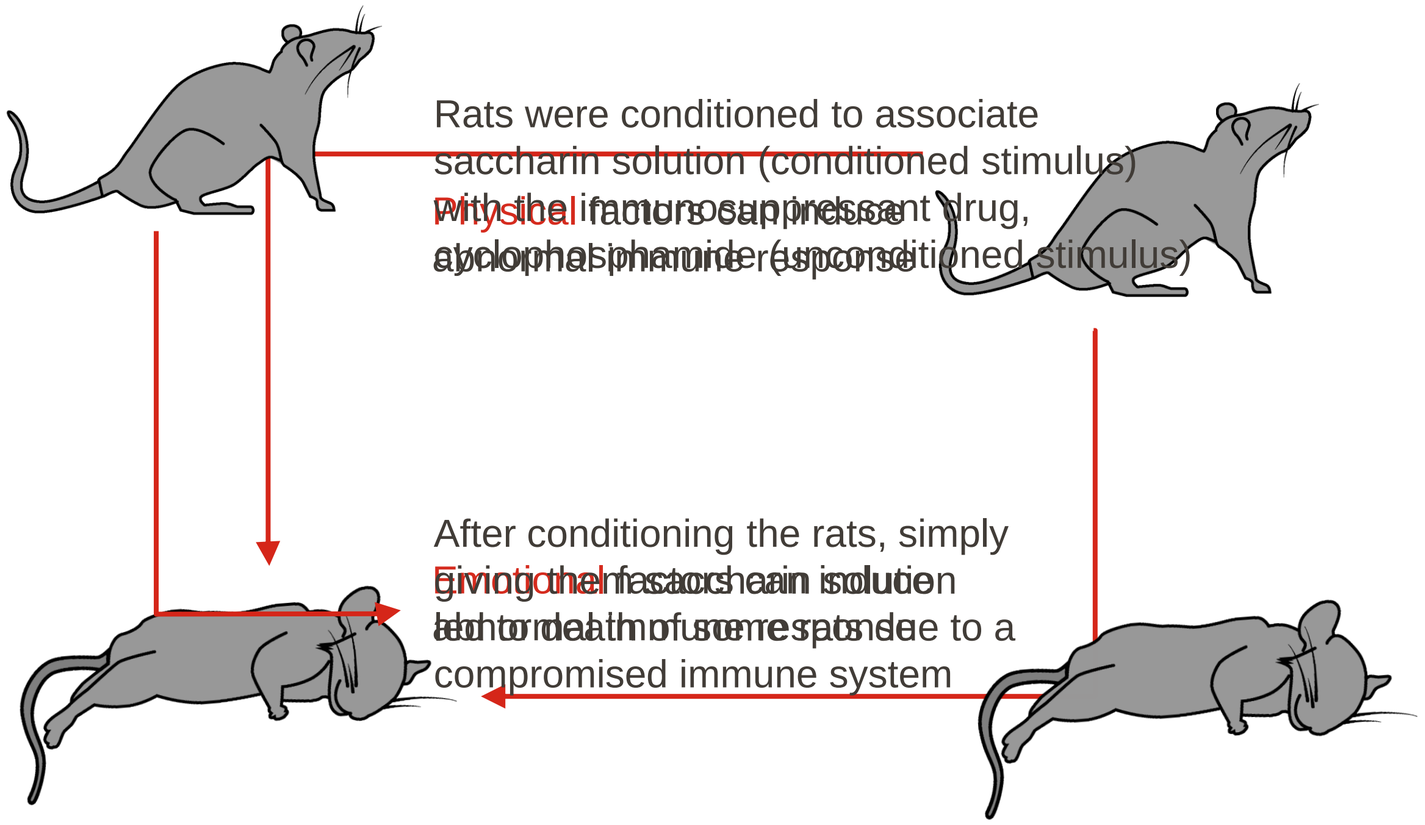
Link Between the Mind and the Immune System

Where It All Began (1975)



The results of this study provide evidence for **behaviorally conditioned immunosuppression**

Immunity responds to **emotions** as it does to **antigens**

Ader R, et al. *Psychosom Med.* 1975;37(4):333-340.

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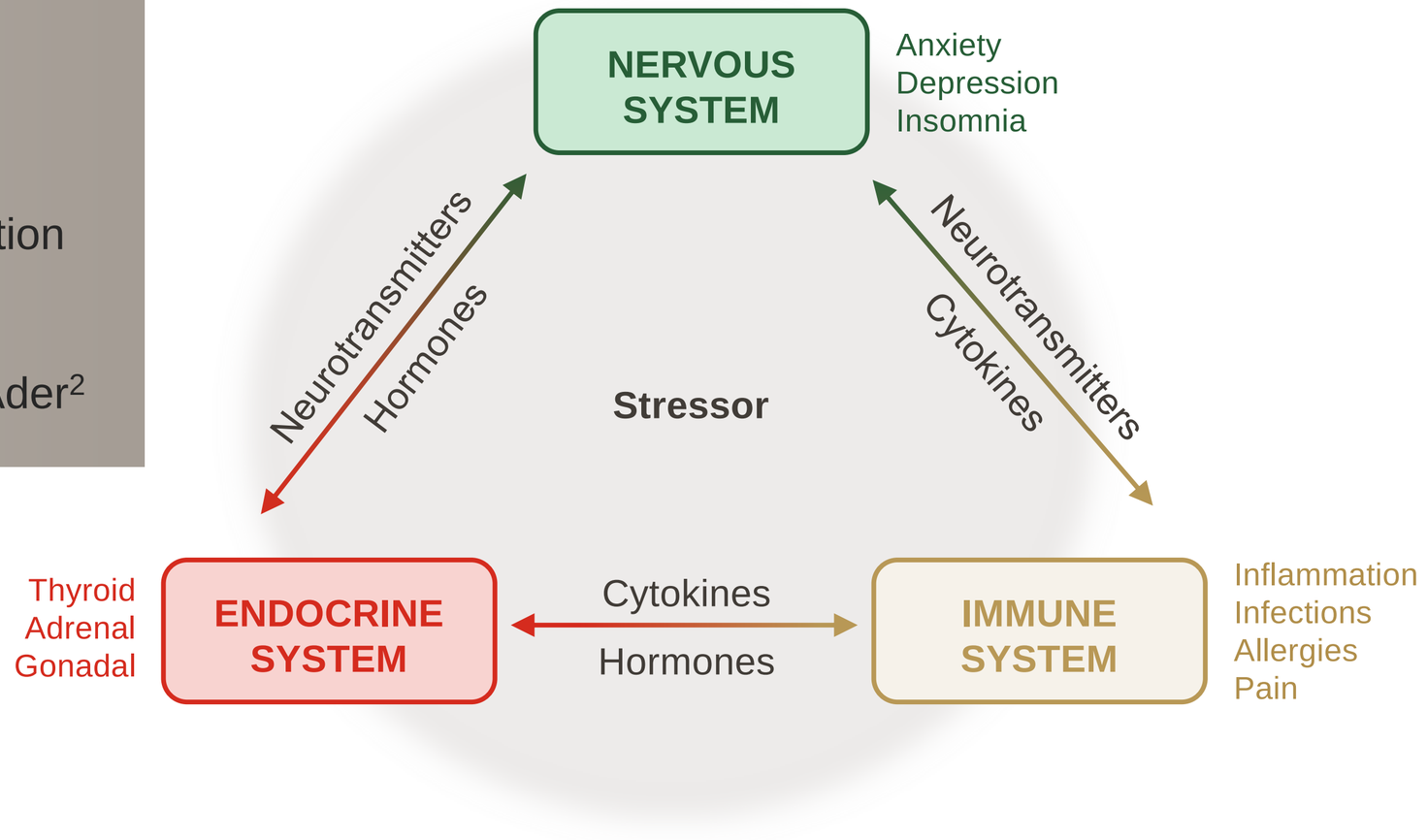
Psychoneuroimmunology (PNI) Explains Brain-Body Link[1]

"**PNI is a convergence of disciplines**—namely the behavioral sciences, the neurosciences, endocrinology, and immunology—intended to achieve a more complete understanding of the way the interaction among these systems serve homeostatic ends and influence health and disease."

– Robert Ader[2]

The Integrated Bidirectional View of PNI[3]



1. Mission statement. Psychoneuroimmunology Research Society website. https://www.pnirs.org/society/index.cfm. Accessed March 2018. 2. Ader R. Psychoneuroimmunology. 4th ed. Amsterdam: Elsevier Academic Press, 2007. Ader R, et al. *Psychosom Med*. 1975;37(4):333-340. 3. Miller AH, et al. *Biol Psychiatry*. 2009;65(9):732-741.

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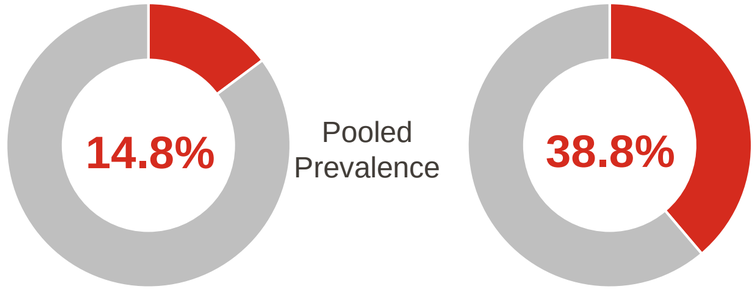
Prevalence of Mental Health Disorders in Rheumatology Practices

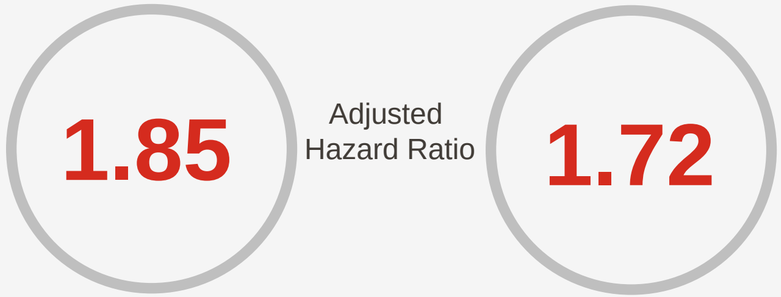
Rheumatoid Arthritis[1]

N=13,189



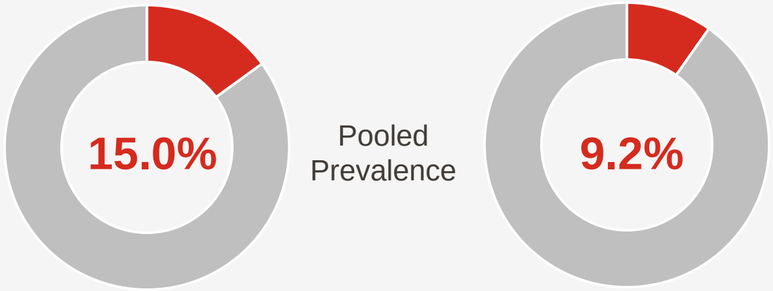
Ankylosing Spondylitis[2]

N=2331



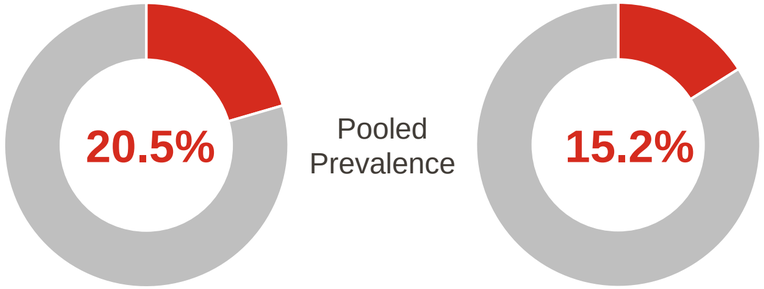
Psoriatic Arthritis[3]

N=306



Inflammatory Bowel Disease[4]

N=158,371



*Moderate or severe.

1. Matcham F, et al. *Rheumatology*. 2013;2(12):2136-2148. 2. Shen CC, et al. *J Rheumatol.* 2016;43(3);625-631. 3. McDonough E, et al. *J Rheumatol*. 2014;41(5):887-896. 4. Neuendorf R, et al. *J Psychosom Res*. 2016;87:70-80.

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PNI Explains How Inflammatory Disorders Connect Our Mind and Body Into One Unitary System

- STIFFNESS
- COGNITIVE DYSFUNCTION
- PAIN
- ANXIETY
- DEPRESSION
- DISEASE ACTIVITY
- WEIGHT GAIN
- FATIGUE
- INSOMNIA

Mental health disorders, such as major depression, are associated with diminished treatment responses in inflammatory disorders such as RA

Data from a UK study in patients with RA on TNF-α inhibitors (N=159) show that reduction in DAS28 at 3 months was lower in patients with depression compared to patients without depression (median change 1.71 [0-2.6] vs 2.2 [1.5-3.2]; *P*=.005)

DAS = Disease Activity Score.

Hider SL, et al. *Rheumatology*. 2009;48(9):1152-1154.

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Summary

Chapter One

Overlap exists between rheumatology and wellness

Many rheumatological disorders exhibit this high overlap

To appreciate this overlap, a deeper understanding of **psychoneuroimmunology (PNI)** is needed

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Psychoneuroimmunology (PNI) Primer for Rheumatology

Chapter Two

Limbic System

Hypothalamus-Pituitary-Adrenal Axis

Autonomic Nervous System

Immune System

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Limbic System

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The Prefrontal Cortex and Limbic System

Entire Neuronal Circuitry Controlling Emotional Behavior and Motivational Drives

Prefrontal cortex[1-3]

Attention

Abstract thinking

Executive functions

ANS and endocrine response regulation

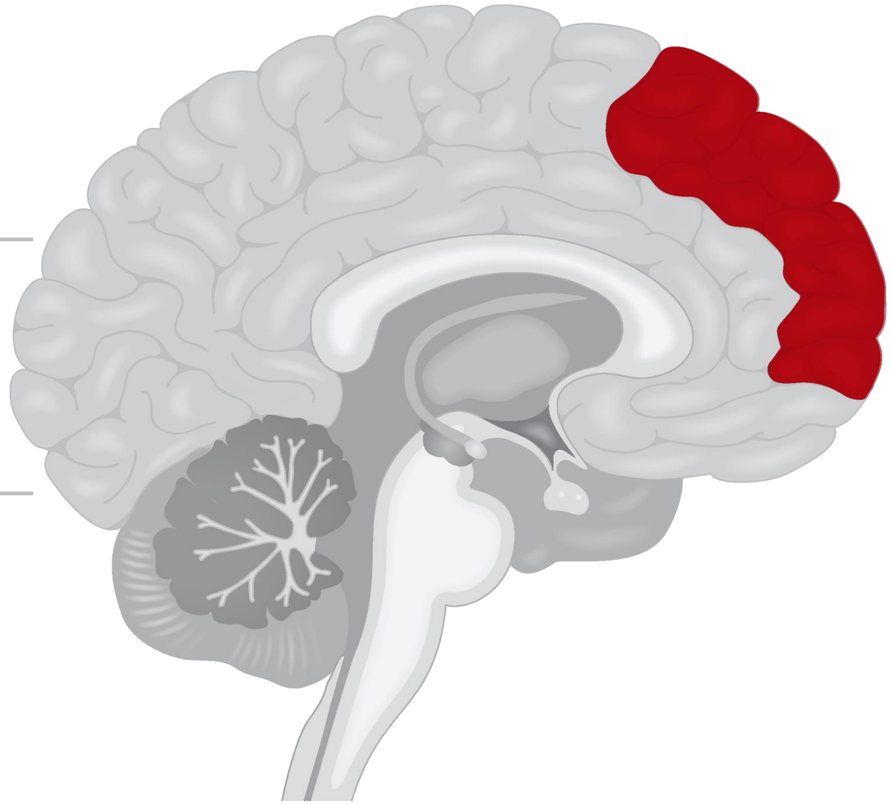
Management of social behavior

Emotional response to pain

Anger/aggression regulation

Anxiety regulation

Fear regulation



Sleep regulation

Endocrine, ANS, and immune systems connection

Appetite regulation

Temperature regulation

Relay of sensory and motor signals

Alertness regulation

Memory

Mood

Learning

1. Siddiqui SV, et al. *Indian J Psychiatry*. 2008;50(3):202-208. 2. Szczepanski SM, et al. *Neuron*. 2014;83(5):1002-1018. 3. Roxo MR, et al. *Scientific World Journal.* 2011;11:2427-2440.

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Anterior cingulate cortex[1-3]

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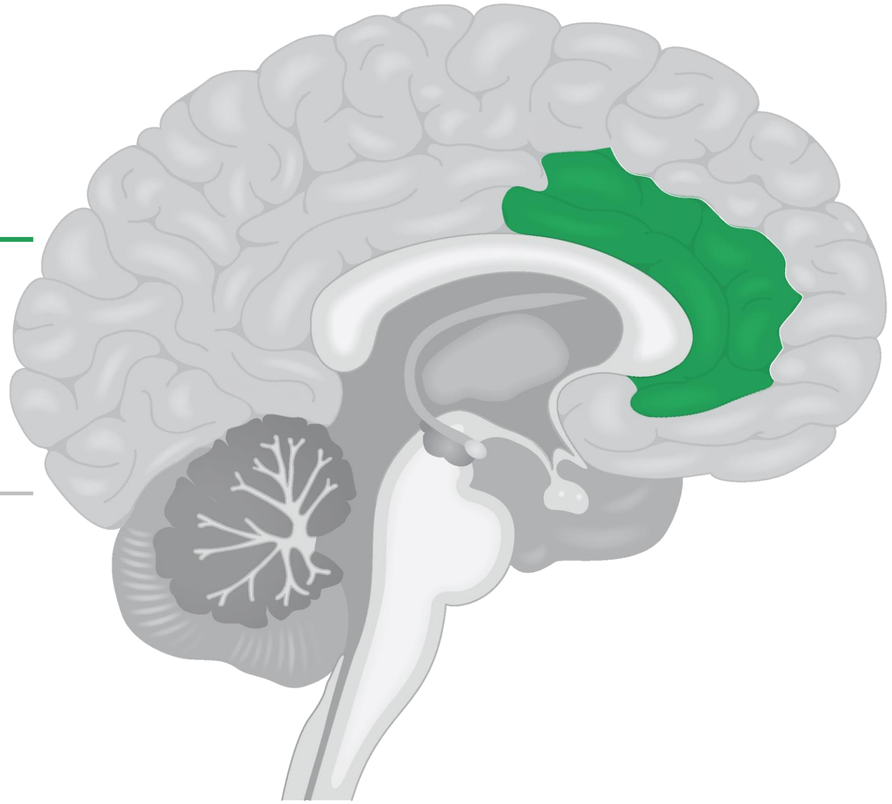

Sleep regulation

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1. Siddiqui SV, et al. *Indian J Psychiatry*. 2008;50(3):202-208. 2. Szczepanski SM, et al. *Neuron*. 2014;83(5):1002-1018. 3. Roxo MR, et al. *Scientific World Journal.* 2011;11:2427-2440.

