Depression, Sleep, and Mindfulness through an Psycho-Neuro-Immunologic Lens

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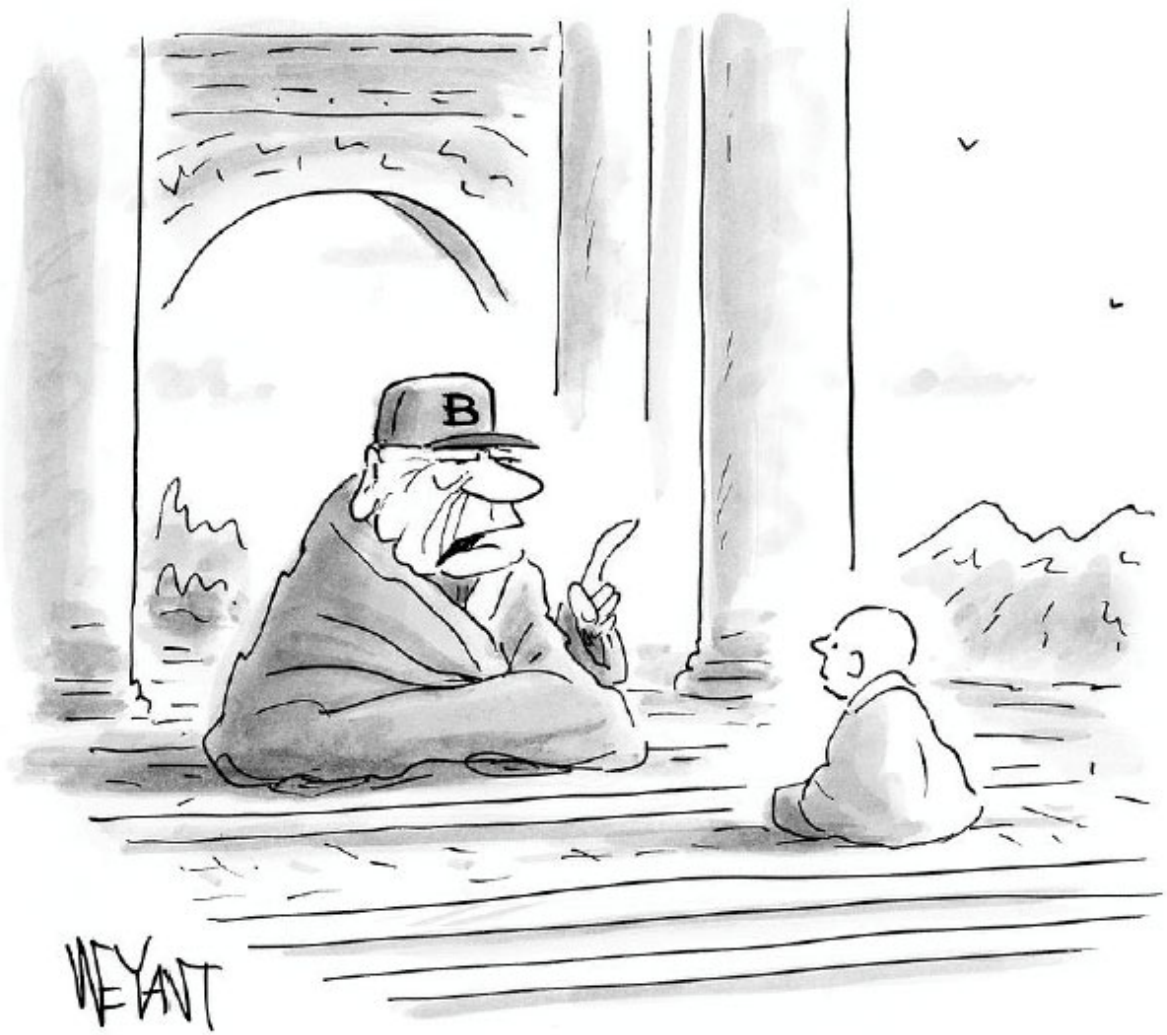
Evidence-Based Medicine

- Cited articles are noted on each slide
- No conflicts of interest and nothing to disclose



"A journey of a thousand miles begins with a single pitch."

Overview

- ***Depression and biobehavioral risk profiles***:

  defining sleep disturbance as a target for depression prevention

- ***Sleep disturbance and the inflammatory biotype of depression***:

  examining sleep regulation of inflammatory dynamics to refine clinical profiles and mechanisms of reward-based treatment of depression

- ***Innovative, mechanistically informed, and community based clinical trials***:

  testing efficacy of mindfulness treatments to optimize sleep health and reverse inflammation

Depression: public health significance

- #1 illness burden globally by 2030
- Depression leads to increased morbidity including cardiovascular disease and dementia
- Depression is associated with increased rates of mortality
- 20% prevalence rate, with two-fold higher rate in women

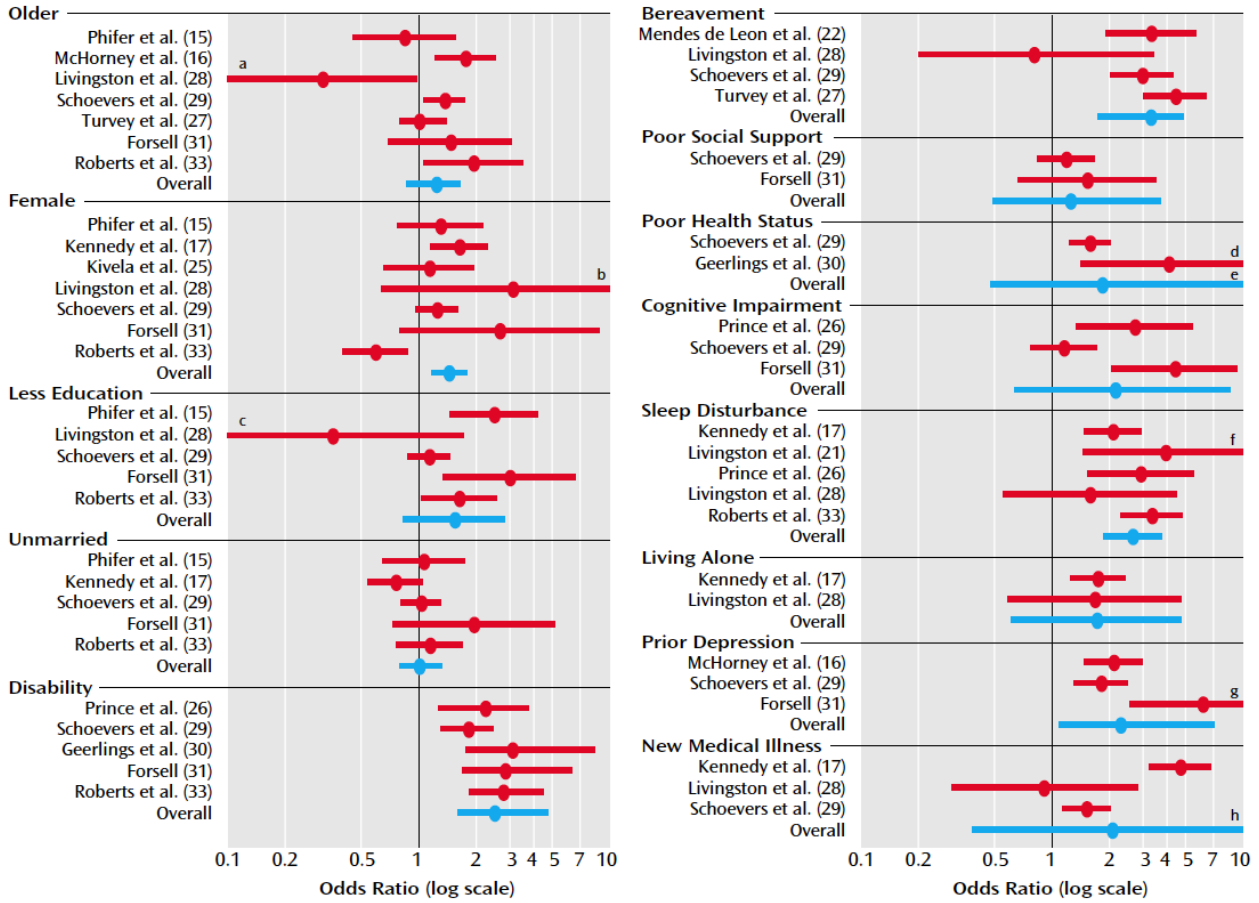
Novel strategies for monitoring risk, treatment, and prevention of depression are needed

- 75% lifetime rate of recurrence
- Only 30% of depressed patients achieve with remission with current treatments
- Identifying modifiable biobehavioral factors of greatest risk salience is needed to guide development of selective monitoring, and targeting depression prevention

Understanding the insomnia risk profile for depression to advance precision-based monitoring and prevention of depression.