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The Prefrontal Cortex and Limbic System

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Amygdala[1,2]

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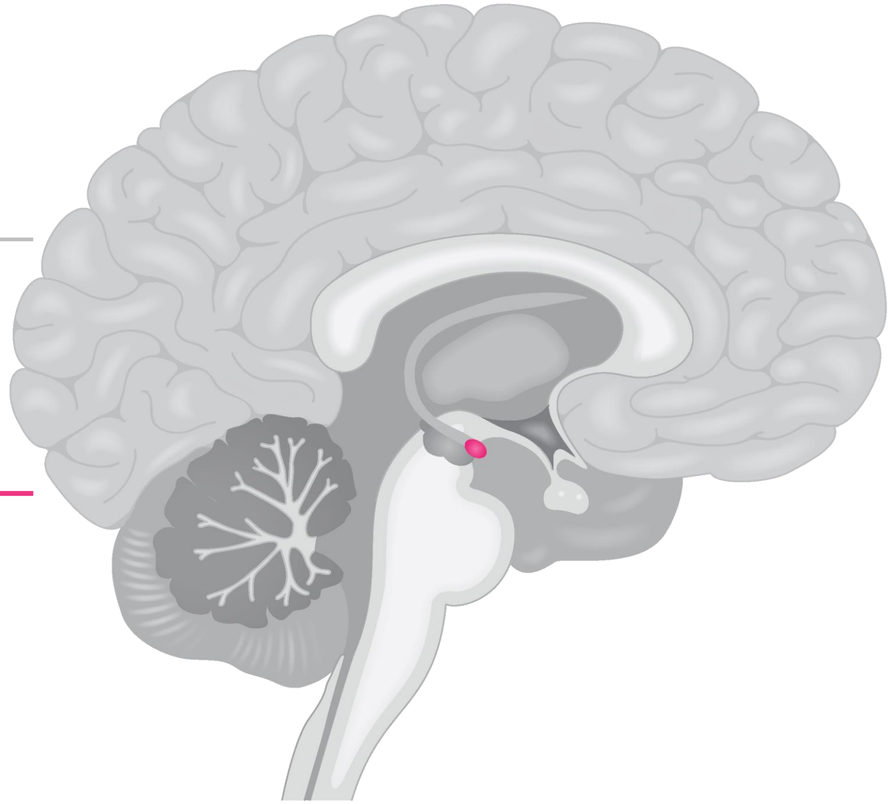

Sleep regulation

Endocrine, ANS, and immune systems connection

Appetite regulation

Temperature regulation

Relay of sensory and motor signals

Alertness regulation

Memory

Mood

Learning

1. Zhu LJ, et al. *PLoS One.* 2014;9(5):e97689. 2. Cai D, et al. *Ann N Y Acad Sci*. 2011;1243:E1-E39.

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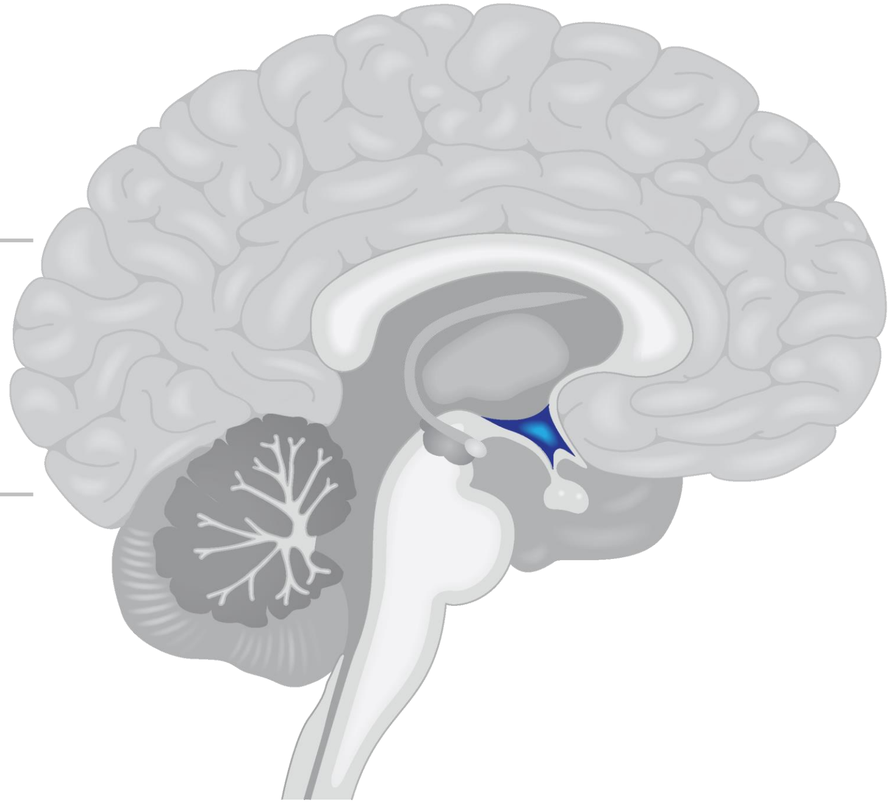
The Prefrontal Cortex and Limbic System

Entire Neuronal Circuitry Controlling Emotional Behavior and Motivational Drives

Hypothalamus[1,2]



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1. Zhu LJ, et al. *PLoS One.* 2014;9(5):e97689. 2. Cai D, et al. *Ann N Y Acad Sci*. 2011;1243:E1-E39.

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The Prefrontal Cortex and Limbic System

Entire Neuronal Circuitry Controlling Emotional Behavior and Motivational Drives

Thalamus[1,2]

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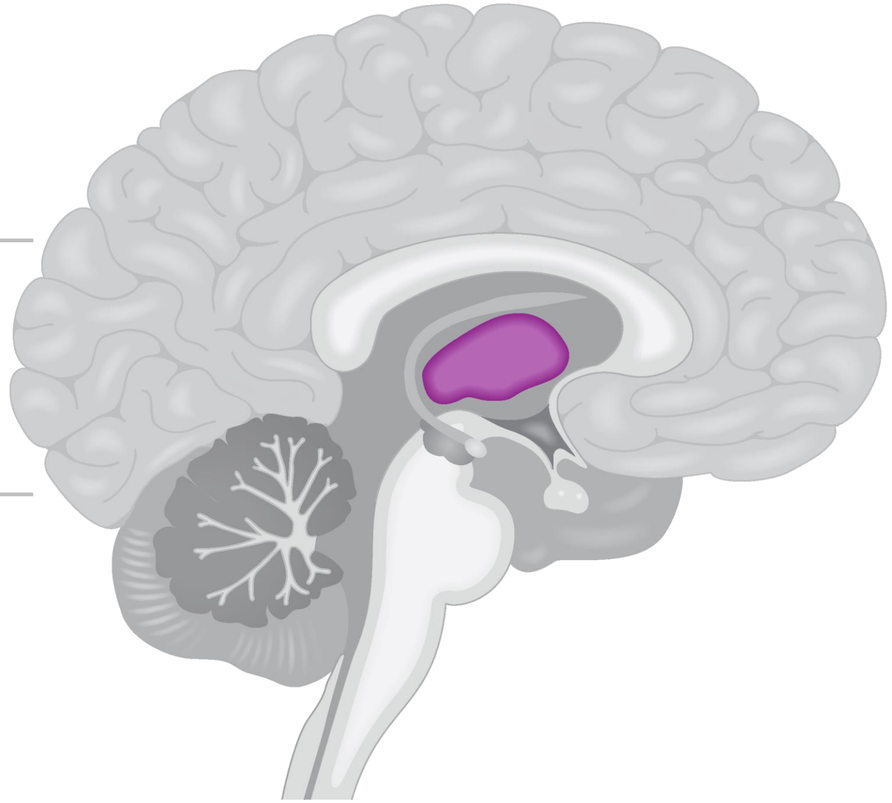

Sleep regulation

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Temperature regulation

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Mood

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1. Szczepanski SM, et al. *Neuron.* 2014;83(5):1002-1018. 2. Roxo MR, et al. *Scientific World Journal.* 2011;11:2427-2440.

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The Prefrontal Cortex and Limbic System

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Hippocampus[1-4]

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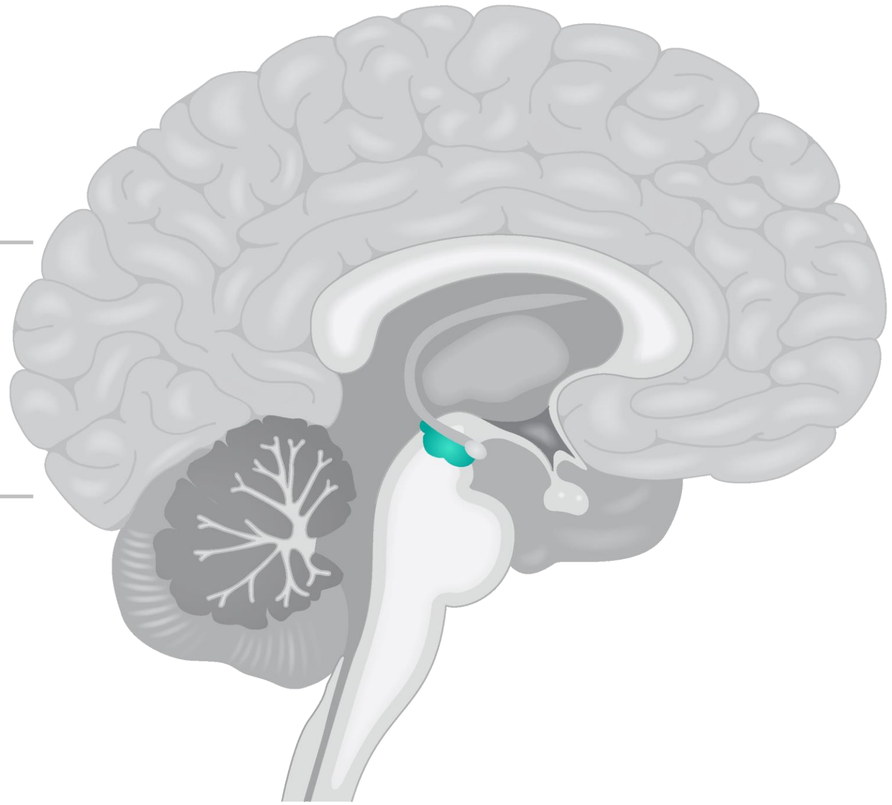

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1. Rovó Z, et al. *J Neurosci*. 2012;32(49):17894-17908. 2. Vertes RP, et al. *Neurosci Biobehav Rev*. 2015;54:89-107. 3. Siddiqui SV, et al. *Indian J Psychiatry*. 2008;50(3):202-208. 4. Roxo MR, et al. *Scientific World Journal.* 2011;11:2427-2440.

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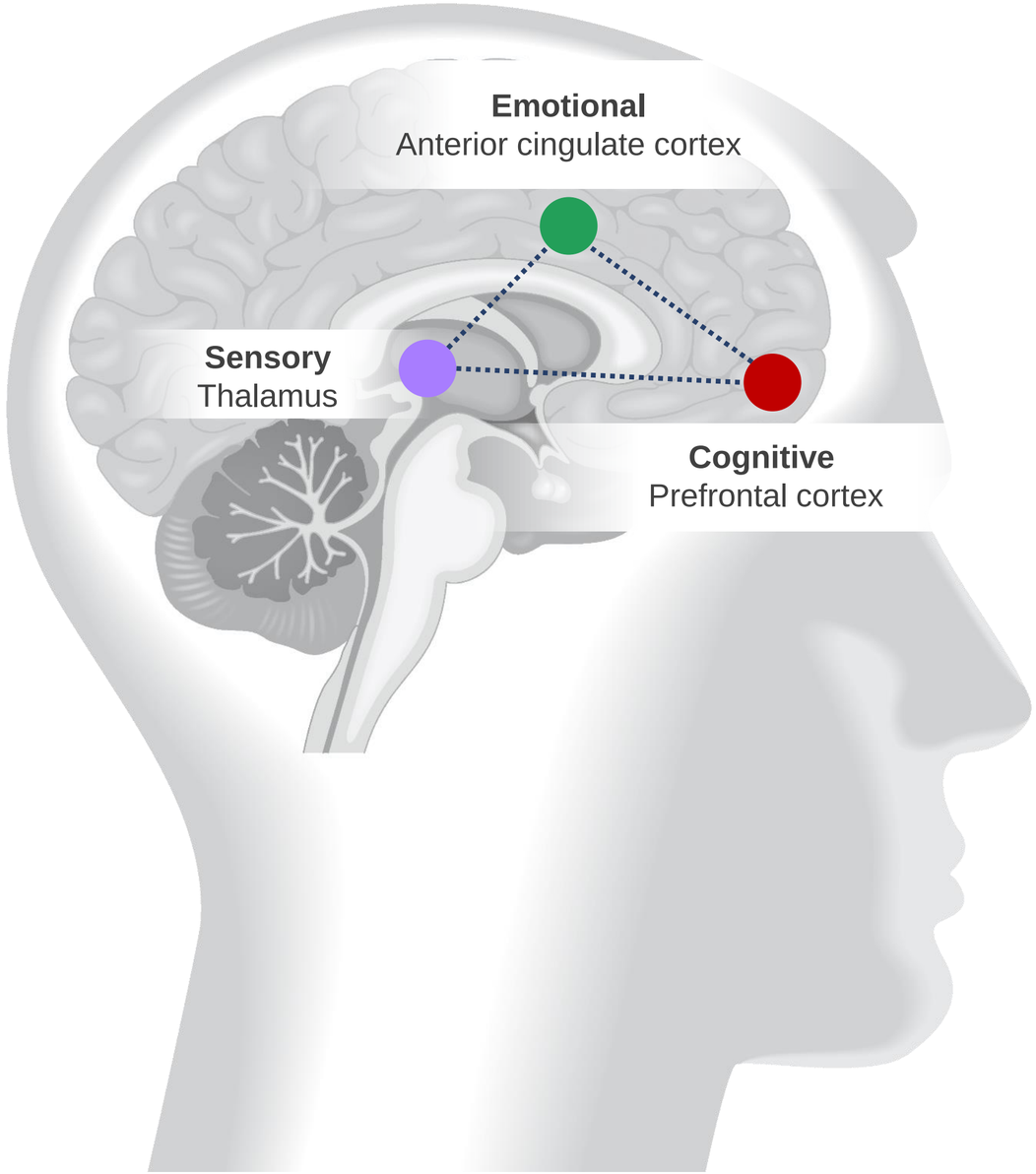

The SEC Model

Emerging evidence reveals PNI factors can influence all 3 in rheumatology:

- **S**ensory functioning
- **E**motional functioning
- **C**ognitive functioning

A recent editorial addressing the overlap between rheumatology and psychiatry:

RHEUMATOLOGY

Editorial

The Odd Couple?—Hardly

The emerging overlap between rheumatology and psychiatry

Peter Taylor and Rakesh Jain

Rheumatology. 2017.doi:10.1093/rheumatology/kex205

SEC = sensory emotional cognitive.

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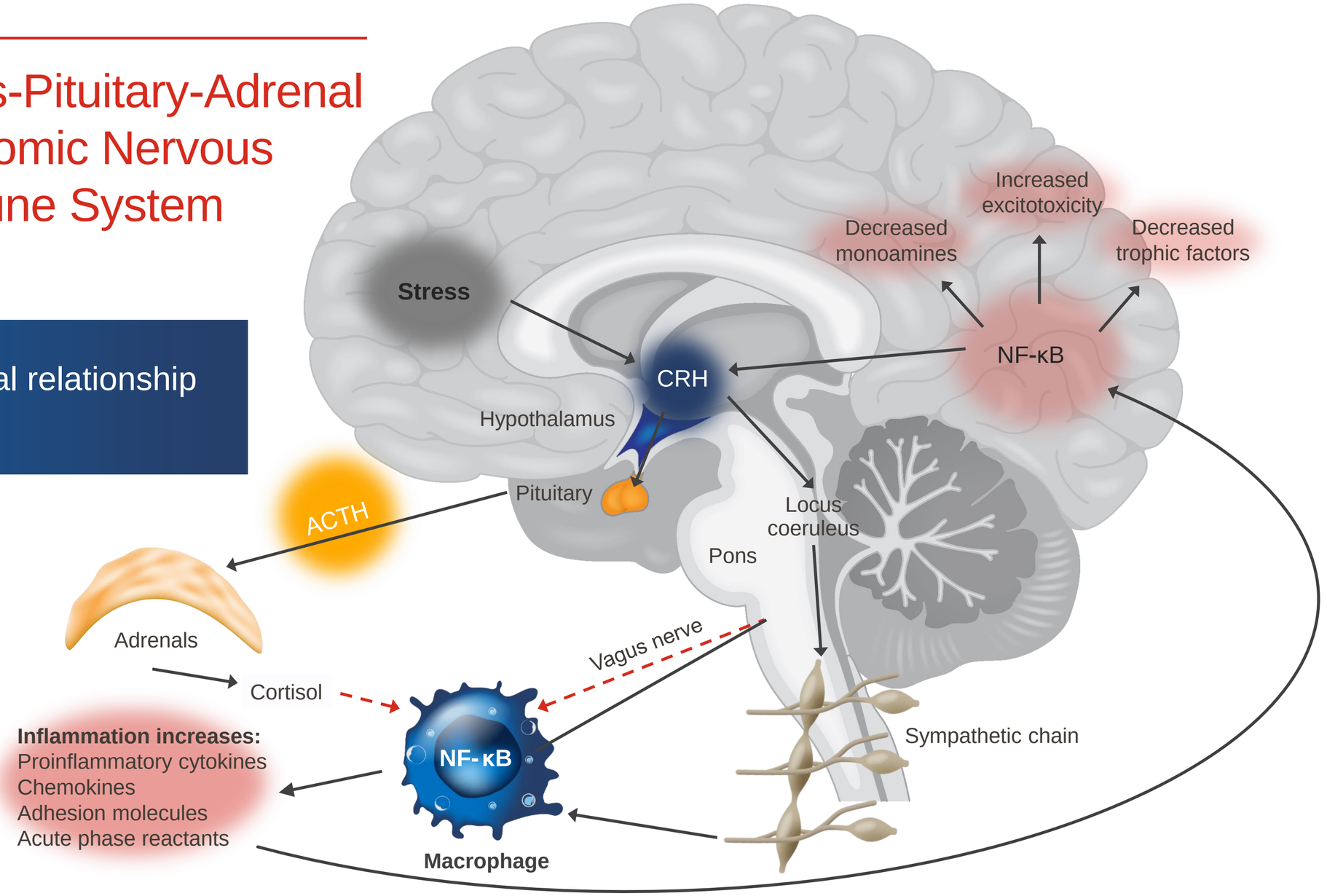
The Hypothalamus-Pituitary-Adrenal (HPA) Axis, Autonomic Nervous System, and Immune System

PNI involves a bidirectional relationship between the 3



ACTH = adrenocorticotropic hormone; CRH = corticotropin-releasing hormone; HPA = hypothalamic-pituitary-adrenal; NF-κB = nuclear factor-kappa-B.

Miller AH, et al. *Biol Psychiatry*. 2009;65(9):732-741.

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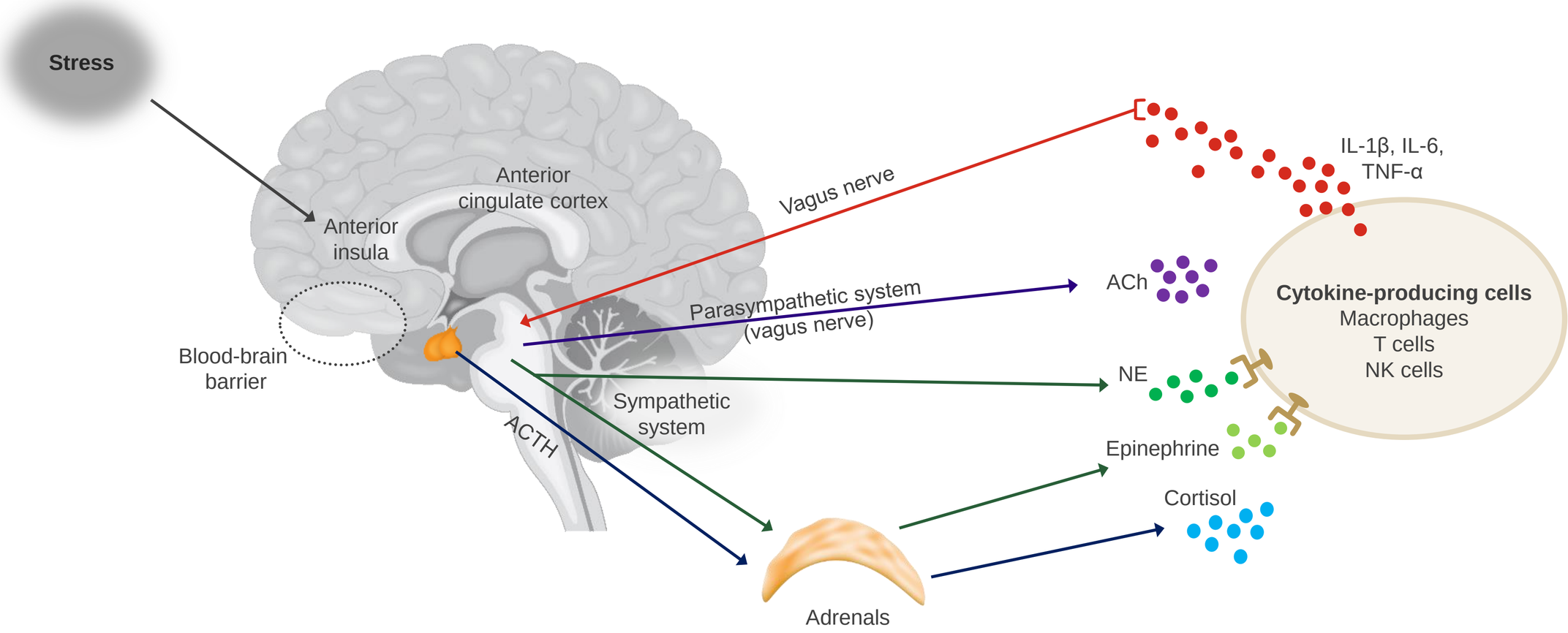
Multiple Brain-Body Pathways Connect Stress to Inflammation

Importance of PNI



ACh = acetylcholine; IL = interleukin; NE = norepinephrine; TNF = tumor necrosis factor.