What are the risk factors for depression?

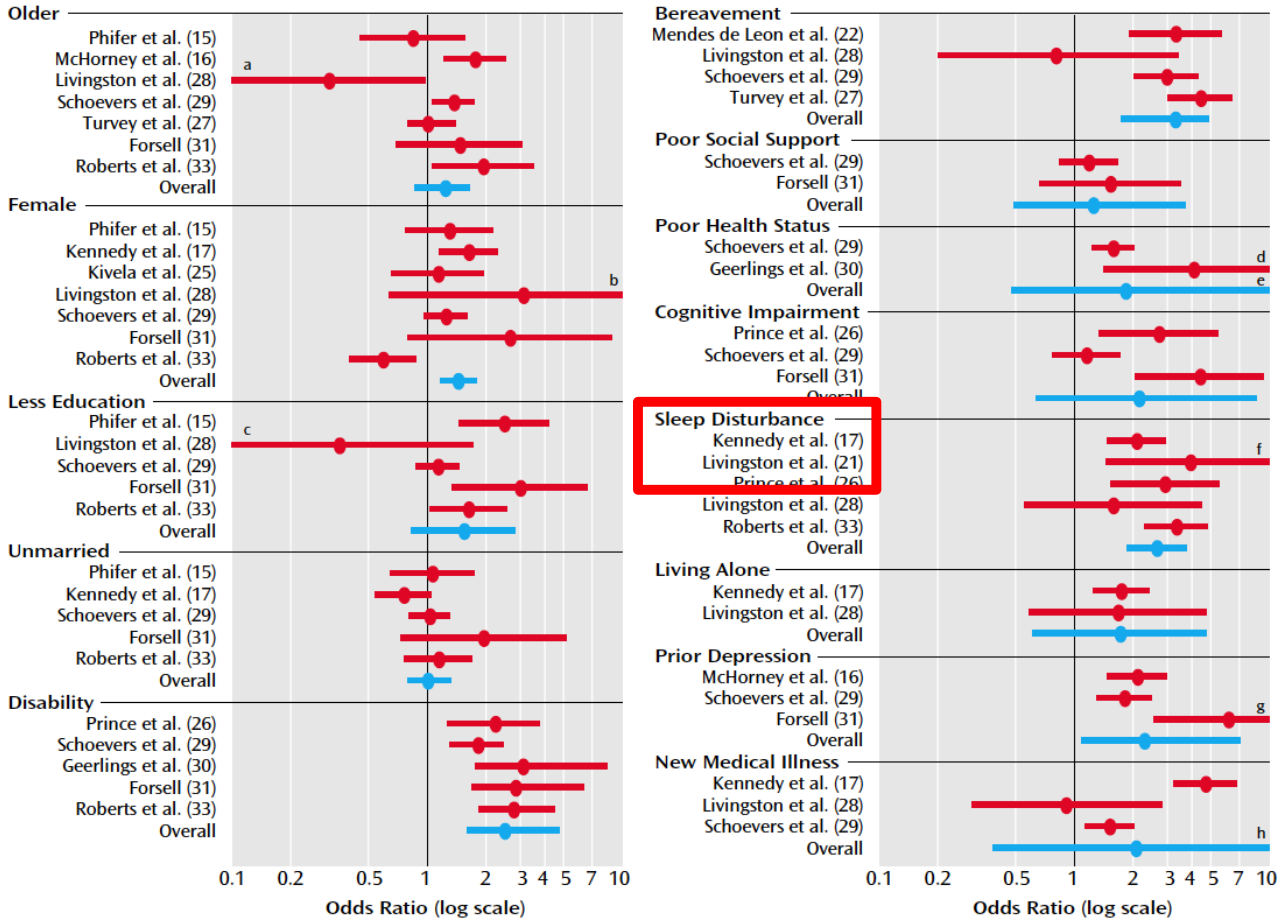
FIGURE 1. Individual and Combined Odds Ratios and 95% Credible Intervals in Prospective Studies of Risk Factors for Depression Among the Elderly



Am J Psychiatry 2003; 160:1147–1156

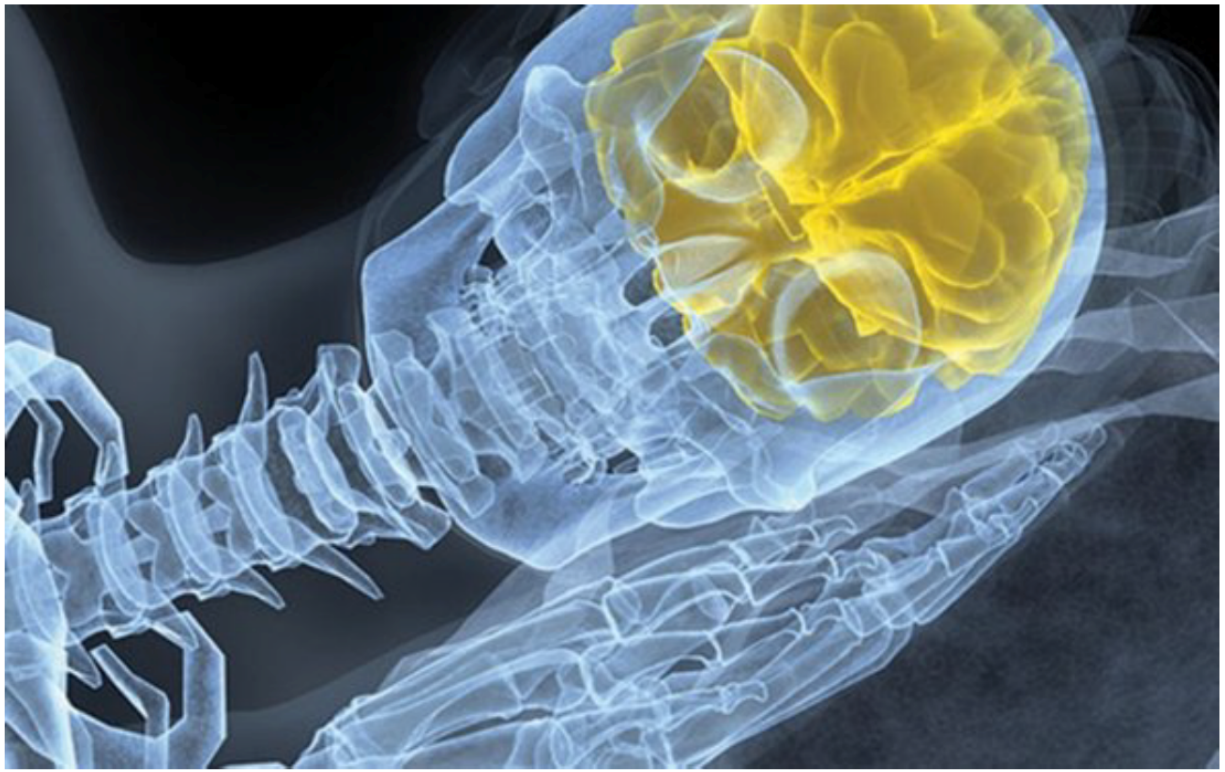
Sleep disturbance: a salient *modifiable* risk factor for depression

FIGURE 1. Individual and Combined Odds Ratios and 95% Credible Intervals in Prospective Studies of Risk Factors for Depression Among the Elderly



Am J Psychiatry 2003; 160:1147–1156

“….a heavy summon lies like lead upon me
And yet I would not sleep: merciful powers
Restrain in me the cursed thoughts that nature
Gives way to in repose” Macbeth, William Shakespeare




INSOMNIA JEOPARDY
WAYS IN WHICH PEOPLE HAVE WRONGED ME
STRANGE NOISES
DISEASES I PROBABLY HAVE
MONEY TROUBLES
WHY DID I SAY/DO THAT?
IDEAS FOR A SCREENPLAY
$10 $10 $10 $10 $10 $10
$20 $20 $20 $20 $20 $20
$30 $30 $30 $30 $30 $30
$40 $40 $40 $40 $40 $40
$50 $50 $50 $50 $50 $50
R. Chast