Slavich GM, et al. *Psychol Bull*. 2014;140(3):774-815.

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Hypothalamus-Pituitary-Adrenal Axis

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The HHPA Axis: An Emerging Paradigm[1,2]

The HPA Axis Is "*So Yesterday*"

Hippocampus

↓

Hypothalamus

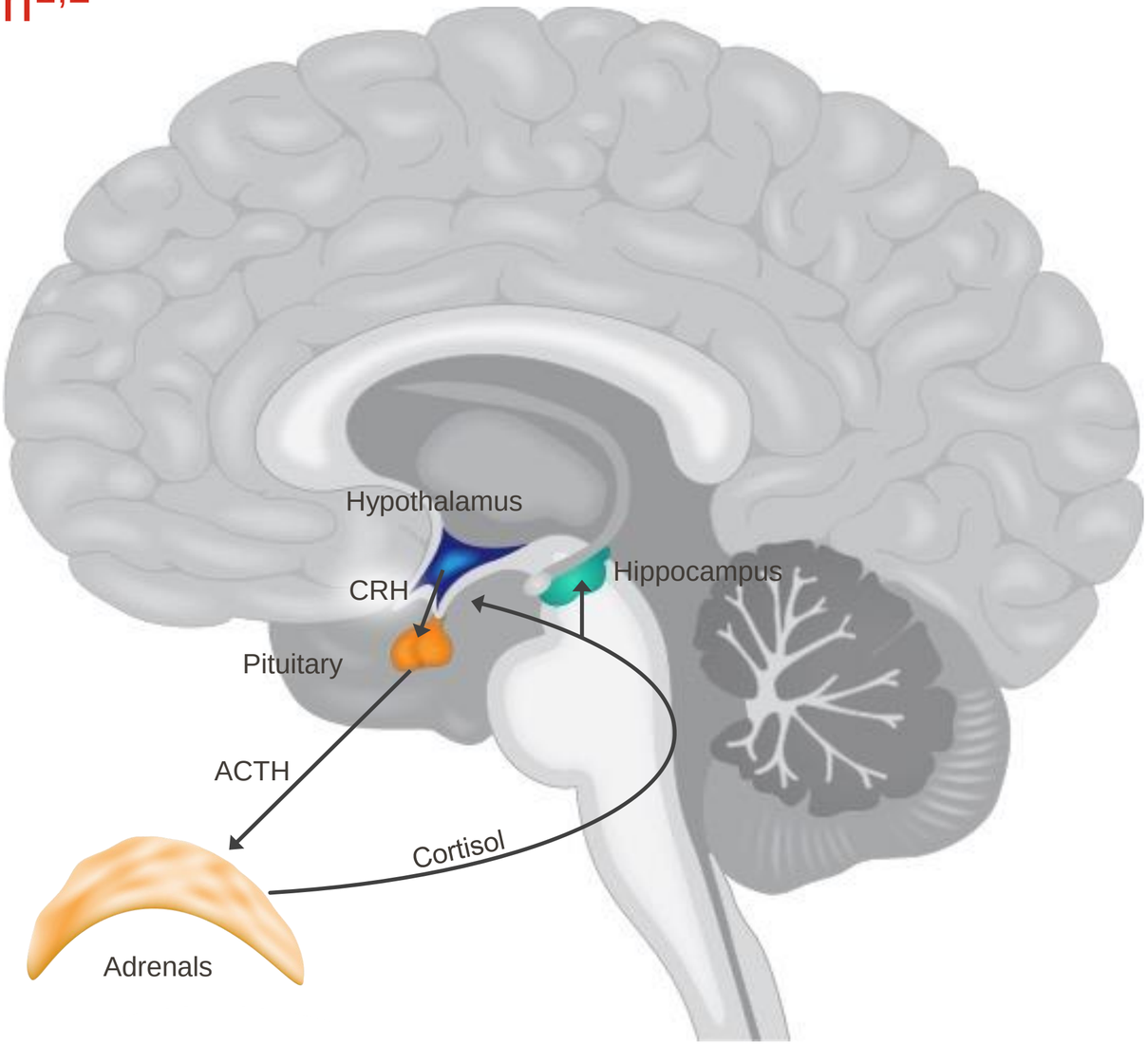
↓ **CRH**

Pituitary

↓ **ACTH**

Adrenals

Cortisol



1. Jain R, et al. *Curr Diab Rep*. 2011;11(4):275-284. 2. Stranahan AM, et al. *Neuromol Med*. 2008;10(2):118-127.

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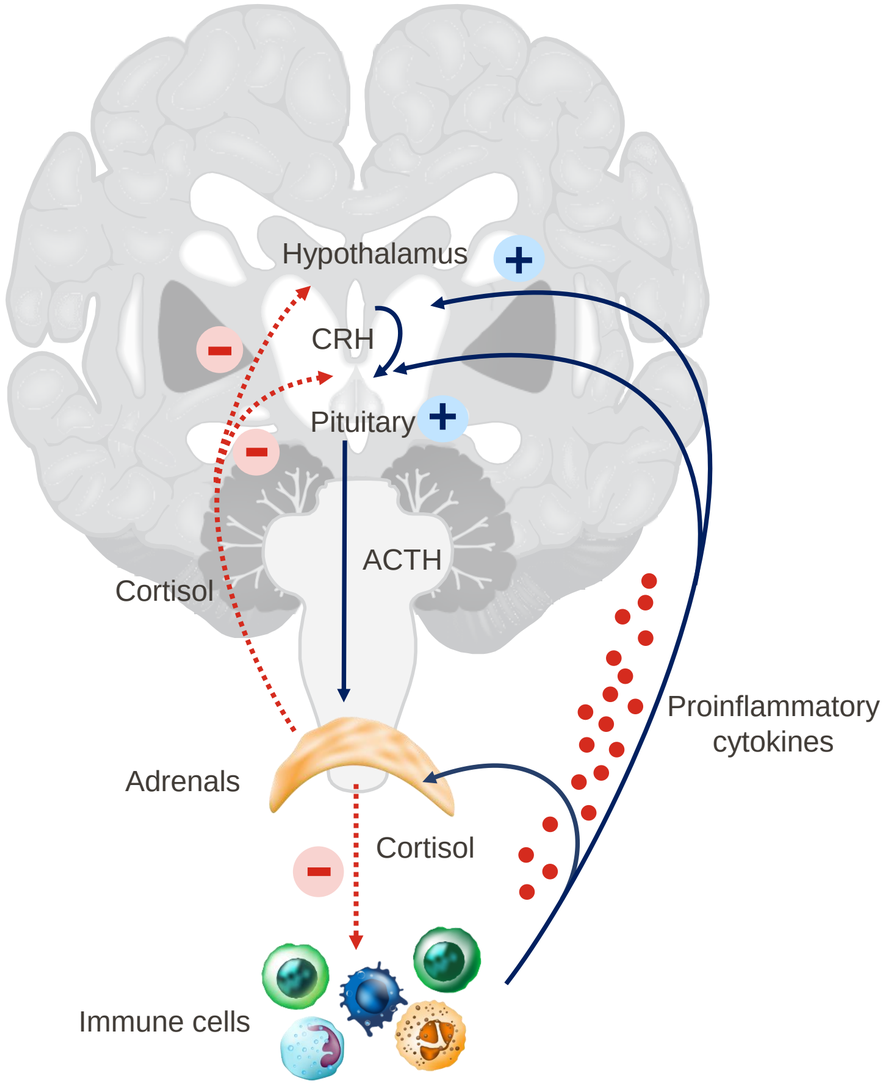
The HPA Axis and Immune System in Healthy Homeostasis

There is **bidirectional** communication between the immune system and the HPA axis

Proinflammatory cytokines, such as TNF, IL-1, and IL-6, stimulate cortisol release by **acting at all 3 levels of the HPA axis.**

In turn, **cortisol** has a negative feedback effect on the immune system to **suppress the further synthesis and release of proinflammatory cytokines.**



Silverman MN, et al. *Ann N Y Acad Sci*. 2012;1261:55-63.

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Autonomic Nervous System

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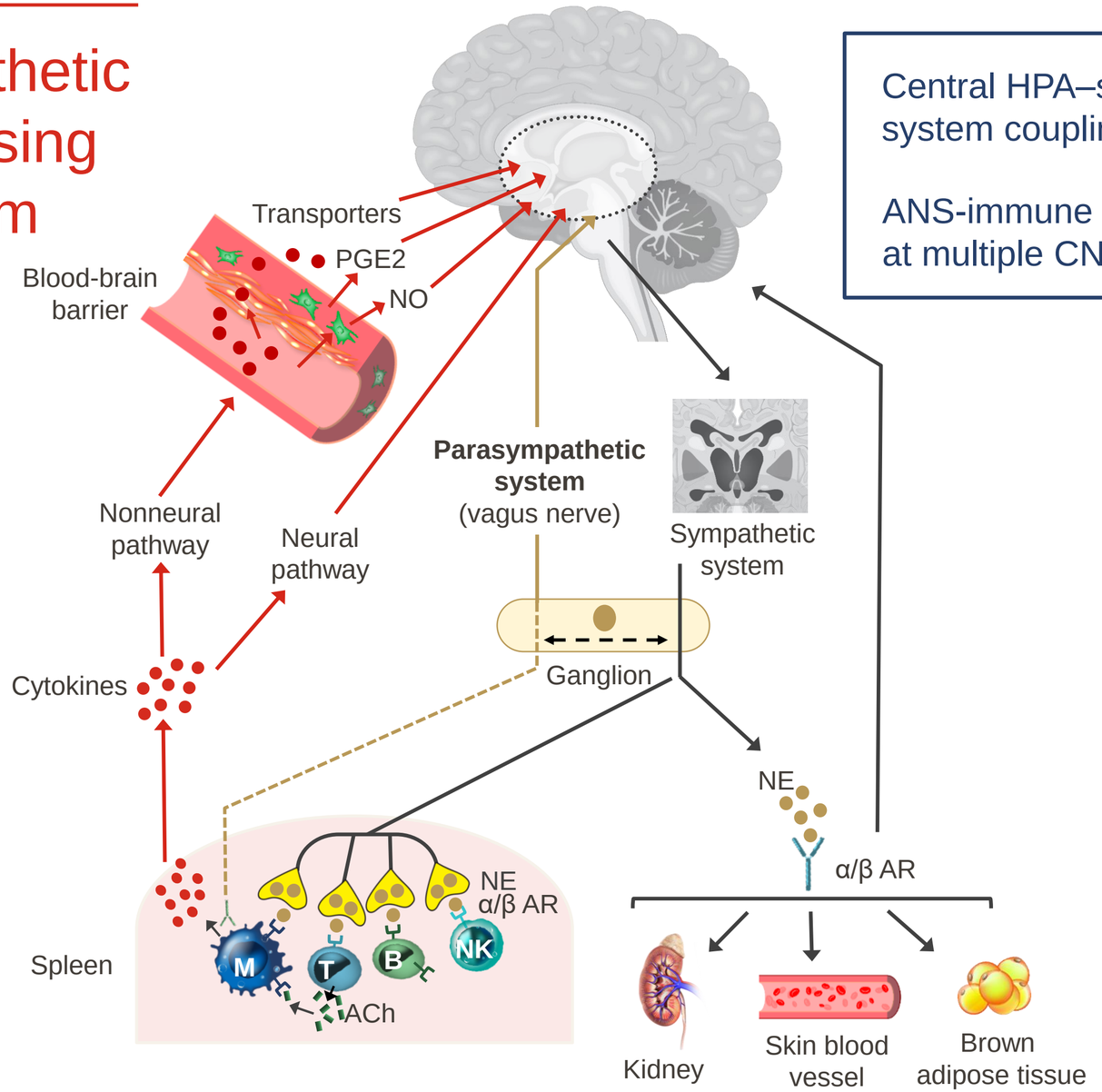
Sympathetic and Parasympathetic Arms of the ANS Exert Opposing Effects on the Immune System



Central HPA–sympathetic system coupling

ANS-immune interactions at multiple CNS sites

AR = adrenergic receptor; B = B cell; CNS = central nervous system; M = macrophage; NO = nitric oxide; PGE2 = prostaglandin E2; T = memory T cell.

Kenney MJ, et al. *Compr Physiol*. 2014;4(3):1177-1200.

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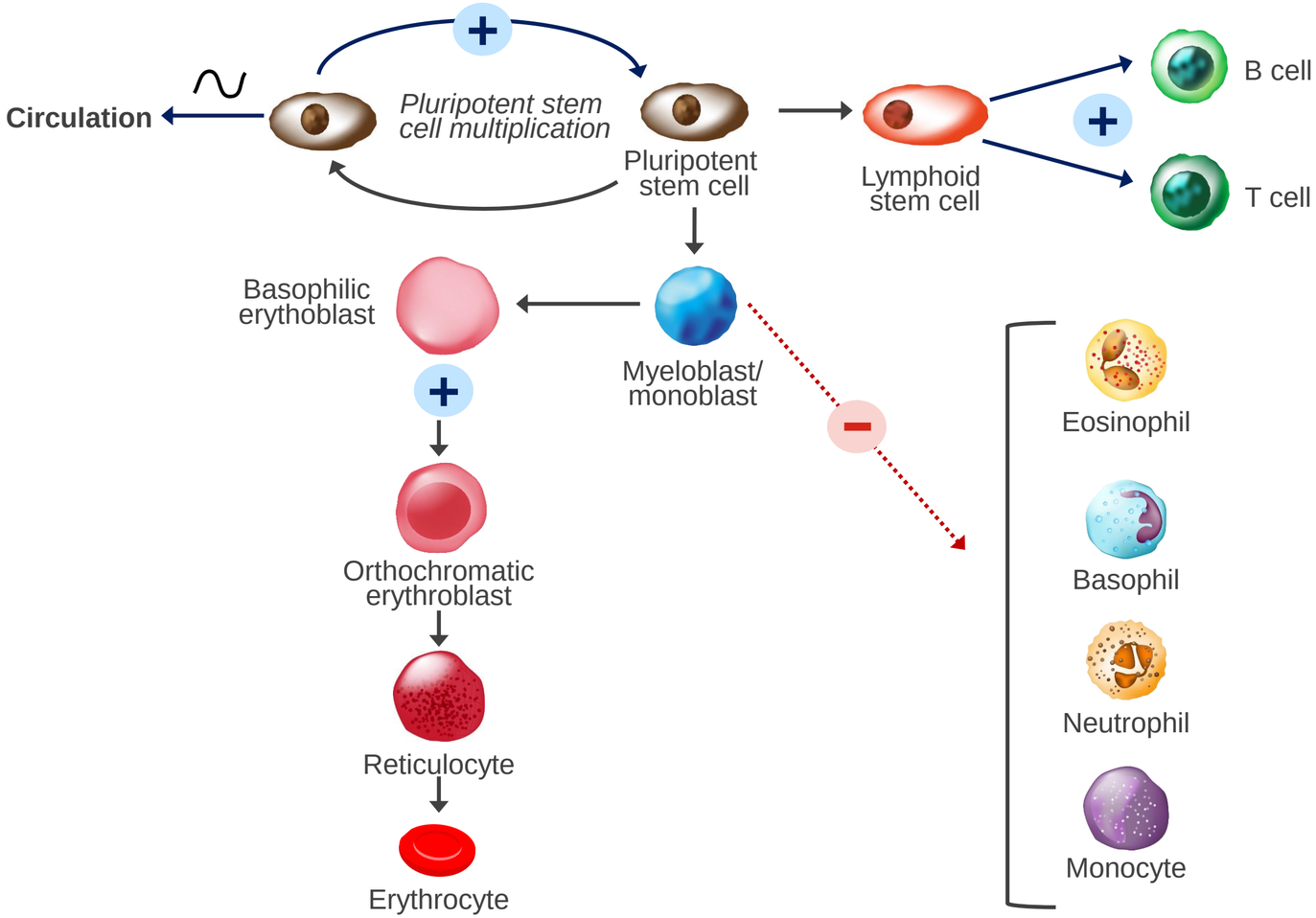
Sympathetic Nervous System Modulates Nearly Every Cell Line of the Immune System



Catecholamines, such as norepinephrine and epinephrine, impact immune cell proliferation

Bellinger DL, et al. *Auton Neurosci.* 2014;182:15-41.

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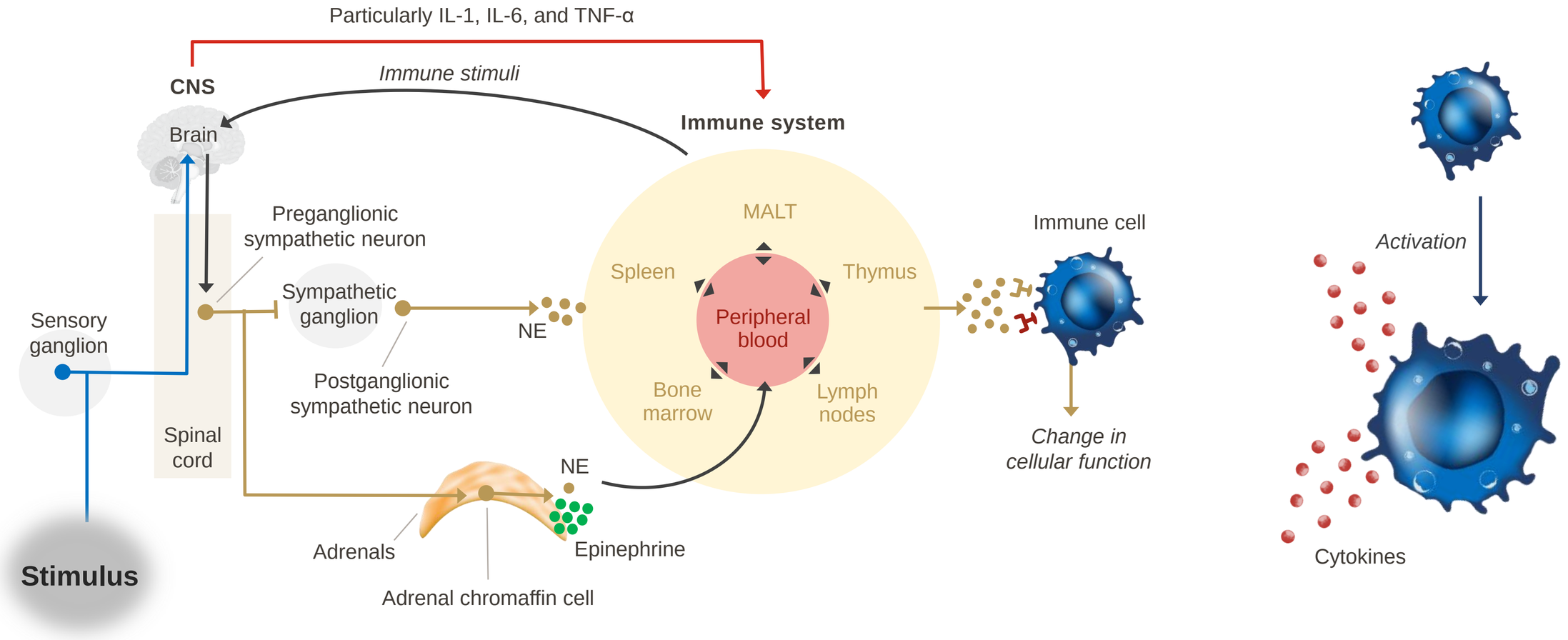
How the Sympathetic System Connects the CNS and Immune System



MALT = mucosa-associated lymphoid tissue.

Bellinger DL, et al. *Auton Neurosci.* 2014;182:15-41.