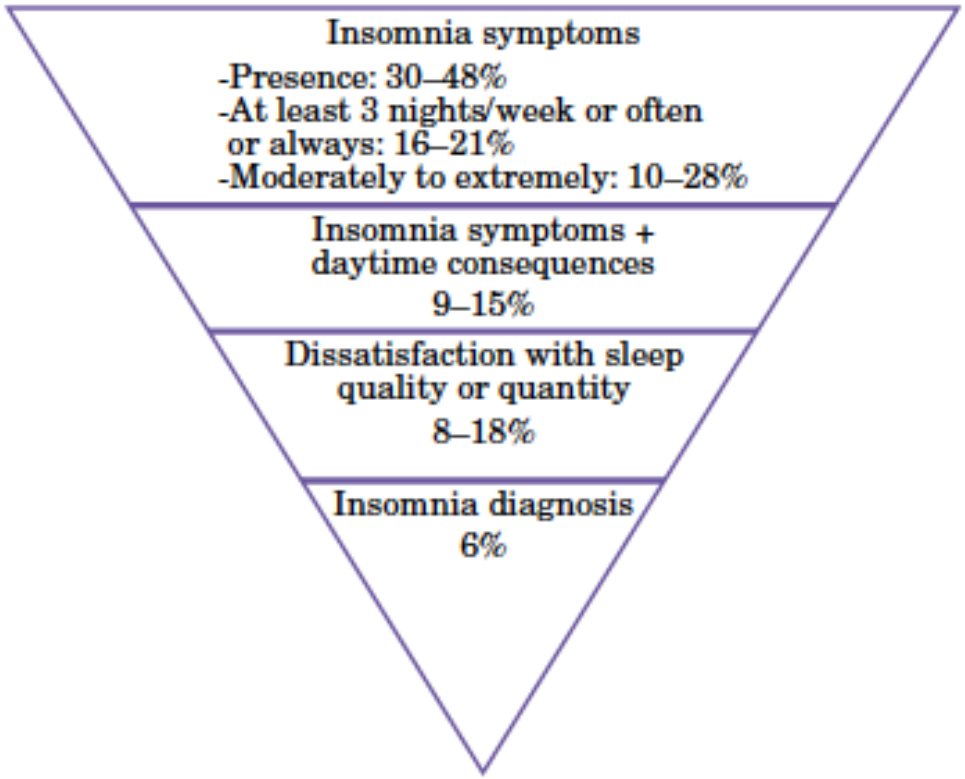
Insomnia Disorder

Diagnostic Criteria

A. A predominant complaint of dissatisfaction with sleep quantity or quality, associated with one (or more) of the following symptoms:
   1. Difficulty initiating sleep. (In children, this may manifest as difficulty initiating sleep without caregiver intervention).
   2. Difficulty maintaining sleep, characterized by frequent awakenings or problems returning to sleep after awakenings. (In children, this may manifest as difficulty returning to sleep without caregiver intervention.)
   3. Early-morning awakening with inability to return to sleep.

B. The sleep disturbance causes clinically significant distress or impairment in social, occupational, educational, academic, behavioral, or other important areas of functioning.
C. The sleep difficulty occurs at least 3 nights per week.
D. The sleep difficulty is present for at least 3 months.
E. The sleep difficulty occurs despite adequate opportunity for sleep.
F. The insomnia is not better explained by and does not occur exclusively during the course of another sleep-wake disorder (e.g., narcolepsy, a breathing-related sleep disorder, a circadian rhythm sleep-wake disorder, a parasomnia).
G. The insomnia is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication).
H. Coexisting mental disorders and medical conditions do not adequately explain the predominant complaint of insomnia.

Over 60% of older adults report sleep disturbance



SLEEP MEDICINE reviews

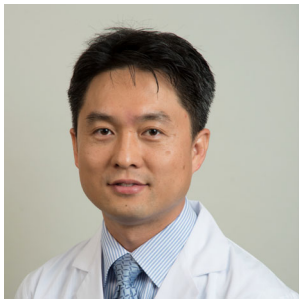
Sleep Medicine Reviews, Vol. 6, No. 2, pp 97–111, 2002

Insomnia is co-morbid with depression

- Insomnia is among the most frequent sleep disturbance in depressed patients
- Sleep disturbance is viewed as a symptomatic dimension of current depression
- Sleep disturbance often lingers and its persistence can represent a residual phase of major mood disorder

Is insomnia a prodromal symptom of depression, or a risk factor that might be targeted for depression prevention?

Self-reported sleep disturbance in non-depressed older adults predicts a 3-fold greater risk of major depression



Article

Sleep Disturbance and Depression Recurrence in Community-Dwelling Older Adults: A Prospective Study

- 2-year prospective study
- 351 community dwelling adults older than 60 years of age
  - 145 with a history of depression
  - 206 without a lifetime history of depression
- DSM-IV diagnosis of depressive episodes

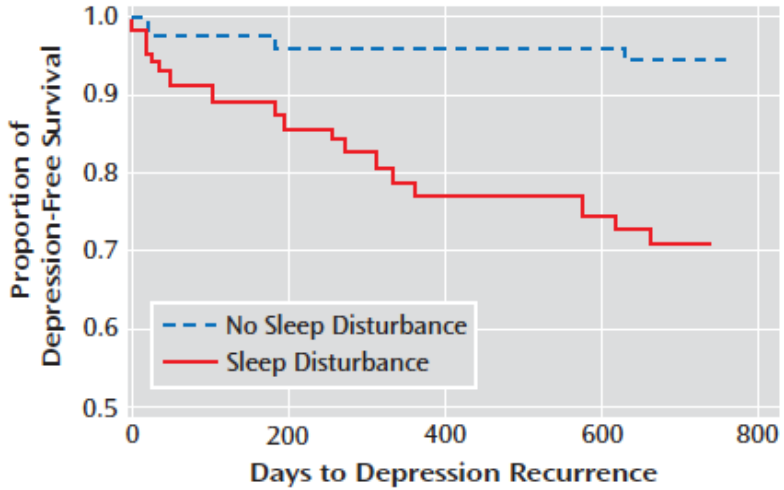
Am J Psychiatry 165:12, December 2008

TABLE 2. Baseline Predictors of Depressive Disorders During Follow-Up

Baseline Predictor	Adjusted Odds Ratio[a]	95% CI	p
Group status (comparison versus prior depression)	38.65	4.72–316.43	0.001
Sleep disturbance (no versus yes)	3.05	1.07–8.75	0.04
Depressive symptoms (Beck Depression Inventory without the sleep item)	1.19	1.07–1.33	0.002
Medical disease (Chronic Disease Score)	1.00	0.80–1.24	0.98
Age (years)	1.00	0.93–1.08	0.10
Gender (male versus female)	0.55	0.20–1.49	0.24
Marital status (married versus nonmarried)	2.00	0.77–5.18	0.16
Education (years)	0.83	0.66–1.04	0.10

[a] Adjusted for all other variables in the table.

FIGURE 1. Time to Depression for Older Adults With a Prior Depression History According to Sleep Disturbance at Baseline



Persistent sleep disturbance over one year in non-depressed older adults predicts a 16-fold greater risk of major depression over following year

Table 3—Predictors of depression recurrence during year 2

Predictors	Adjusted hazard ratio[a,b] (95% CI)	P
Persistent sleep disturbance	16.05 (1.21-213.06)	0.04
Intermittent sleep disturbance	5.61 (0.47-66.96)	0.17
Age[c]	0.84 (0.74-0.96)	0.01
Sex	0.70 (0.19-2.60)	0.59
Marital status[d]	12.24 (1.83-82.08)	0.01
Education[e]	0.55 (0.38-0.79)	0.001
Chronic medical burden	1.00 (0.70-1.44)	0.99
Depressive symptoms[f]	0.81 (0.67-0.97)	0.02
Use of antidepressant medications[g]	5.01 (1.39-18.07)	0.01
Use of sedative-hypnotic medications	1.32 (0.28-6.15)	0.72
Depression group status[h]	6.74 (0.80-56.83)	0.08

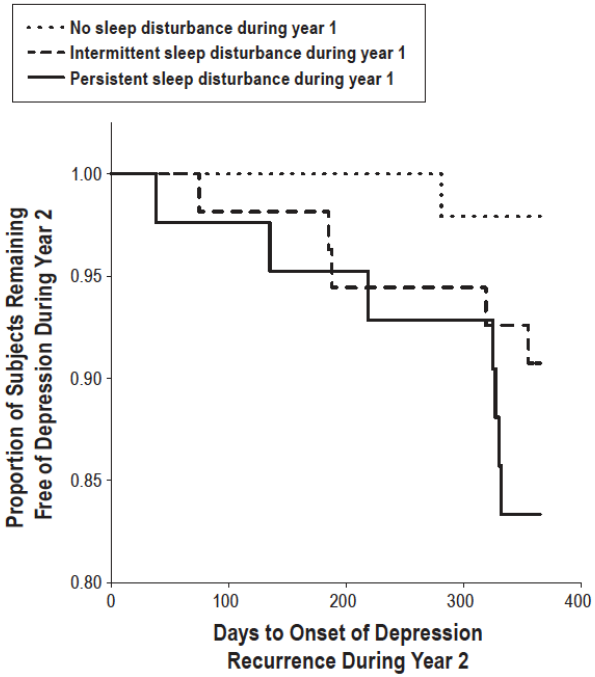


Figure 2—Time to onset of depression recurrence during year 2 stratified by sleep disturbance during year 1.