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Immune System

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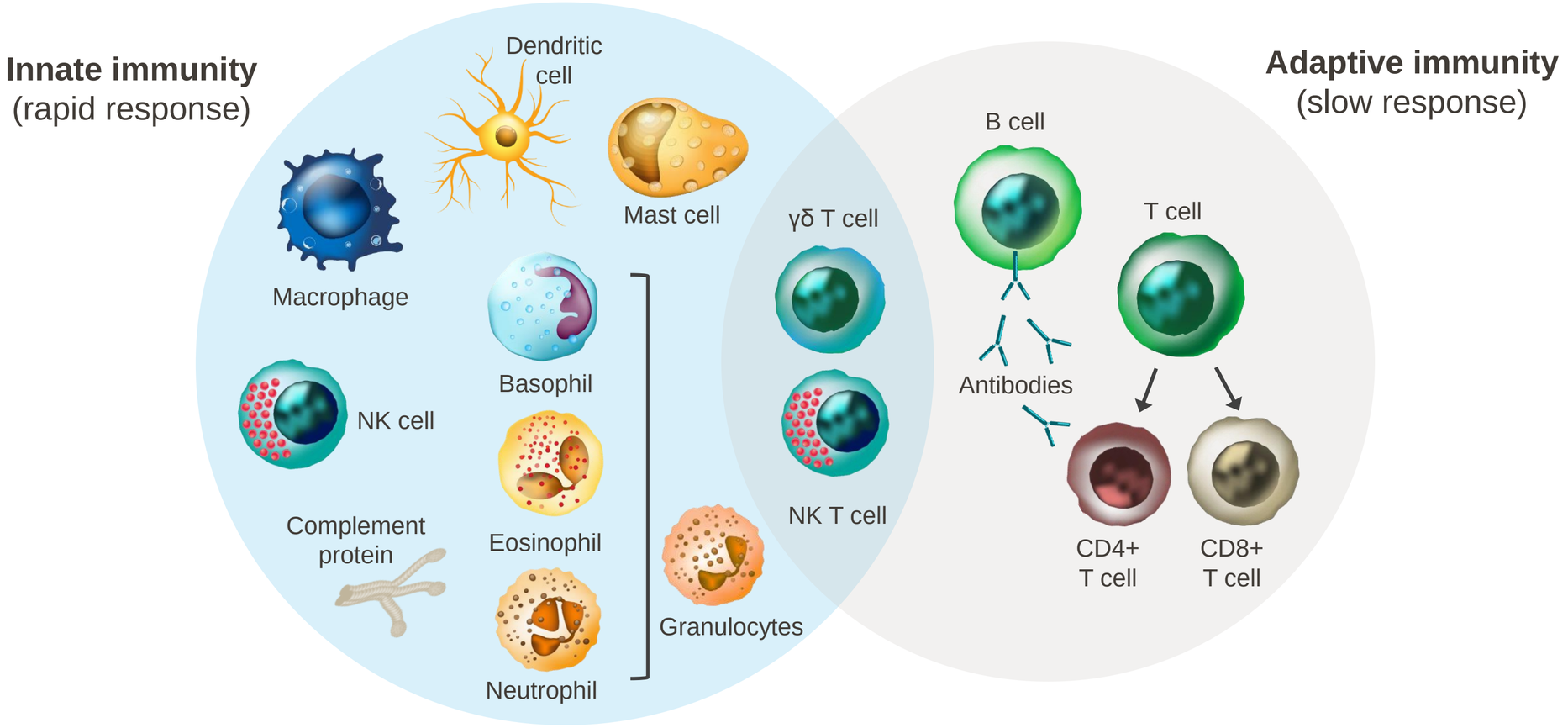
Innate and Adaptive Immunity



CD = cluster of differentiation.

Dranoff G. *Nat Rev Cancer*. 2004;4(1):11-22.

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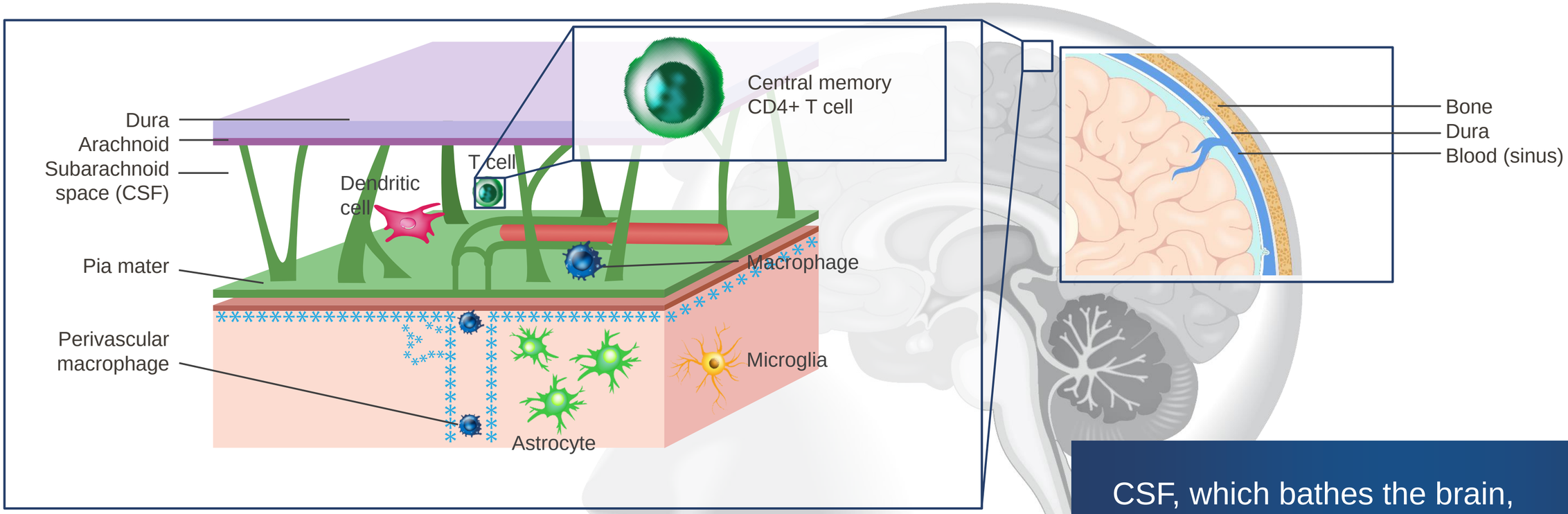
Immune Presence in the Brain Is Far More Extensive Than Previously Known



CSF, which bathes the brain, contains T cells

CSF = cerebrospinal fluid.

Prinz M, et al. *Nat Neurosci*. 2017;20(2):136-144.

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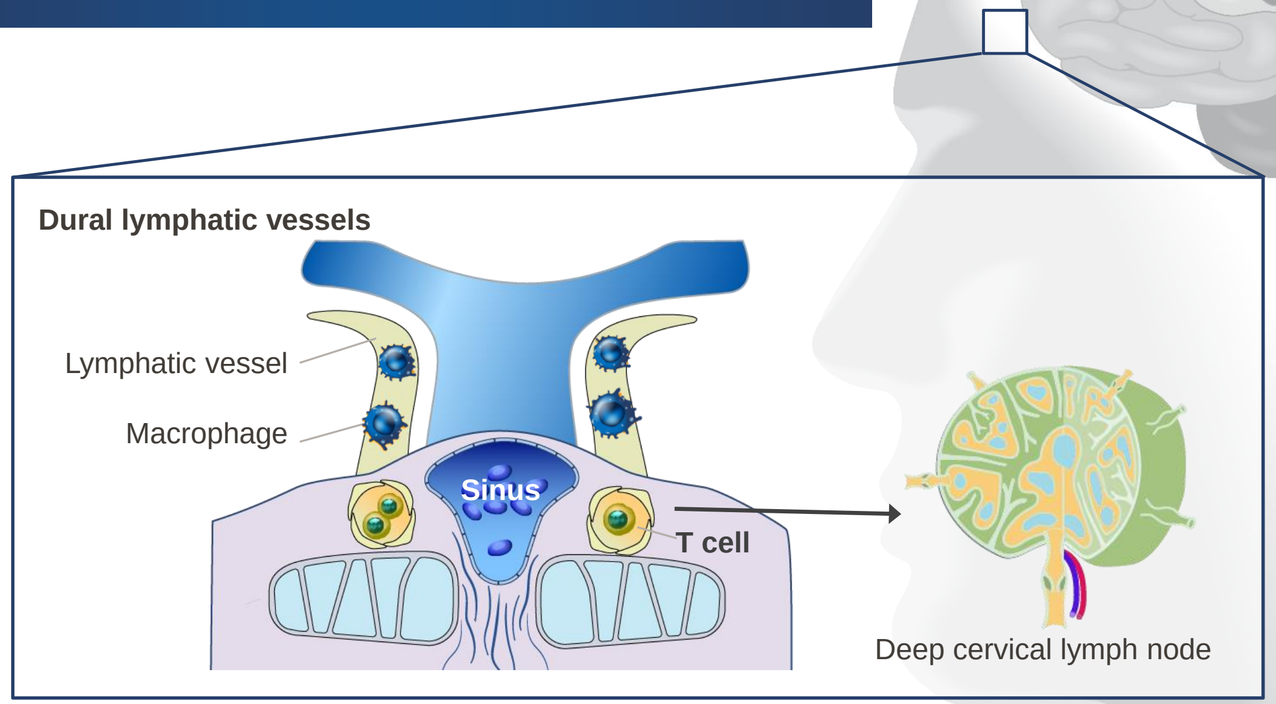
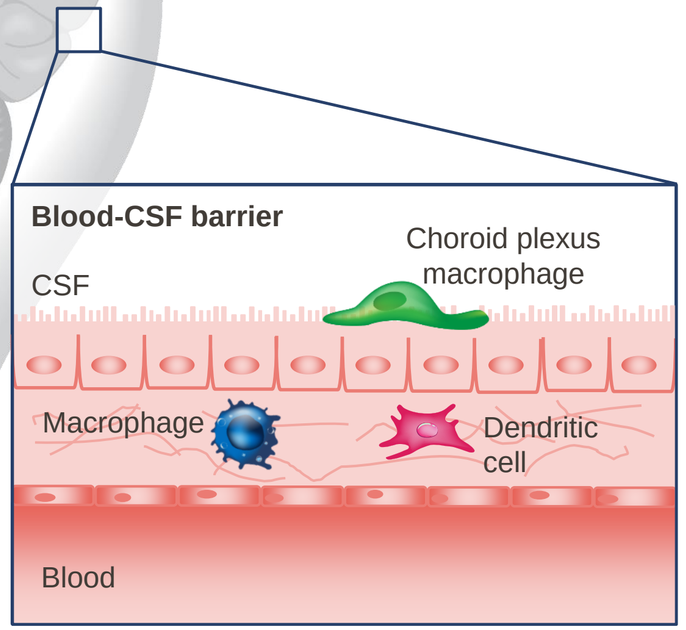
Immune Presence in the Brain Is Far More Extensive Than Previously Known (cont.)

Immune cells and proteins in CSF may be drained through meningeal lymphatic structures to reach the deep cervical lymph nodes

The only endogenous immune cells within the CNS are parenchymal (eg, microglia) and nonparenchymal (eg, perivascular, meningeal, choroid plexus) macrophages





Prinz M, et al. *Nat Neurosci*. 2017;20(2):136-144.

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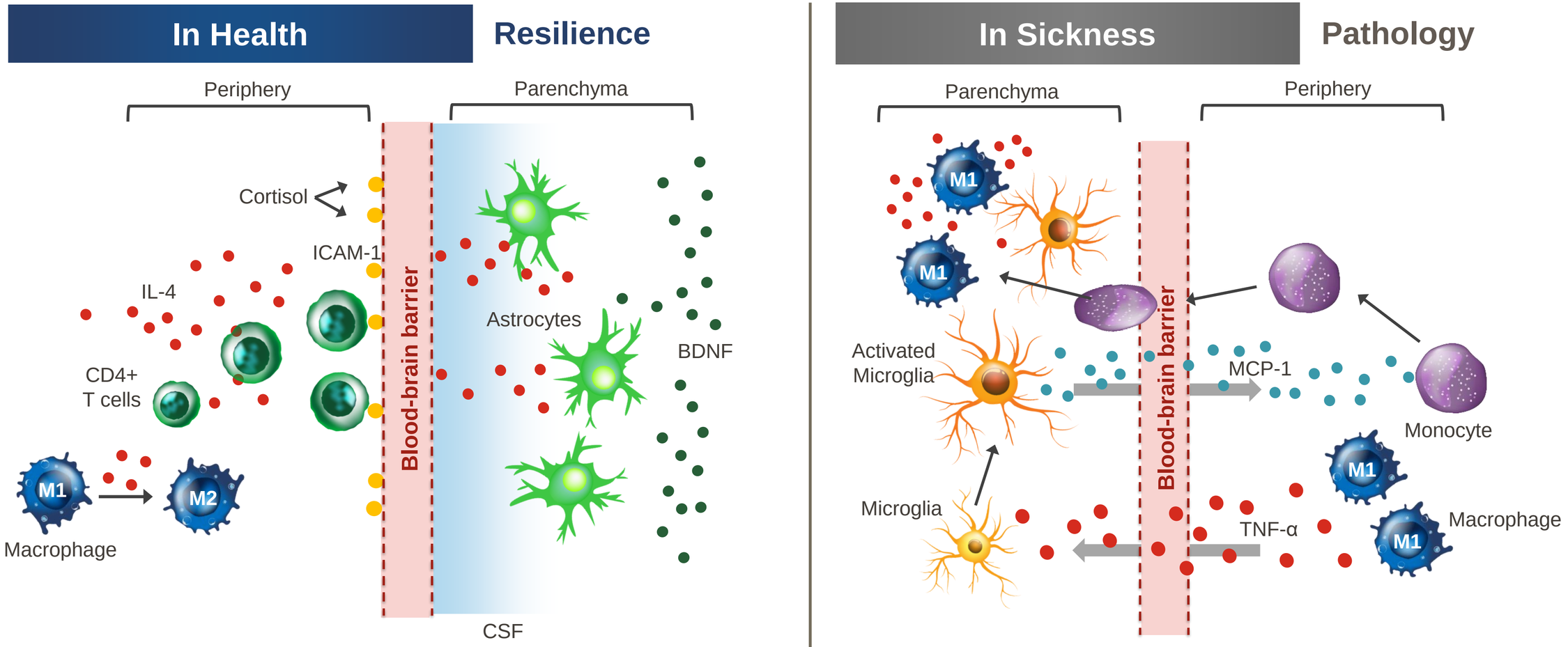
How Peripheral Inflammation Causes Central Inflammation



BDNF = brain-derived neurotrophic factor; ICAM = intercellular adhesion molecule; MCP = monocyte chemotactic protein.
Haroon E. et al. *Neuropsychopharmacol Rev*. 2012;37(1):137-162.

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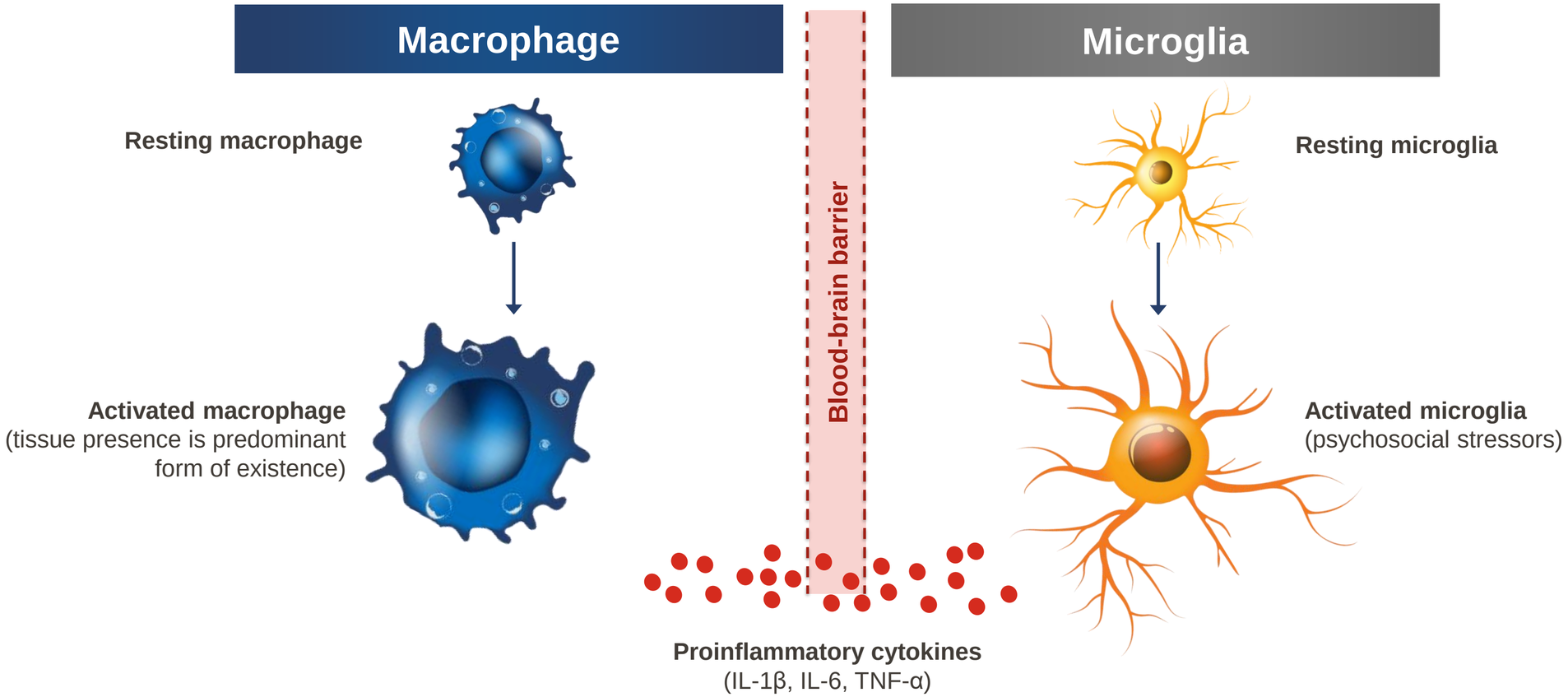
Macrophage-Microglia Interaction[1,2]



1. Haroon E, et al. *Neuropsychopharmacol Rev*. 2012;37(1):137-162. 2. Raison CL, et al. *Trends Immunol*. 2006;27(1):24-31.

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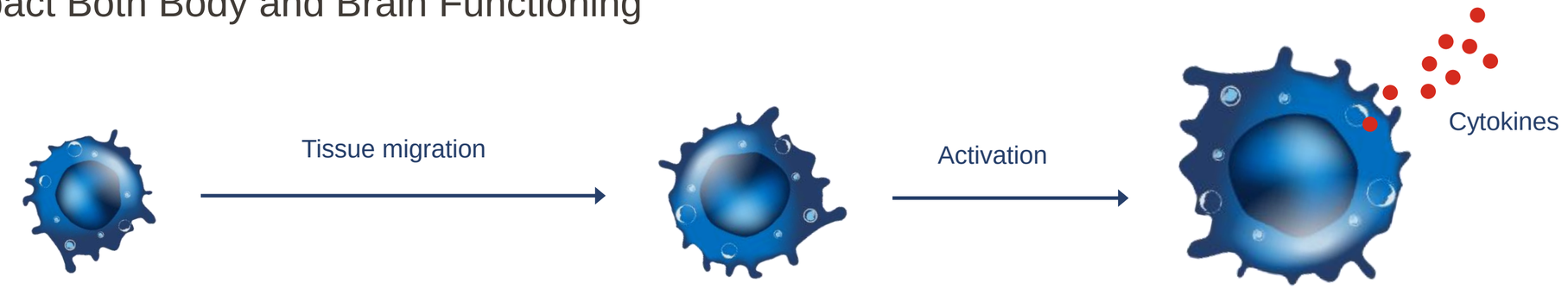
Activated Macrophages Produce Cytokines[1,2]

Cytokines Impact Both Body and Brain Functioning



Reasons why cytokines are important:

1. Cytokines have easy access to the CNS, primarily microglia
2. Microglia respond to peripheral cytokines and produce cytokines
3. Cytokines interact with pathophysiologic domains that characterize neuropsychiatric disorders (eg, depression)[2]

1. Haroon E, et al. *Neuropsychopharmacol Rev*. 2012;37(1):137-162. 2. Raison CL, et al. *Trends Immunol*. 2006;27(1):24-31.