Citation: Lee E; Cho HJ; Olmstead R; Levin MJ; Oxman MN; Irwin MR. Persistent sleep disturbance: a risk factor for persistent or recurrent depression in community-dwelling older adults. *SLEEP* 2013;36(11):1685-1691.

A two-hit model of depression: the combined impact of insomnia and inflammation

- Inflammation is a risk factor depression.
- Patients with an inflammatory disorder show a 2-4 fold greater prevalence of depression.
- Similarly, patients with an inflammatory disorder show an over 3-fold greater prevalence of insomnia.

Do insomnia and inflammation interact to increase risk of depression?

Sleep disturbance in HIV infected men who have elevated rates of inflammation leads to a 2-fold greater risk of depression than either sleep disturbance or HIV status alone

EBioMedicine
Published by THE LANCET

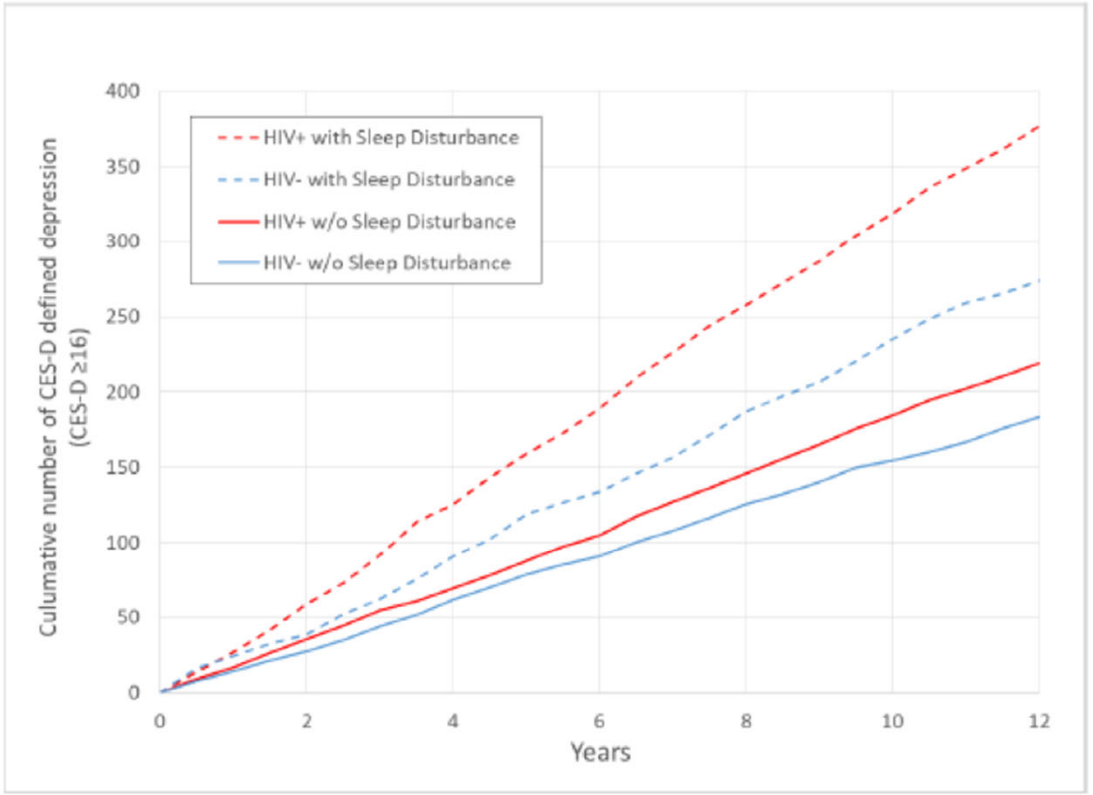
- Multicenter AIDS Cohort Study, a population-based prospective study of men who have sex with men
- Sample:
  - HIV+(N=1054; 9,556 person-visits)
  - HIV- (N=1217; 12,680 person-visits)
- Assessments:
  - Every 6 months over 12 years
  - Self-reported sleep disturbance (>2 weeks)
  - Depression defined by Clinical Epidemiologic Scale for Depression >16
- Analyses:
  - Logistic regression tested whether sleep disturbance predicted depression (CES-D$\geq$16) at the immediate subsequent visit, and so on over 12 years
  - Linearly estimated average incidence of depression and normalized cumulative rate of depression over 12 years

EBioMedicine 36 (2018) 454–460

Sleep disturbance in HIV infected men who have elevated rates of inflammation leads to a nearly 2-fold greater risk of depression than either sleep disturbance or HIV status alone

Incidence per 100 subjects:

HIV+ with sleep disturbance, 31.8 per year (95% CI: 31.6-32.0)
HIV+ w/o sleep disturbance, 18.2 per year (95% CI: 18.1-18.4)
HIV- with sleep disturbance, 23.1 (95% CI: 22.8-23.3)
HIV- w/o sleep disturbance, 15.4 (95% 15.3 – 15.5)



EBioMedicine 36 (2018) 454–460

Insomnia and regulation of affective mechanisms

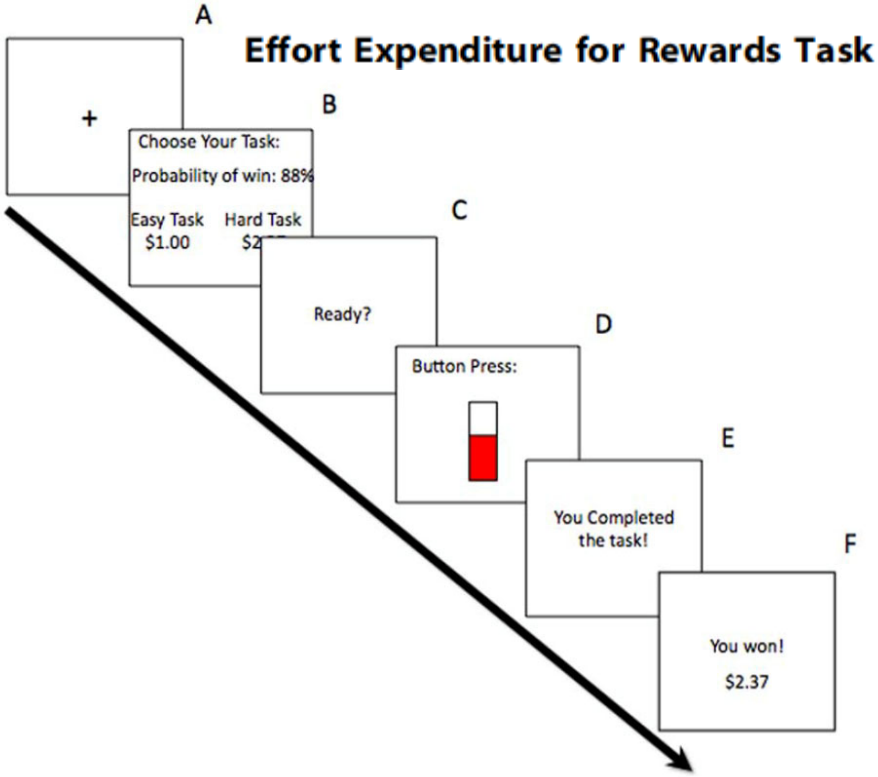
Reward or anhedonia

- Reduced motivation for reward (i.e., reduced “wanting”)
- Reduced sensitivity for reward (i.e., reduced “liking”)
- Reward prospectively predicts depressive symptoms, suicide risk, and depressive episodes

Facial emotion perception

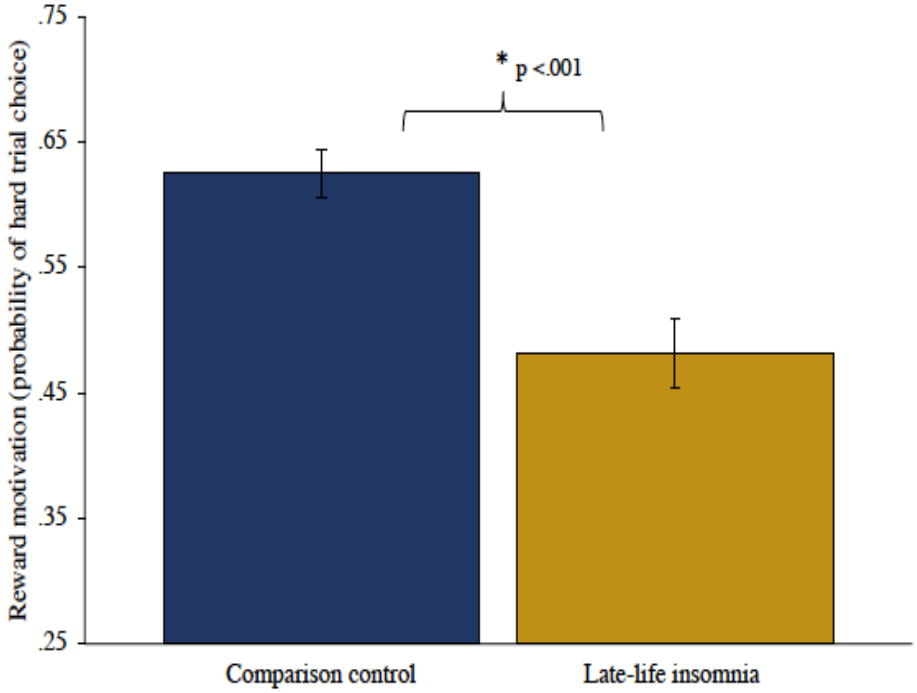
- Sensory ability to detect and discriminate salient emotional information from facial expressions
- Impaired in depressed patients: delay in the ability to recognize sad faces