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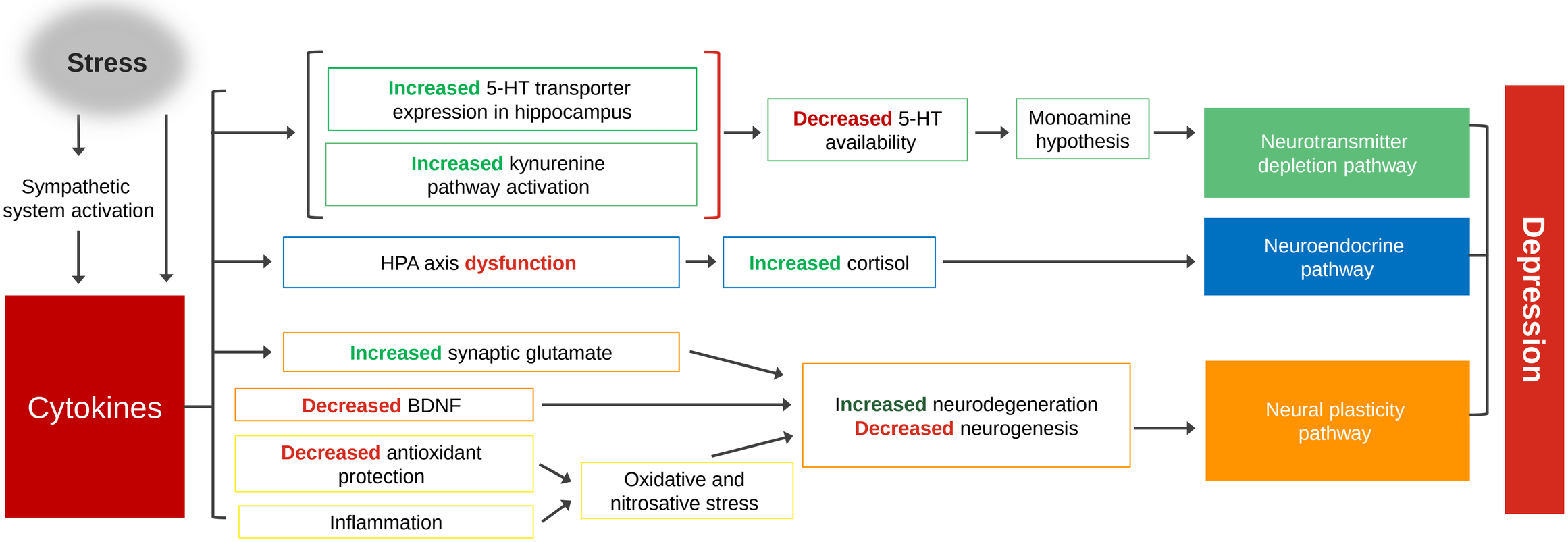
A Bidirectional Relationship Exists Between Raised Inflammatory Cytokine Levels and Depression



HT = hydroxytryptamine.

Jeon SW, et al. *World J Psychiatry.* 2016;6(3):283-293.

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Summary

Chapter Two

PNI is the great connector between the body and the brain

The HPA axis (or, more accurately, the **HHPA axis**), **ANS**, and **immune systems** have a **bidirectional** relationship with inflammation

This PNI link may not be widely known in rheumatology

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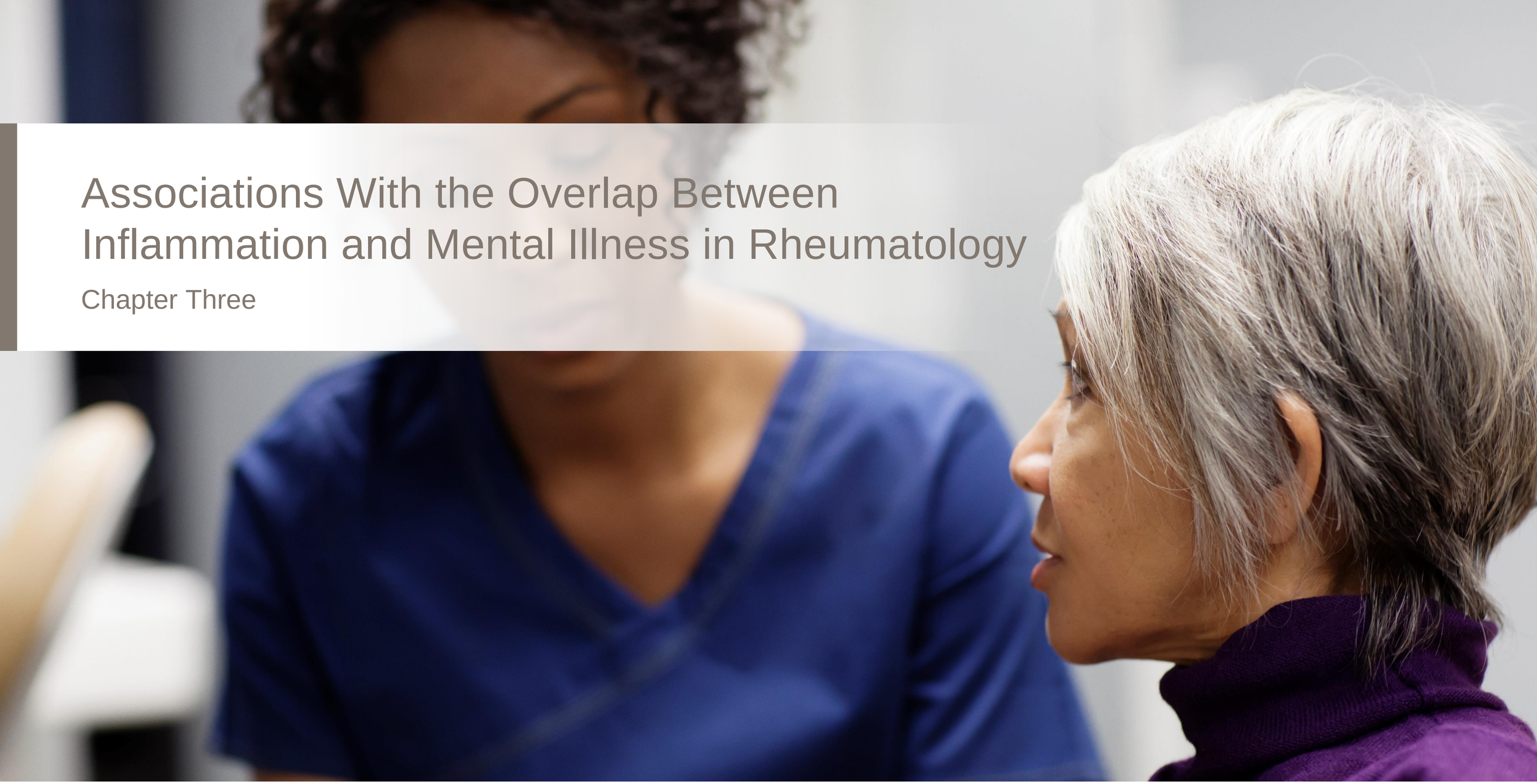

Associations With the Overlap Between Inflammation and Mental Illness in Rheumatology

Chapter Three

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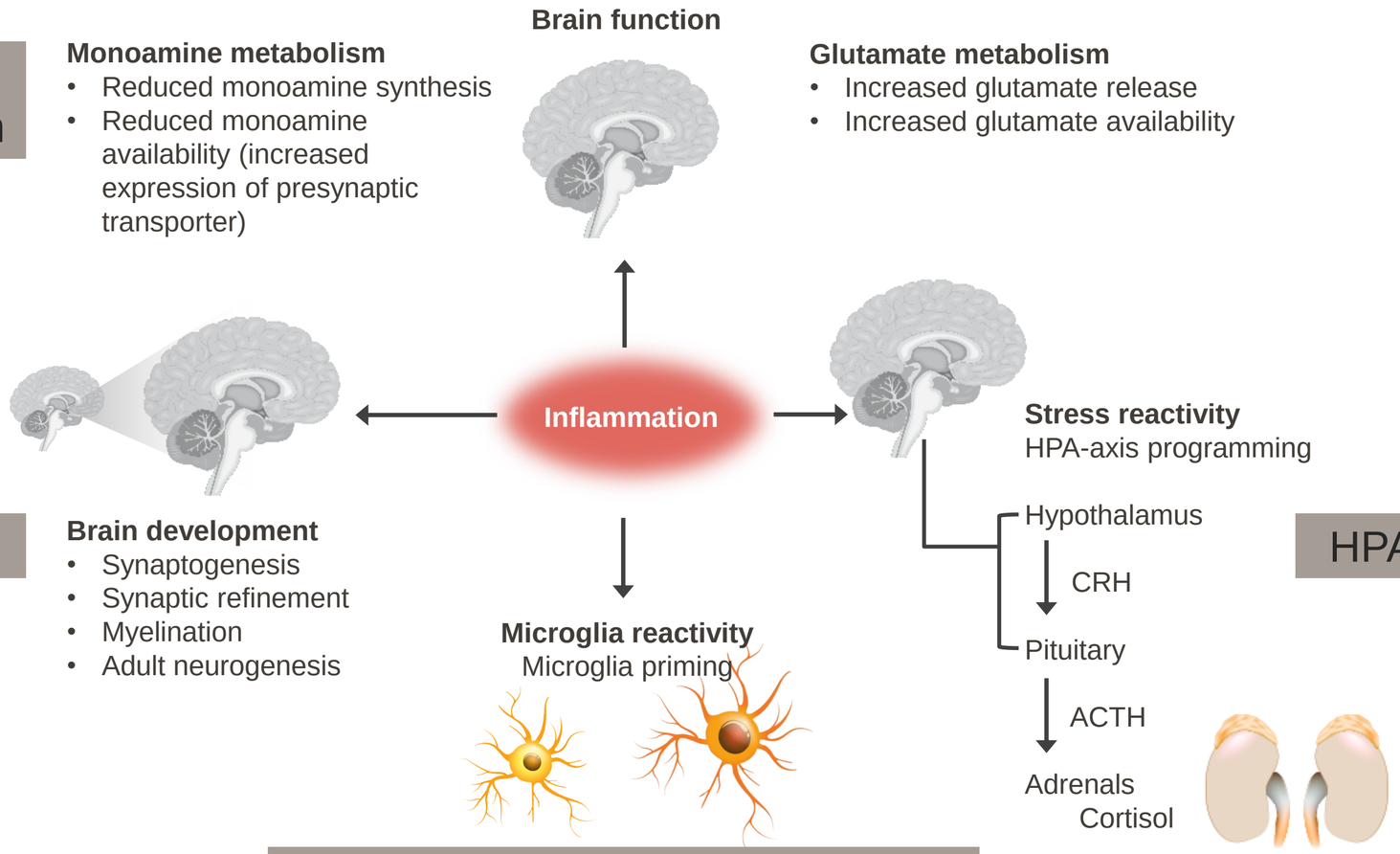
Stress Can Set Off an Inflammatory Chain Reaction With Multiple Adverse Consequences



Danese A, et al. *Neuropsychopharmacol Rev*. 2017;42(1):99-114.

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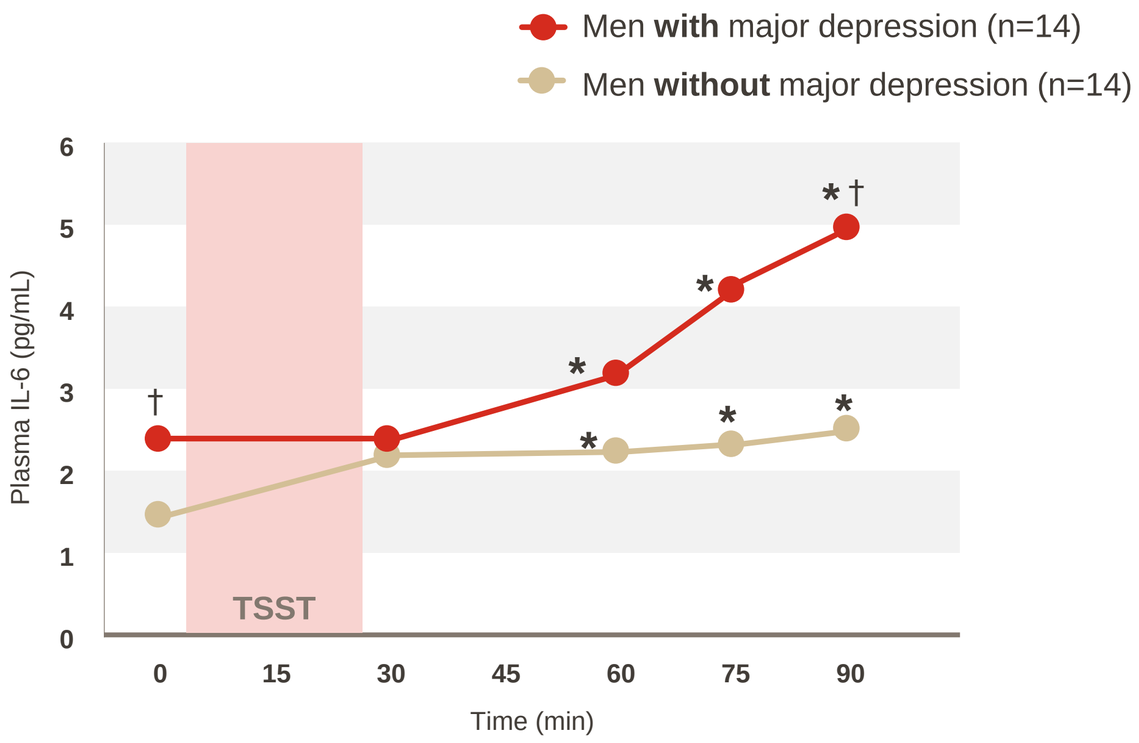
Psychosocial Stress Can Induce Inflammatory Response in Major Depression

Plasma IL-6 Levels Before and After a Psychosocial Stressor Challenge (TSST)

N=28



Participants with major depression had **increased early-life stress**‡

Participants with major depression had **significantly higher IL-6 levels** at baseline and 90 minutes after the stressor, as well as a greater IL-6 response to the stressor

*P<.05 vs baseline; †P<.05 between groups; ‡On Childhood Trauma Questionnaire.
TSST = Trier social stress test.
Pace TWW. *Am J Psychiatry*. 2006;163(9):1630-1633.

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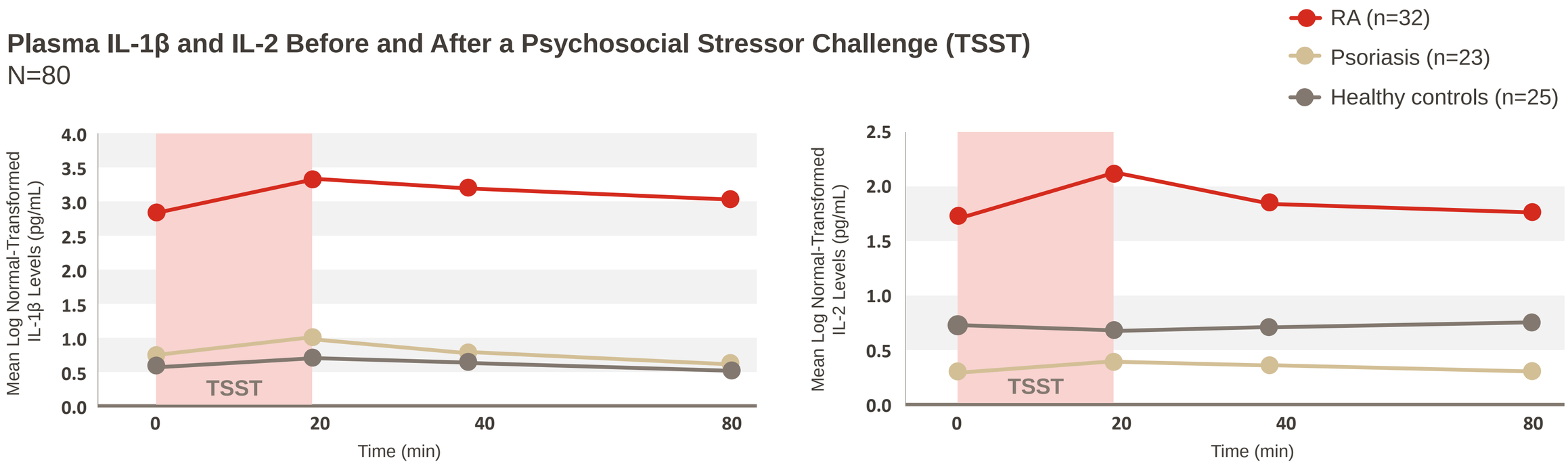
Immune Response to Stress in RA and Psoriasis

Plasma IL-1β and IL-2 Before and After a Psychosocial Stressor Challenge (TSST)
N=80



Patients with RA had significantly higher baseline and stress-induced* levels of IL-1β and IL-2 compared to patients with psoriasis and healthy controls

Not only are levels of inflammation higher at baseline for patients with RA, inflammation further increases with stress.

*After correction for baseline.

De Brouwer SJM, et al. *Rheumatology.* 2014;53(10):1844-1848.

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Summary

Chapter Three

Cytokine levels increase in stress and patients with depression have even higher stress-induced cytokine responses

Patients with RA have higher stress-induced cytokine responses

Cytokines appear to be the currency utilized in the transaction process

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Mental Wellness, Inflammation, and Rheumatology

Chapter Four

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High Positive Affect = Lower Inflammation

Positive Emotions Predicting IL-6
N=119

Dispositional Positive Emotions Scale	IL-6*
Awe	- 0.33
Amusement	- 0.02
Compassion	- 0.09
Contentment	- 0.20
Joy	- 0.23
Love	- 0.1
Pride	- 0.21

Dispositional joy, contentment, pride, and awe each negatively predicted IL-6 levels.

Positive affect predicted lower levels of the proinflammatory cytokine, IL-6

*β values for positive emotions predicting IL-6 and controlling for participant's BMI. Emotions were separately entered into regressions.
Stellar JE. *Emotion*. 2015;15(2):129-133.

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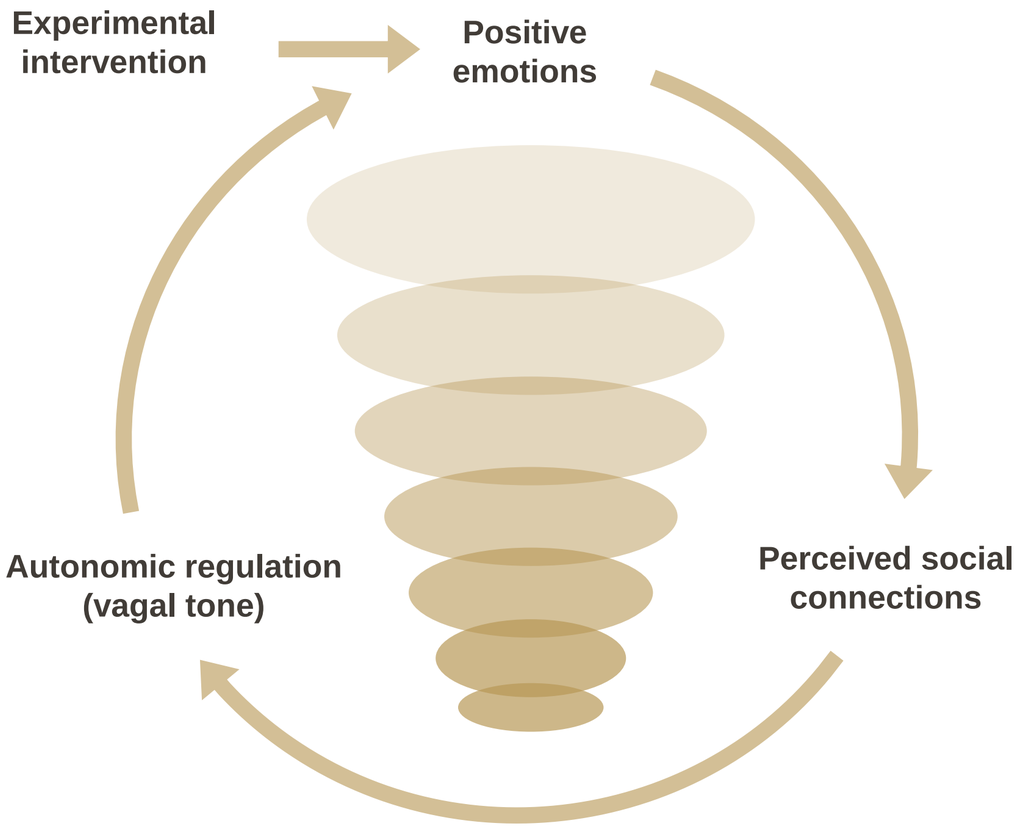
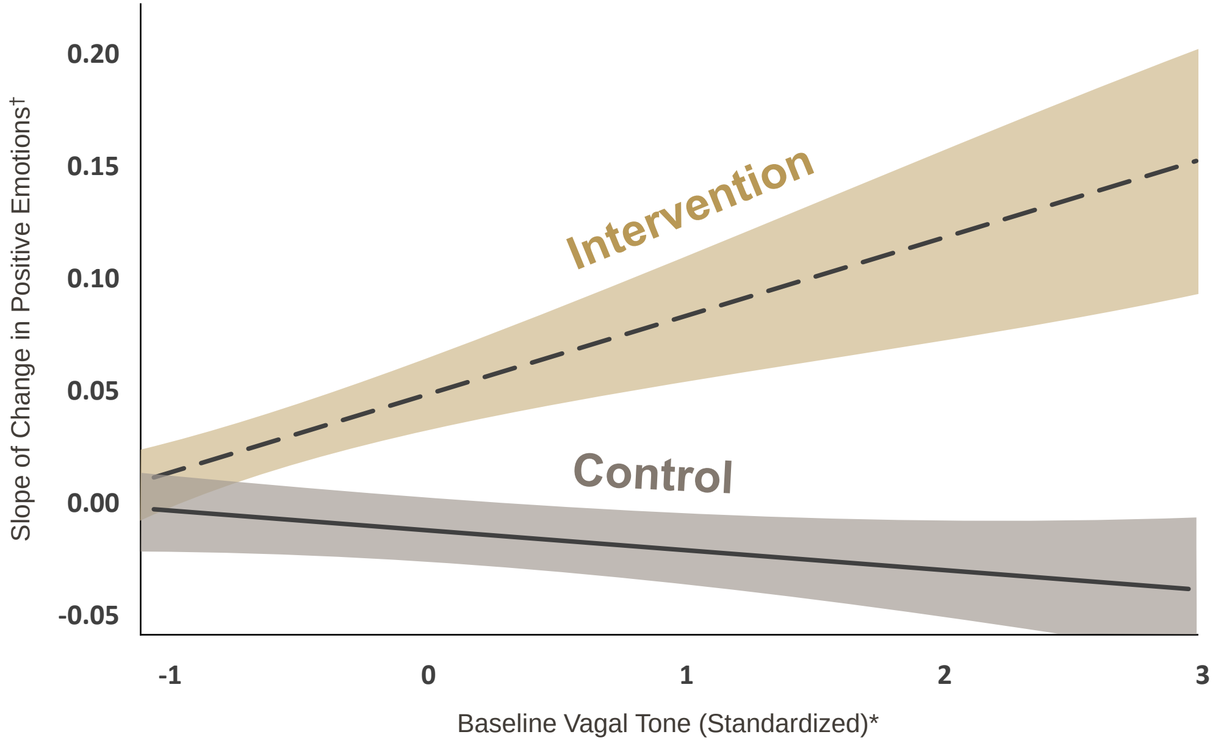
Upward Spiral: Interventional Study Shows Positive Emotions Can Change Vagal Tone



Relationship Between Baseline Vagal Tone and Change in Positive Emotions

N=65



*Vagal tone was assessed using spectral frequency analysis of heart rate data to obtain high-frequency heart rate variability; †Shaded areas represent 95% confidence interval.