Insomnia blunts motivation and sensitivity to monetary reward, especially in men and those with inflammation

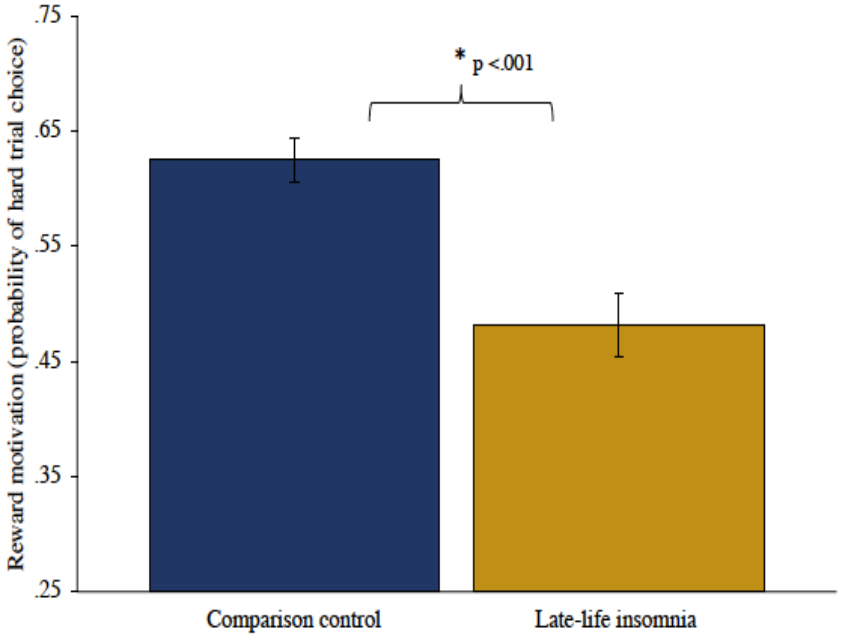


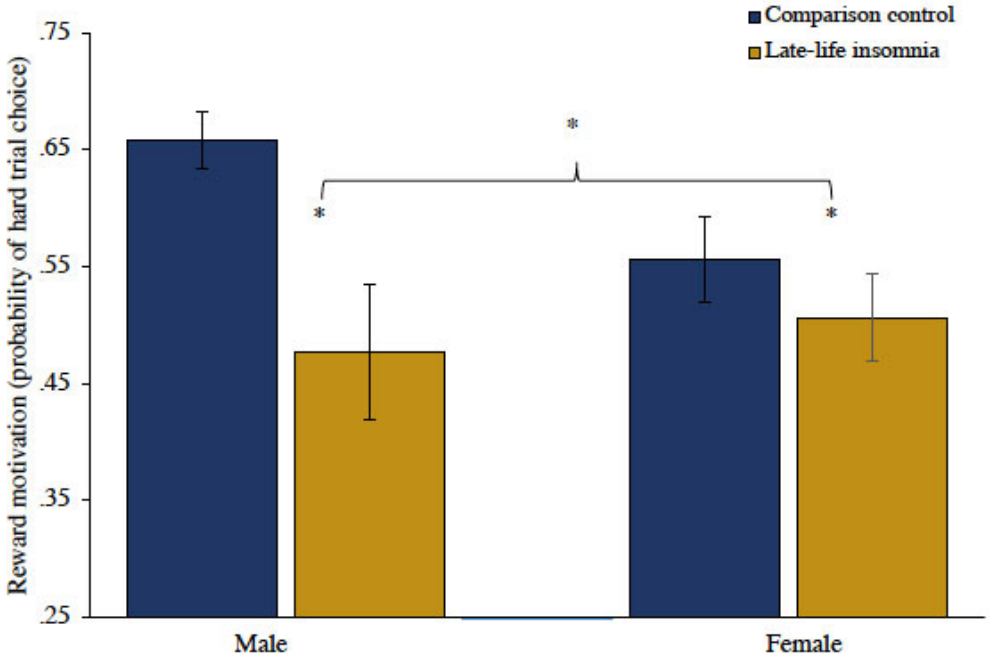
- Community dwelling older adults (n=103; aged 60-80)
  - Insomnia (n=31)
  - Comparison controls (n=72)
- Behavioral reward task, EEfRT
- Systemic inflammation: C-reactive protein.

Insomnia blunts motivation and sensitivity to monetary reward



Insomnia blunts motivation and sensitivity to monetary reward, *especially in men*





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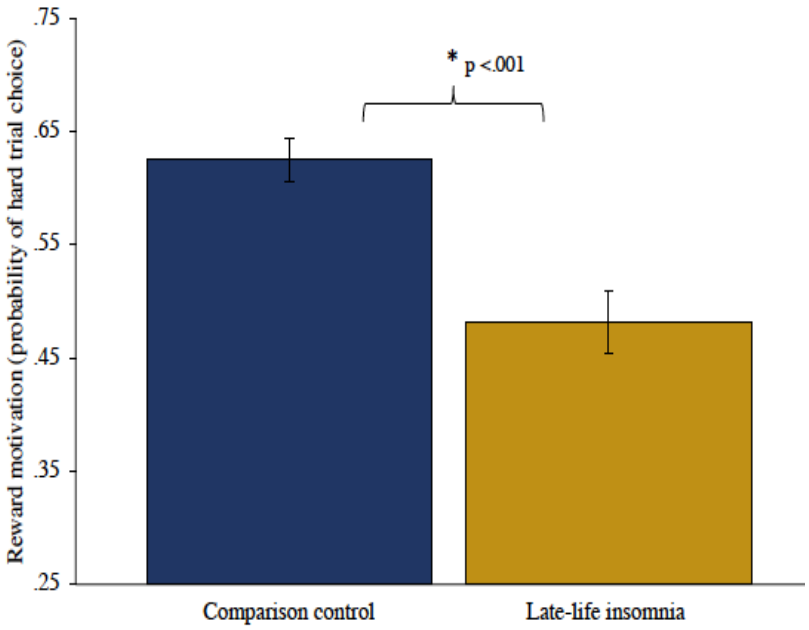
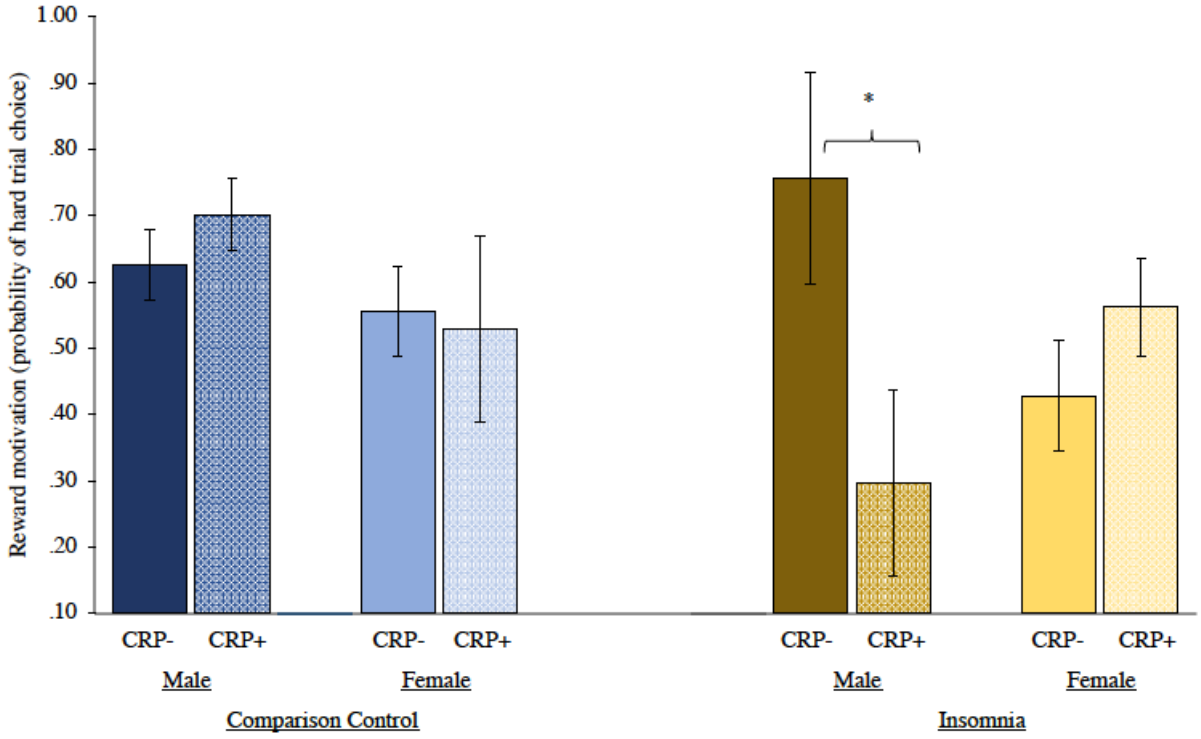
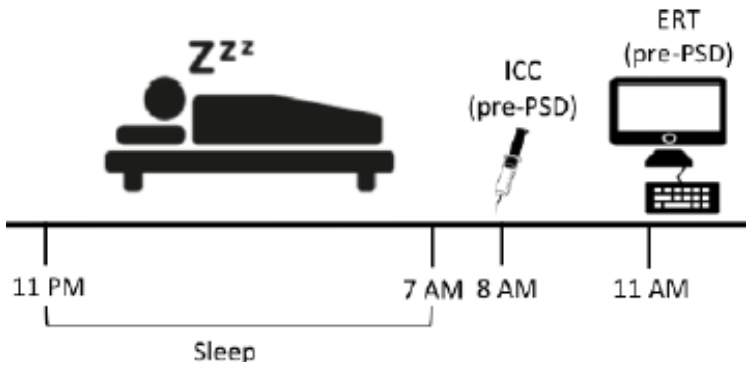