Kok BE, et al. *Psychol Sci.* 2013;24(7):1123-1132.

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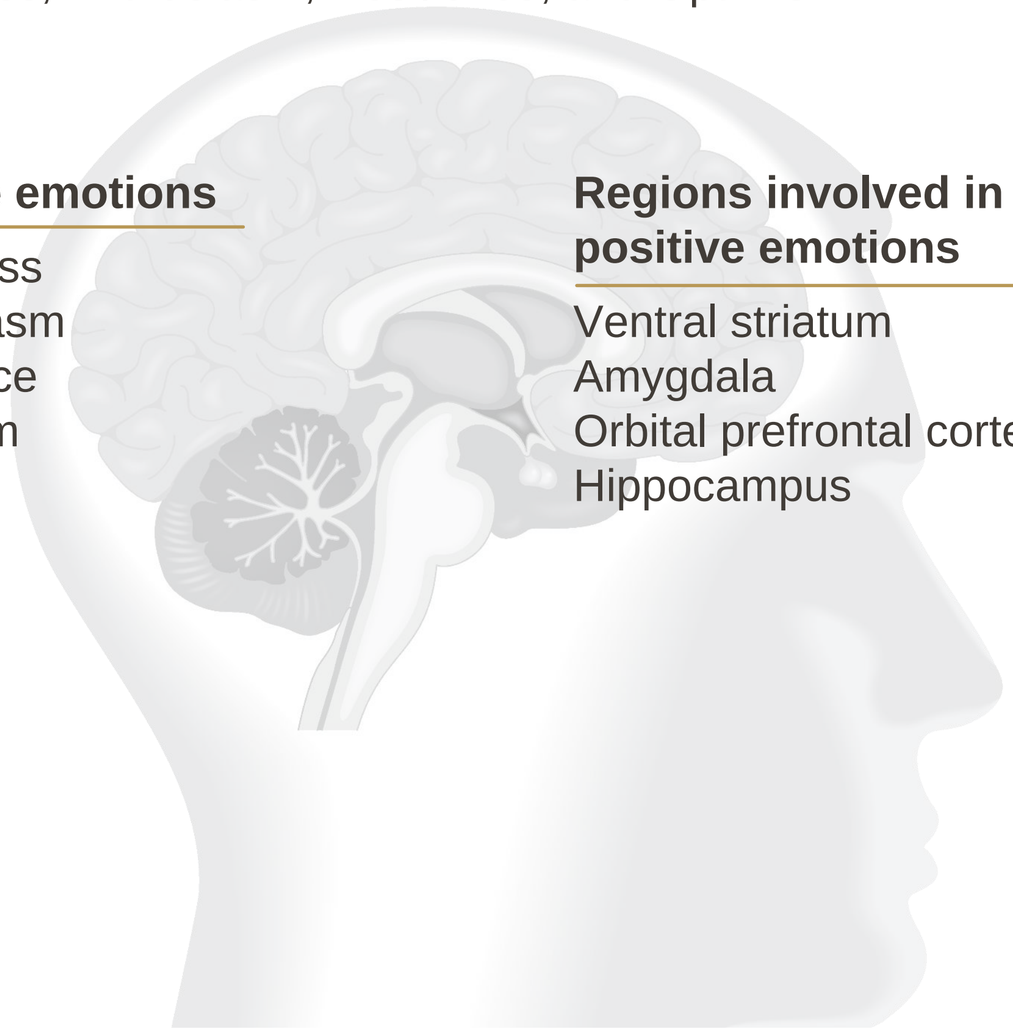
Neurobiology of Positive Emotions

Happiness, Enthusiasm, Resilience, and Optimism



Positive emotions

Happiness
Enthusiasm
Resilience
Optimism
Others

Regions involved in positive emotions

Ventral striatum
Amygdala
Orbital prefrontal cortex
Hippocampus

Neurotransmitters involved in positive emotional processing

Dopamine
GABA
Endogenous opioids
Endogenous cannabinoids

GABA = gamma-aminobutyric acid.

Burgdorf J, et al. *Neurosci Biobehav Rev*. 2006;30(2):173-187.

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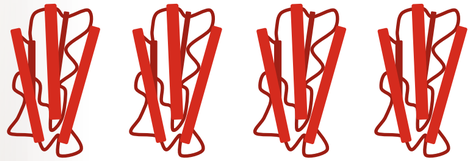
Happiness and Its Relationship to Inflammation



Lower perceived happiness was associated with **higher** IFN-γ levels

Higher perceived happiness was associated with **lower** IFN-γ levels

In addition, touching and warm/positive emotion induction from the touch of a loved one **reduced peripheral IFN-γ levels**

IFN-γ = interferon gamma.

Matsunaga M, et al. *Neuro Endocrinol Lett*. 2011;32(4):458-463.

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Can a Wellness Trait Like Optimism Change the Brain?

- Several studies have shown that dispositional optimism is beneficial to physical and psychological well-being
- High levels of optimism may be associated with
  - **Lower activation of the amygdala** when viewing negative stimuli
  - **Higher activation of the anterior cingulate cortex** when viewing positive stimuli

Associations Between Regional Gray-Matter Volume and Dispositional Optimism in Healthy Participants (N=361)

Individual **dispositional optimism was significantly and positively correlated with gray-matter volume** in a cluster that mainly included areas in the left thalamus/left pulvinar, which extended to the left parahippocampal gyrus

Yang J, et al. *Neurosci Lett*. 2013;553:201-205.

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Summary

Chapter Four

Positive affect may be associated with lower levels of inflammation

Increased positive emotions mediated by perceived social connection improves physical health

Perceived happiness may be associated with lower levels of proinflammatory cytokines

Individual dispositional optimism has been shown to be positively correlated with gray-matter volume

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Mental Health Scales and Screeners

Chapter Five

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Simple Scales and Screeners

Depression	Patient Health Questionnaire-9 (**PHQ-9**)[1]
Anxiety	Generalized Anxiety Disorder 7 (**GAD-7**)[2]
Sleep	Sleep Condition Indicator (**SCI**)[3]
Wellness	**H**appiness, **E**nthusiasm, **R**esilience, **O**ptimism (**HERO**)[4]

1. Kroenke K, et al. J *Gen Intern Med*. 2001;16(9):606-613. 2. Spitzer RL, et al. *Arch Intern Med*. 2006;166(10):1092-1097. 3. Espie CA, et al. *BMJ Open.* 2014;4:e004183. doi:10.1136/bmjopen-2013-004183. 4. Jain S, et al. Presented at: 29th Annual US Psychiatric and Mental Health Congress; October 2016; San Antonio, Texas.

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HERO Wellness Scale

- Self-reported tool
- Brief (only 5 questions)
- Takes a few minutes to complete

Scoring:

Add all circled numbers to calculate total score

Score range = 0 to 50

A higher score indicate a higher level of wellness

HERO WELLNESS SCALE

*Please circle **ONE NUMBER** for each question below.*

1. On average, during the last 7 DAYS, how happy have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all happy		Mildly happy			Moderately happy			Highly happy		Extremely happy

2. On average, during the last 7 DAYS, how enthusiastic have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all enthusiastic		Mildly enthusiastic			Moderately enthusiastic			Highly enthusiastic		Extremely enthusiastic

3. On average, during the last 7 DAYS, how resilient have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all resilient		Mildly resilient			Moderately resilient			Highly resilient		Extremely resilient

4. On average, during the last 7 DAYS, how optimistic have you felt?

0	1	2	3	4	5	6	7	8	9	10
Not at all optimistic		Mildly optimistic			Moderately optimistic			Highly optimistic		Extremely optimistic

5. On average, during the last 7 DAYS, how would you rate your mental wellness?

0	1	2	3	4	5	6	7	8	9	10
Not at all good		Mildly good			Moderately good			Markedly good		Extremely good

SCORING: To calculate total score, add all circled numbers. TOTAL SCORE: 0 - 50

HIGHER SCORES INDICATE HIGHER LEVELS OF WELLNESS

SCORE

Jain S, et al. Presented at: 29th Annual US Psychiatric and Mental Health Congress; October 2016; San Antonio, Texas. https://www.wild5wellness.com/uploads/3/3/6/9/3369689/uspc_-_hero_w.

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Behaviors to Repair PNI Disruptions in Rheumatologic Disorders

Chapter Six

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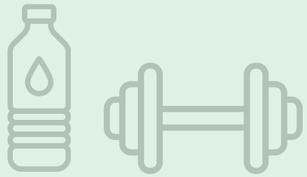
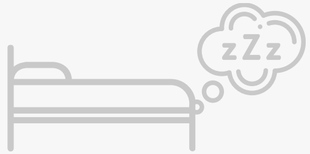
Wellness Behaviors With Anti-Inflammatory Effect



Exercise



Sleep

Nutrition

Mindfulness

Social Connectedness

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Exercise
and Its Impact on Inflammation

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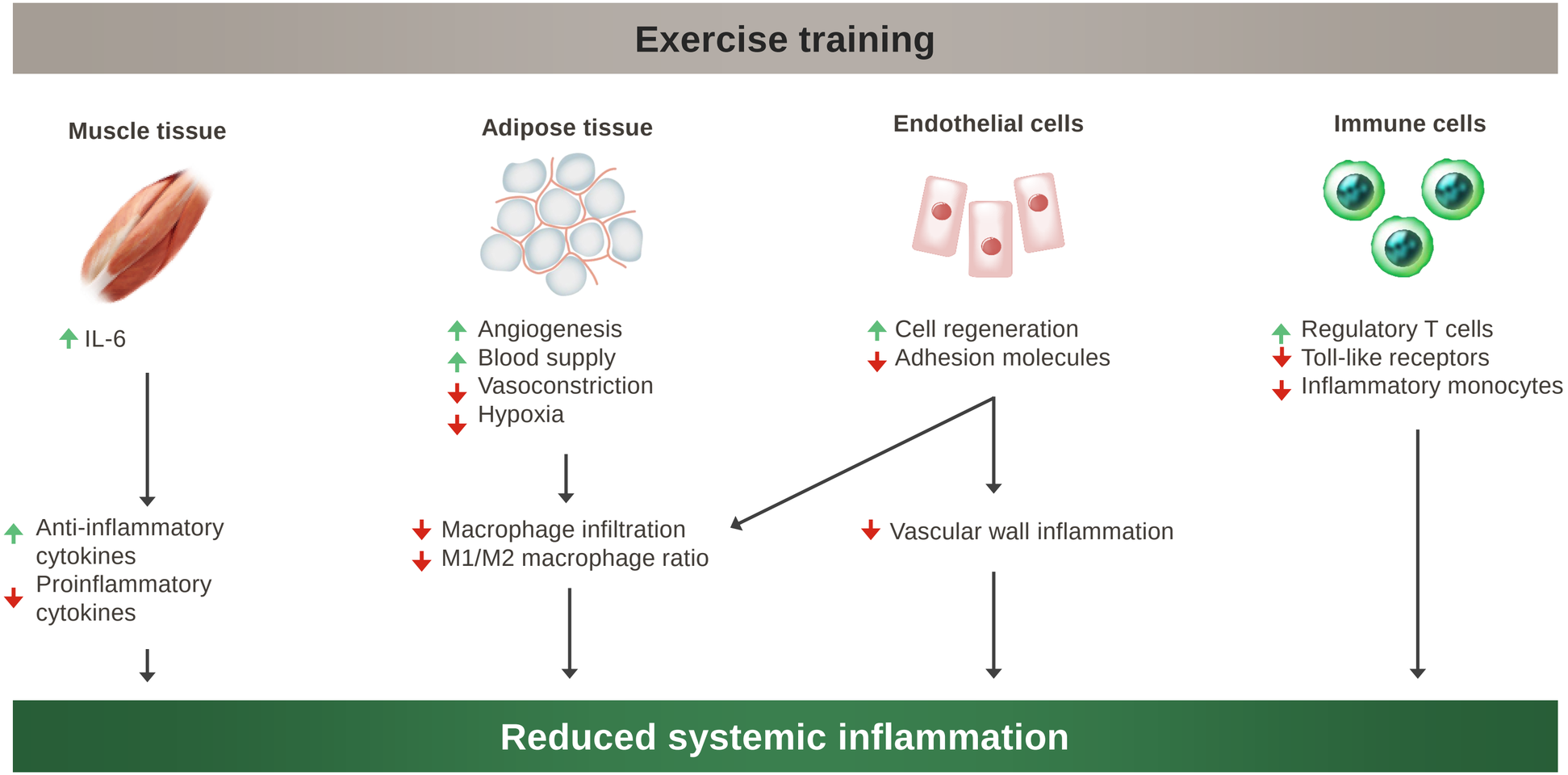
Potential Mechanisms Through Which Exercise Reduces Chronic Inflammation



M1/M2 = proinflammatory/anti-inflammatory macrophage ratio.

You T, et al. *Sports Med*. 2013;43(4):243-256.

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Exercise Improves Gray-Matter Density and Brain Connectivity

Effects of Regular Physical Exercise on Gray and White–Matter Density and Neurotrophic and Metabolic Blood Markers in Overweight to Obese Individuals
N=16

Findings:

- Reduced BMI
- Reduced serum leptin concentrations, elevated HDL-C, and alterations of serum BDNF concentrations, which suggest changes of metabolic and neurotrophic function
- Increased gray-matter density in the left hippocampus, insular cortex, and left cerebellar lobule
- Observed exercise-dependent changes of diffusivity parameters in surrounding white-matter structures, as well as in the corpus callosum

BDNF = brain-derived neurotrophic factor; BMI = body mass index; HDL-C = high-density lipoprotein-cholesterol.
Mueller K, et al. *Front Hum Neurosci*. 2015;9:372.

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Sleep
and Its Impact on Inflammation

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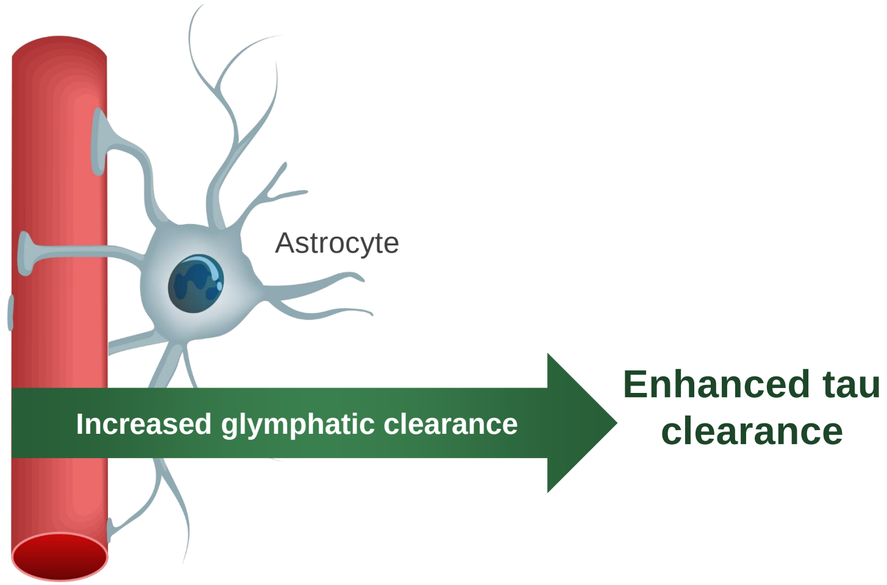
Why Care About Sleep?

Sleep and Its Immune Implications

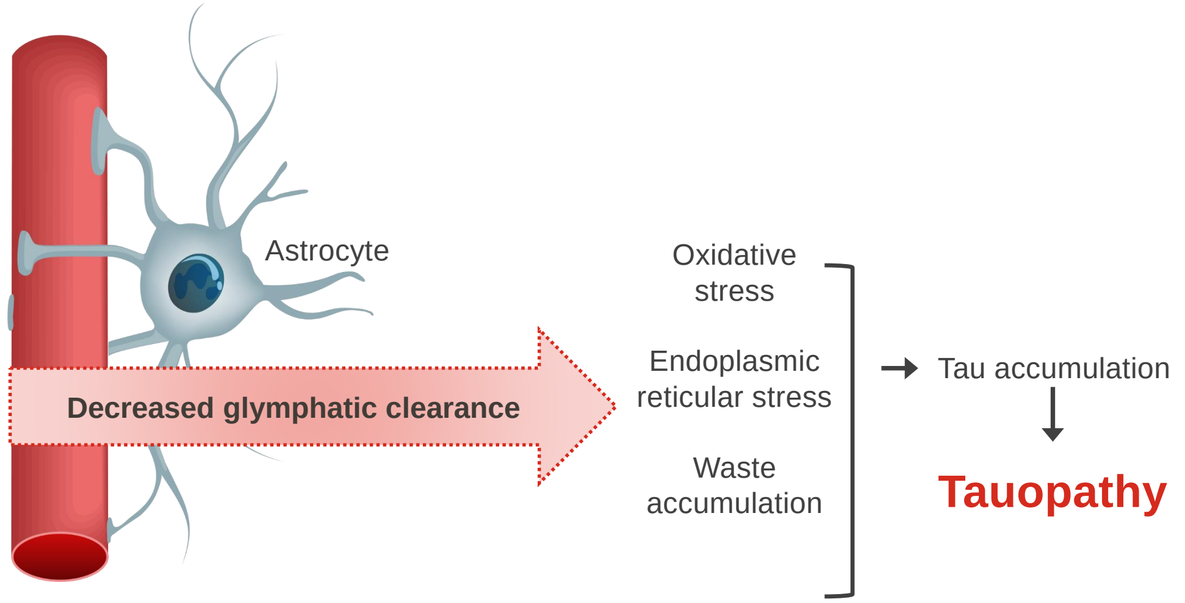
Normal Sleep

Increased intracellular ATP → Enhanced cellular repair mechanisms → **Decreased** inflammatory response → Enhanced cell survival



Sleep Deprivation

Decreased intracellular ATP → Inhibited cellular repair mechanisms → Increased inflammatory response → **Decreased** cell survival



ATP = adenosine triphosphate.

Lucke-Wold BP, et al. *Neurosci Biobehav Rev*. 2015;55:68-77.