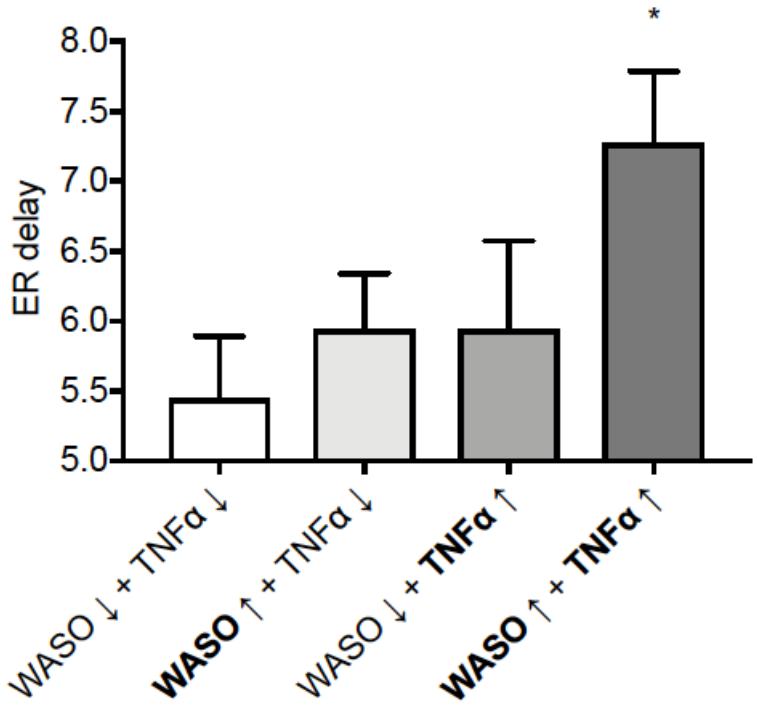


Disturbance in sleep continuity and inflammation interact to predict impaired facial emotion perception

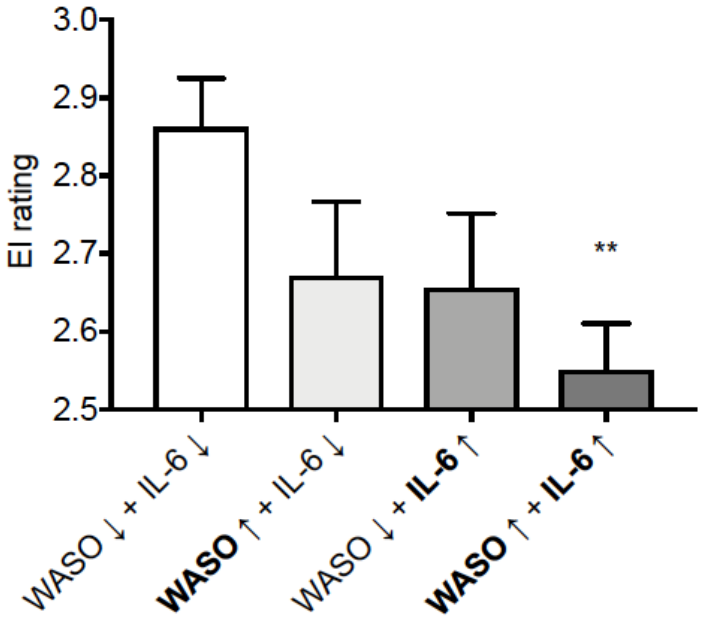


- Older adults (N=39, 71.7±6.8y, 56.4% female)
- Assessment of sleep continuity by polysomnography
- Morning assessment of systemic inflammation (interleukin-6 and tumor necrosis factor alpha)
- Exposure to three facial emotional stimuli (sad, happy, angry) for each task
- Exposure in two tasks: emotion recognition (ER) and perceived emotion intensity (EI)

Disturbance in sleep continuity and inflammation interact to predict impaired recognition of sad facial emotion



Disturbance in sleep continuity and inflammation interact to predict impaired perception of sad facial emotion



“Slumber……the chief nourisher in life's feast”

William Shakespeare

What are the pathways linking sleep disturbance and depression risk?

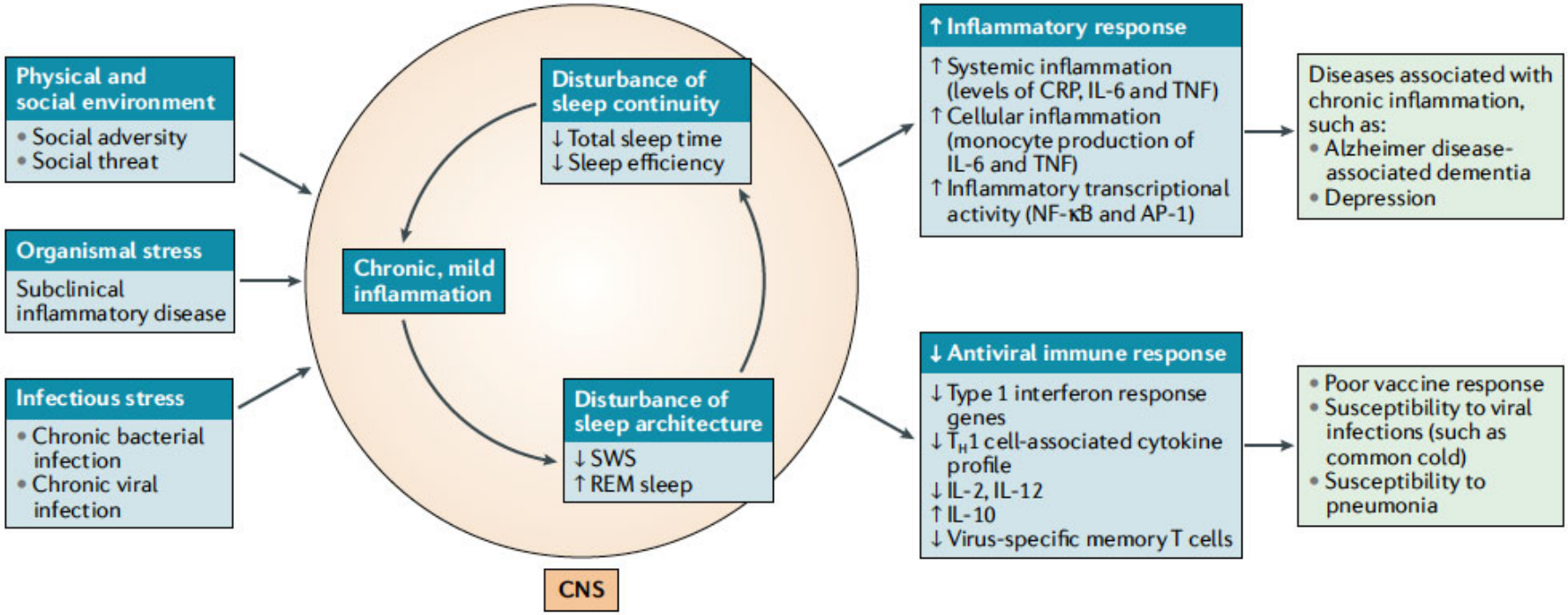
Does sleep disturbance activate inflammatory mechanisms?