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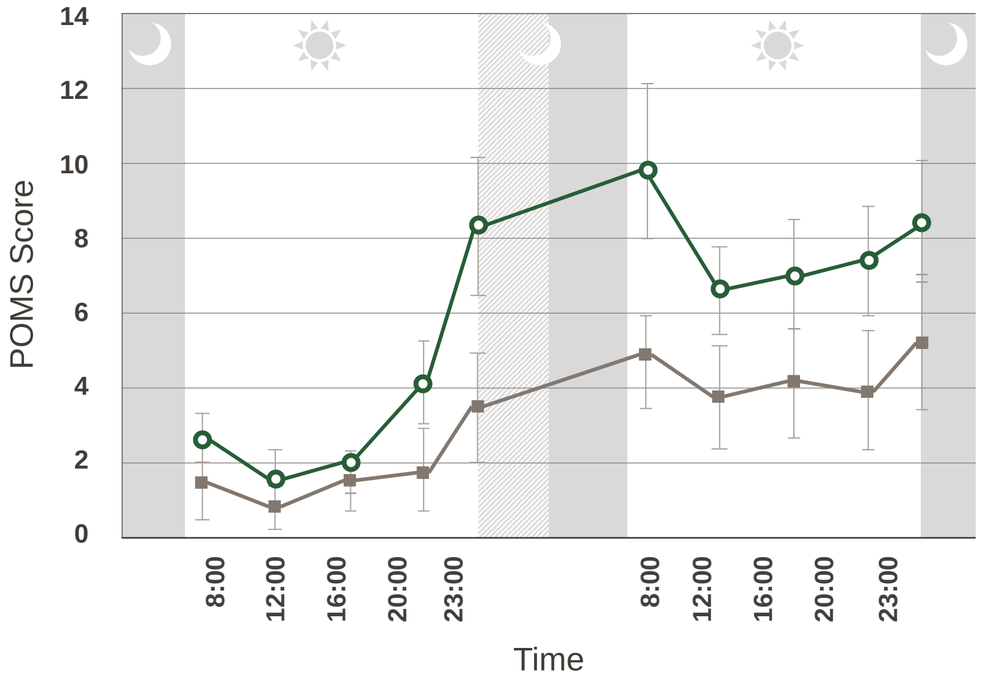
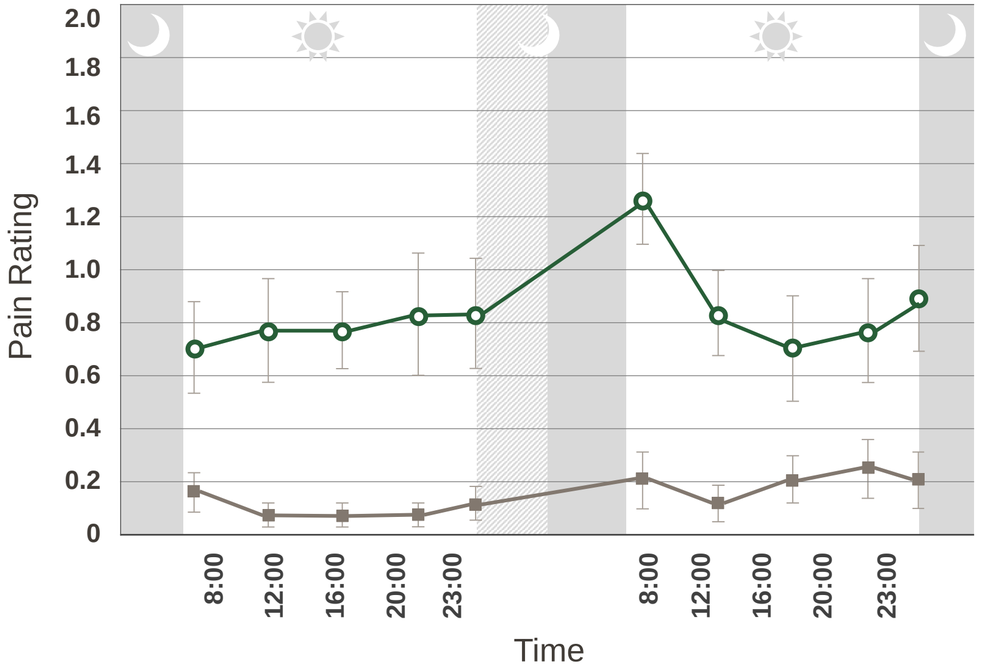
Sleep Deprivation Impacts Patients With RA More Than Controls

Effects of Partial Night Sleep Deprivation on Self-Reported Fatigue and Pain in Patients With RA

POMS Fatigue



McGill Pain Summary



Patients with RA (n=27)

Controls (n=27)

Sleep deprivation interval

POMS = Profile of Mood States.

Irwin MR, et al. *Sleep*. 2012;35(4):537-543.

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Nutrition
and Its Impact on Inflammation

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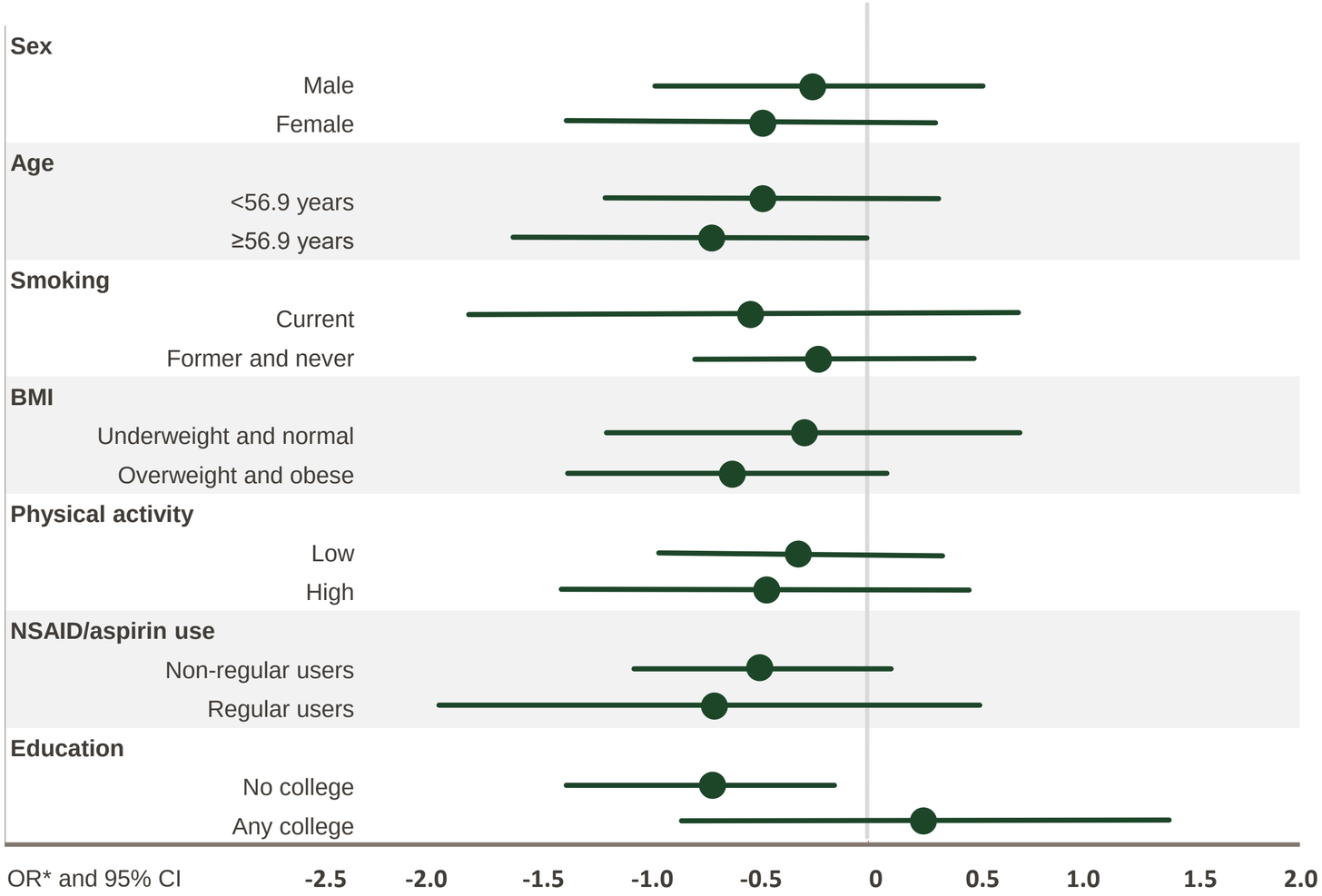
Mediterranean Diet and Inflammation

Associations of the Mediterranean Diet Scores With Plasma hsCRP Concentration



Data are from a pooled cross-sectional study of an elective outpatient colonoscopy population (N=646)

Diets that are Mediterranean-like may be associated with lower levels of systemic inflammation

*Transformed by natural logarithm.
CI = confidence interval; hsCRP = high-sensitivity C-reactive protein; NSAID = nonsteroidal anti-inflammatory drug; OR = odds ratio.
Whalen KA, et al. *J Nutr*. 2016;146(6):1217-1226.

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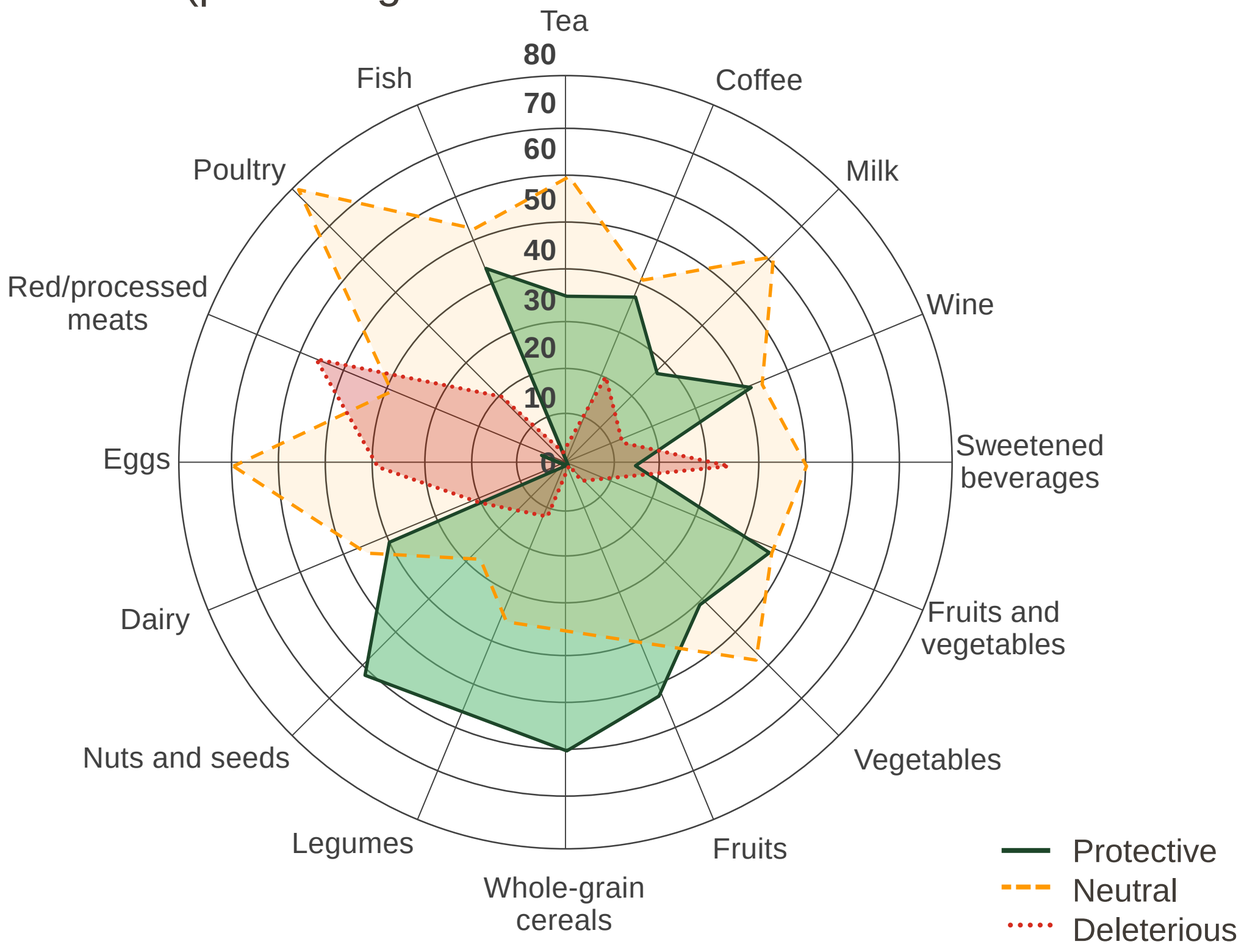
Are We What We Eat?

Radar Plots for Food Groups and Beverages vs Number of References (percentages from 0%-100% are shown on concentric circles)



Review of 304 studies examining the link between nutrition and **chronic disease** show that **plant food groups are more protective** than animal food groups against diet-related chronic diseases (obesity, type 2 diabetes, mental health disorders, skeletal disorders, cardiovascular diseases, and cancers)

Fardet A, et al. *Nutr Rev*. 2014;72(12):741-762.

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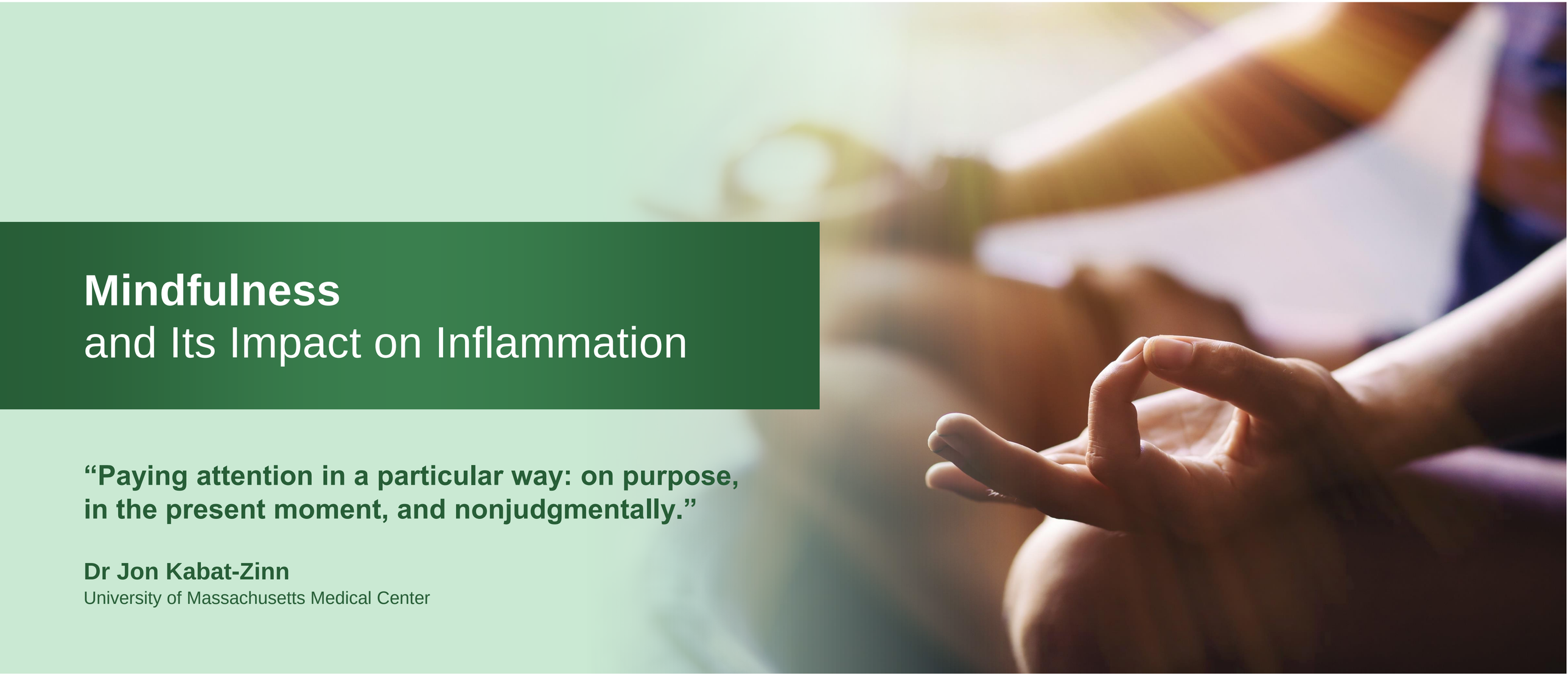
Mindfulness
and Its Impact on Inflammation



“Paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally.”

Dr Jon Kabat-Zinn
University of Massachusetts Medical Center

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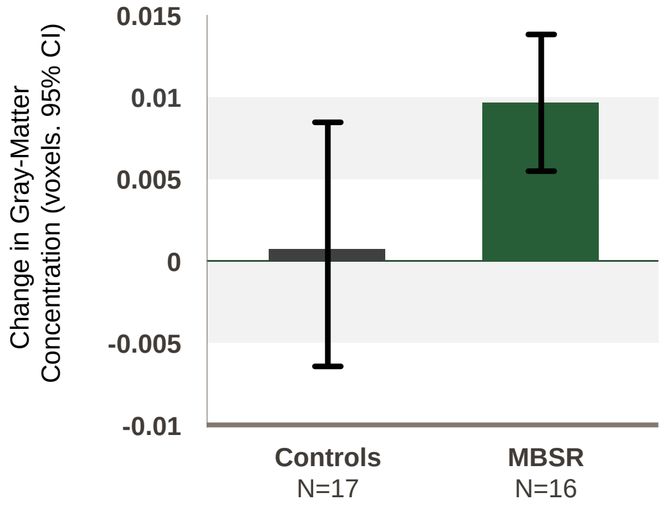
Volumetric Changes in the Hippocampus With 8 Weeks of Mindfulness-Based Therapy

Change in Gray-Matter Concentration in the Left Hippocampus



Participation in **mindfulness-based stress reduction (MBSR) was** associated with changes in gray-matter concentration in brain regions involved in learning and memory processes, emotion regulation, self-referential processing, and perspective taking

Hölzel BK, et al. *Psychiatry Res*. 2011;191(1):36-43.

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Meditative Practice and Therapeutic Benefits in Chronic Inflammatory Conditions

- Compared to meditation-naive participants (N=37), long-term meditators (N=31) had:
  - **Significantly lower** stress-evoked cortisol (*P*<.05), perceived stress (*P*<.01), and smaller neurogenic inflammatory response (*P*<.05)

- Long-term meditators also reported higher levels of psychological factors associated with well-being and resilience

Long-term meditation practice may reduce stress reactivity and have therapeutic benefit in chronic inflammatory conditions characterized by neurogenic inflammation

Rosenkranz MA, et al. *Psychoneuroendocrinol*. 2016;68:117-125.

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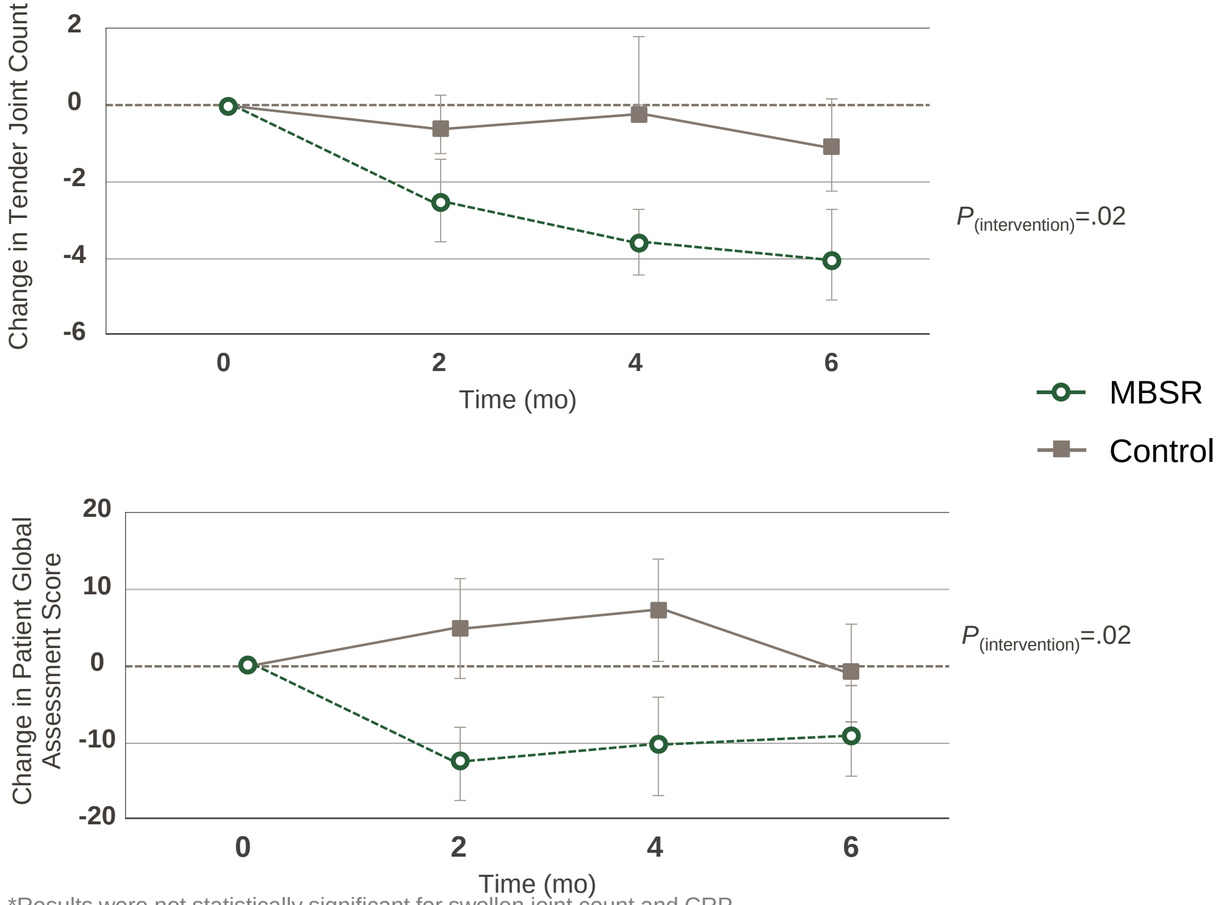
Mindfulness Can Positively Impact Disease Activity Measures in RA

Effect of Mindfulness-Based Stress Reduction (MBSR) on Disease Activity in Patients With RA



These results may offer clinicians preliminary evidence for the utility of mindfulness-based interventions in patients with RA to help reduce experienced disease activity (tender joints and patient global assessment)*

*Results were not statistically significant for swollen joint count and CRP.
CRP = C-reactive protein.
Fogarty FA, et al. *Ann Rheum Dis.* 2015;74(2):472-474.

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Social Connectedness
and Its Impact on Inflammation

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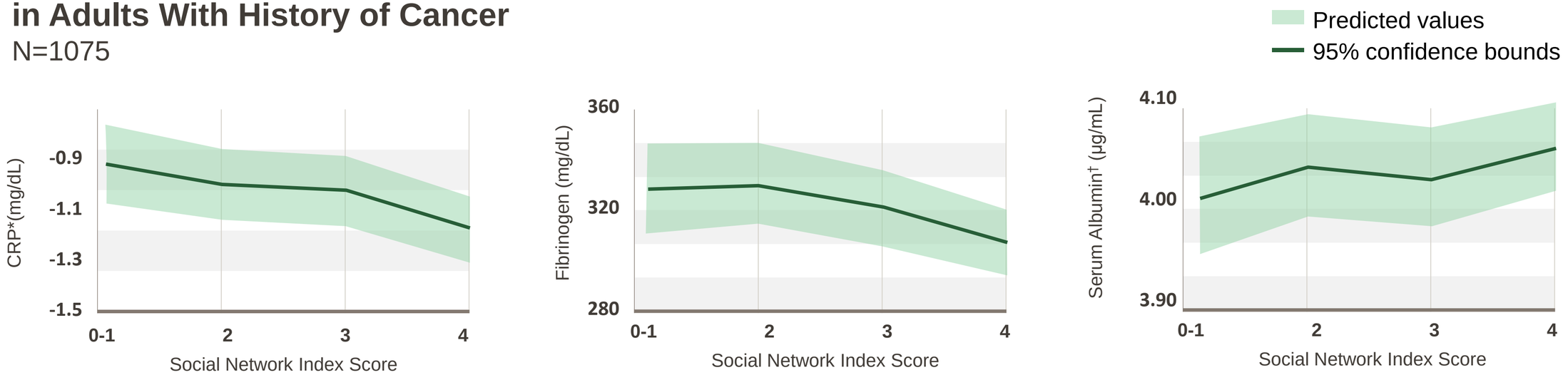
Social Network Ties and Inflammation

Predicted Values of Inflammatory Markers by Social Network Index Score in Adults With History of Cancer

N=1075



Lower Social Network Index scores were associated with greater inflammation marked by CRP (*P*=.028), fibrinogen (*P*=.038), and albumin‡

*Transformed by natural logarithm; †Higher albumin values indicate less albumin values; ‡ Not statistically significant.

Yang YC, et al. *Biodemography Soc Biol*. 2014;60(1):21-37.

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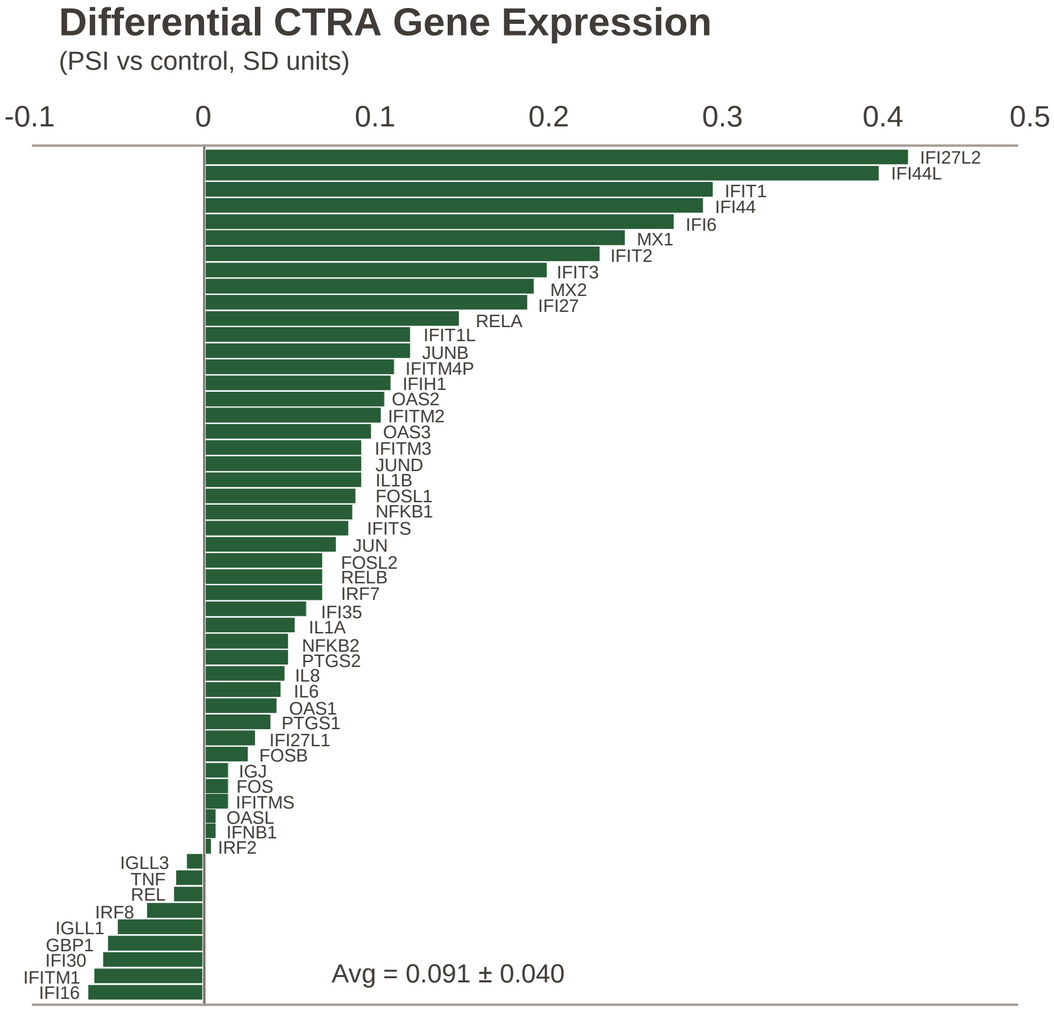
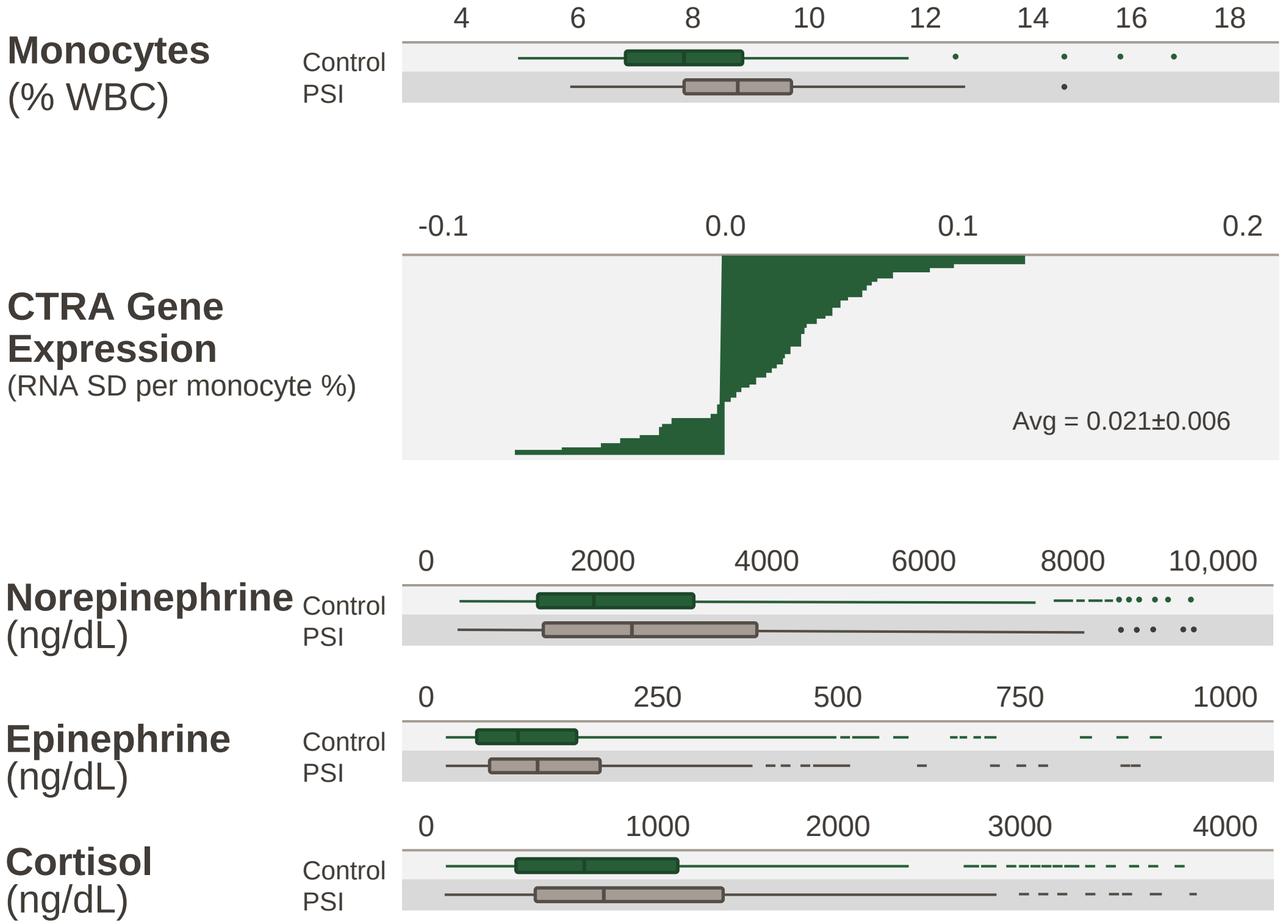
Effect of Loneliness and Social Isolation





CTRA = conserved transcriptional response to adversity; PSI = perceived social isolation; WBC = white blood cell.

Cole SW, et al. *Proc Natl Acad Sci USA.* 2015;112(49):15142-15147.

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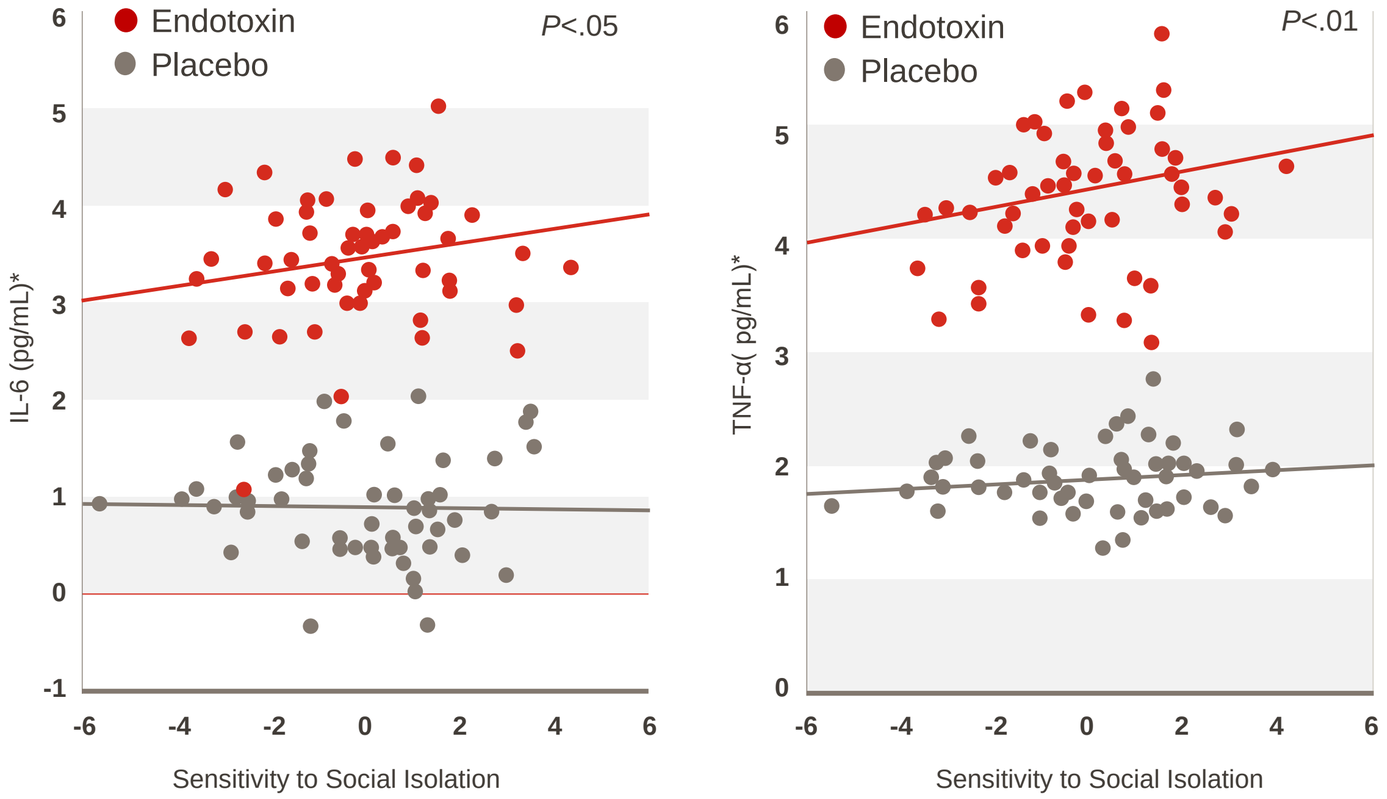
Social Isolation May Be Associated With Enhanced Inflammatory Response to Stress

Relationship Between Sensitivity to Social Disconnection and TNF-α or IL-6 Response to Endotoxin



Greater sensitivity to social isolation was related to more inflammation in response to endotoxin

This was found for both proinflammatory cytokines and multiple gene transcripts

*Cytokine values (pg/mL) transformed and plotted on a natural log scale.

Moieni M, et al. *Psychoneuroendocrinology*. 2015;62:336-342.

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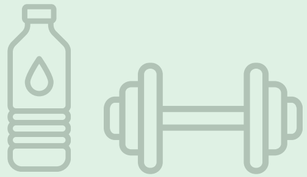
Anti-Inflammatory Wellness Behavior Examples

 Exercise	Exercise **30 minutes daily**; aim for at least **moderate** intensity
 Sleep	Implement **sleep hygiene** practices daily
 Nutrition	**Log** your daily meals/snacks/beverages/alcohol daily
 Mindfulness	Practice mindfulness for at least **8 minutes daily**
 Social Connectedness	**Call** a friend or family member daily

Jain S, et al. Presented at: 29th Annual US Psychiatric and Mental Health Congress; October 2016; San Antonio, Texas.

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Summary

Chapter Six

The 5 behaviors (exercise, sleep, nutrition, mindfulness, social connectedness) exert protective **anti-inflammatory effects**

Assessing and counseling on the lifestyle habits in wellness may be beneficial

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Backup Slide

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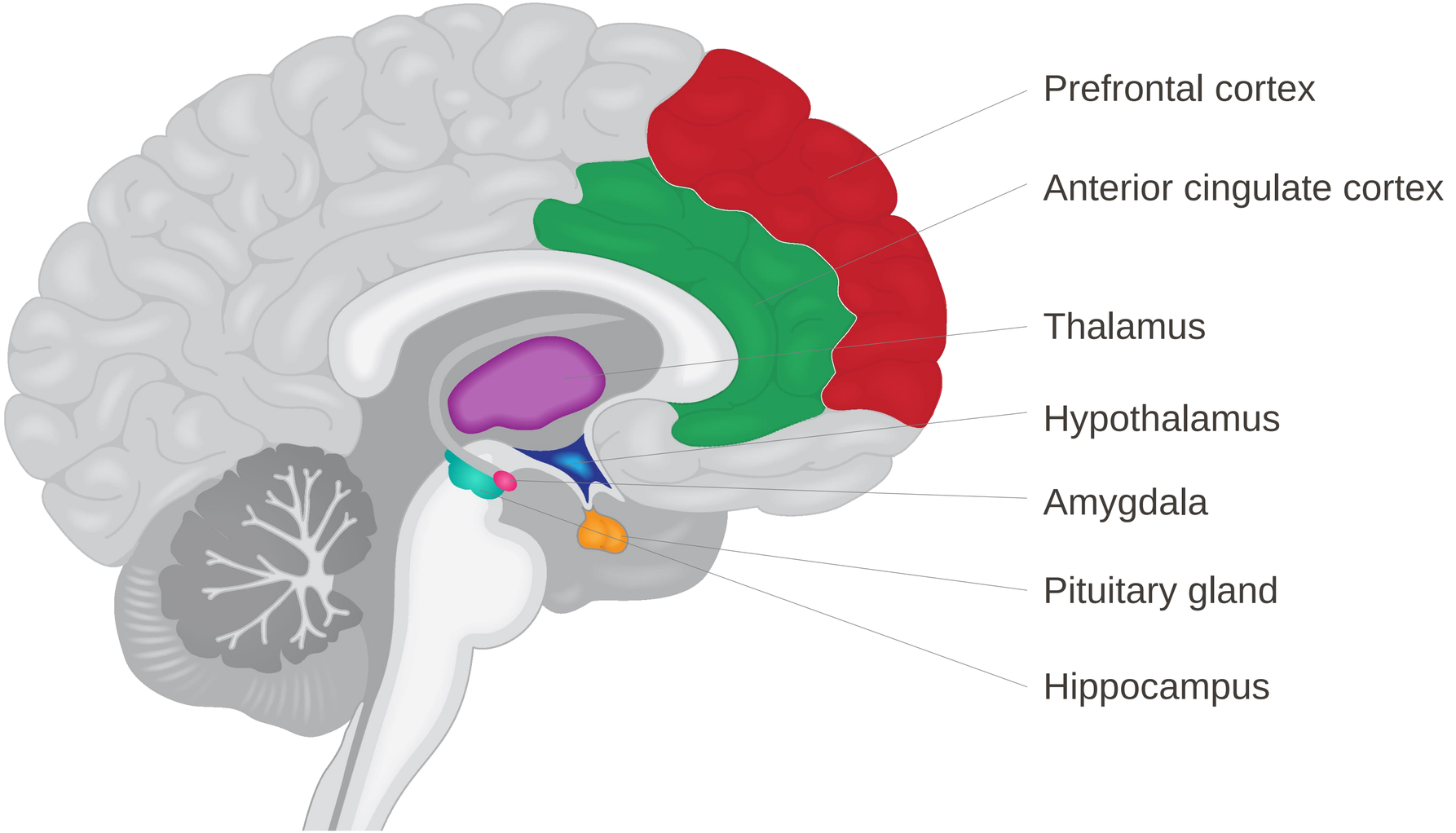
The Limbic System[1-7]



1. Siddiqui SV, et al. *Indian J Psychiatry*. 2008;50(3):202-208. 2. Szczepanski SM, et al. *Neuron*. 2014;83(5):1002-1018. 3. Roxo MR, et al. *Scientific World Journal.* 2011;11:2427-2440. 4. Zhu LJ, et al. *PLoS One.* 2014;9(5):e97689. 5. Cai D, et al. *Ann N Y Acad Sci*. 2011;1243:E1-E39. 6. Rovó Z, et al. *J Neurosci*. 2012;32(49):17894-17908. 7. Vertes RP, et al. *Neurosci Biobehav Rev*. 2015;54:89-107.

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assisted with the creation of this slide deck

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