Interrogating the role of sleep in the regulation of inflammatory dynamics

NATURE REVIEWS | IMMUNOLOGY

Sleep and inflammation: partners in sickness and in health

Michael R. Irwin



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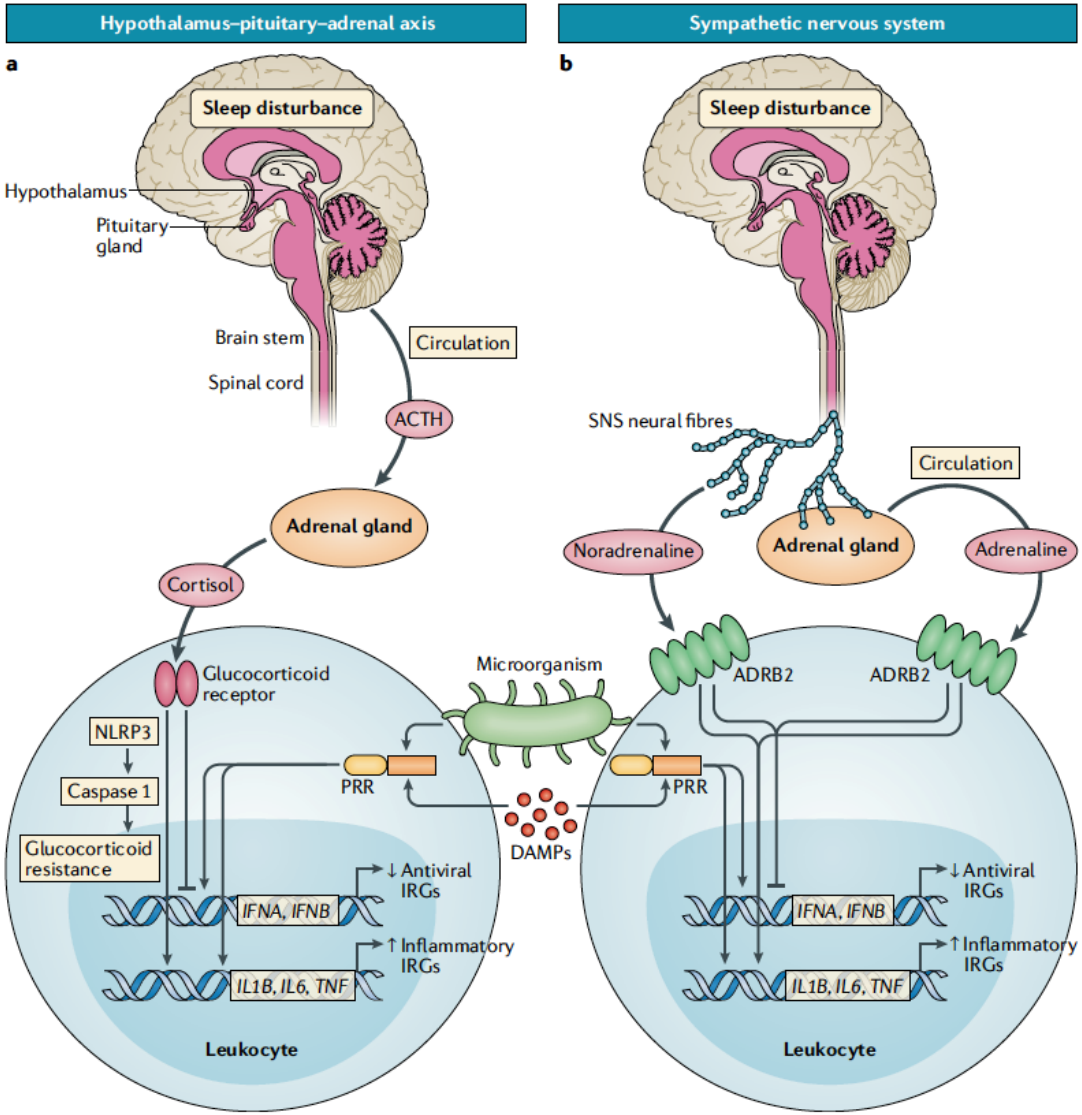


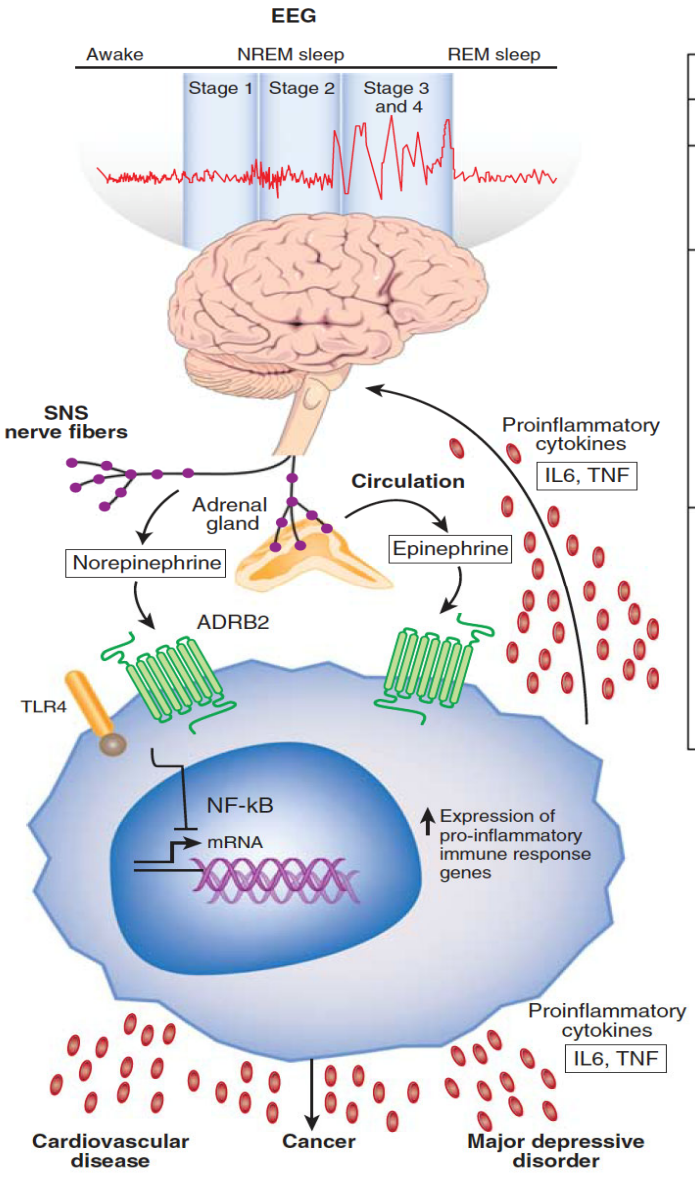


Table 1: Vertically Integrated Comprehensive Assessment of Inflammation/Immune Activation

Level	Source	Assay Type	Outcome
Systemic	Serum, plasma, OMT, CSF	Immunoassay (ELISA, Luminex)	Circulating concentrations of pro-inflammatory (e.g., IL6, IL8, TNF), anti-inflammatory cytokines; other biomarkers of immune activation
Cellular	WBC, PBMC, cell subsets (lymphocytes, monocytes)	Flow cytometry	Number and % of cell population of interest; activation status
		TLR-4 activation	% Monocytes secreting IL6 and/or TNF (in vitro capacity to respond to inflammatory challenge by LPS)
		STAT signaling	Quantitation of transcription factor signaling
	PBMC extracts	NFκB signaling	Quantitation of pro-inflammatory signaling
		Telomerase	Quantitation of telomerase enzyme activity
Molecular/ Genomic	RNA extracts, (PBMC or cell subsets)	Genome-wide gene expression	Bioinformatic analyses of patterns of pro- and anti-inflammatory gene expression; evaluation of senescence-associated secretory phenotype (SASP)
	DNA (WBC, PBMC)	Telomere length	Quantitation of telomere length
		SNP	DNA polymorphisms in inflammation-related and other genes
		DNA methylation	Bioinformatic analyses of biologic age

Irwin Ann Rev Psychol 2015

Michael R Irwin*,1 and Mark R Opp2

Neuropsychopharmacology REVIEWS (2017) 42, 129–155

Archival Report

Biological Psychiatry

Sleep Disturbance, Sleep Duration, and Inflammation: A Systematic Review and Meta-Analysis of Cohort Studies and Experimental Sleep Deprivation

Michael R. Irwin, Richard Olmstead, and Judith E. Carroll

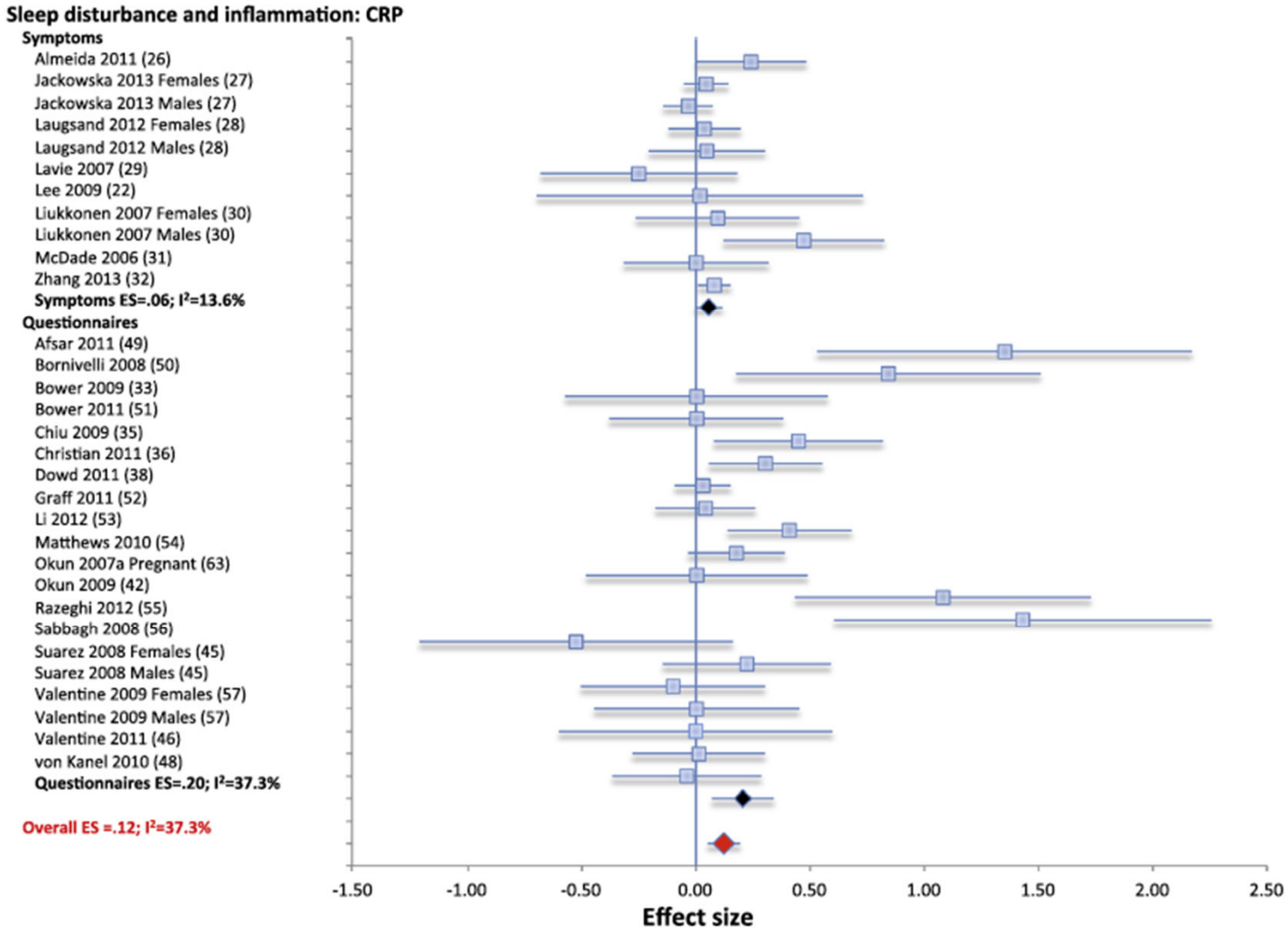
Sample: 72 studies (n > 50,000)

Measures:

C-reactive protein, interleukin-6, and tumor necrosis factor alpha

Sleep disturbance: self-reported items, questionnaires, diagnosis

Sleep duration: long (>8 h) and short (<7 h), self report, actigraphy



Irwin et al, Biol Psychiatry 2015

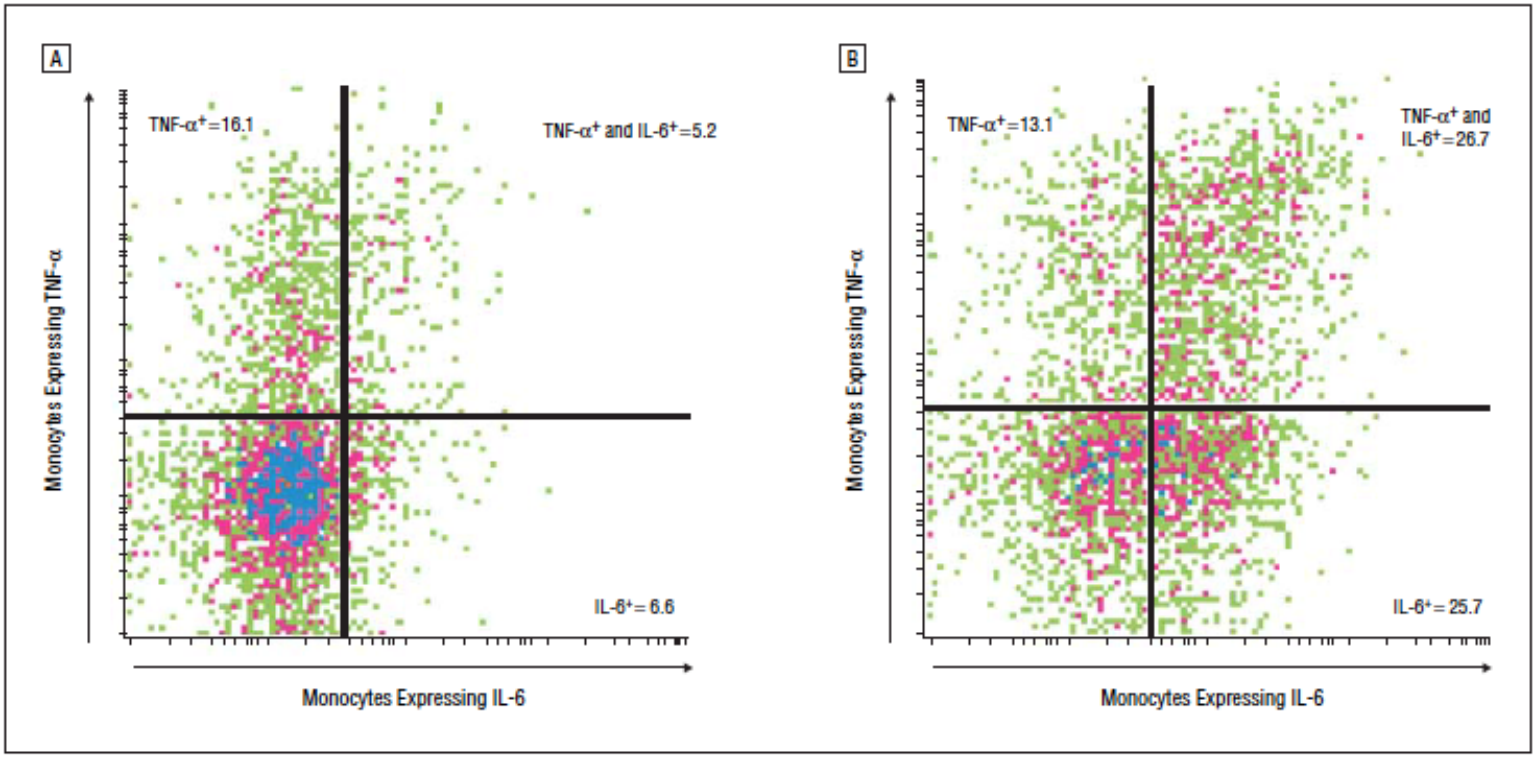
ORIGINAL INVESTIGATION

Sleep Deprivation and Activation of Morning Levels of Cellular and Genomic Markers of Inflammation

Michael R. Irwin, MD; Minge Wang, MSN; Capella O. Campomayor, MS; Alicia Collado-Hidalgo, PhD; Steve Cole, PhD

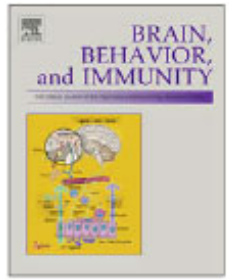
Uninterrupted sleep: 11 p.m. to 7 a.m.

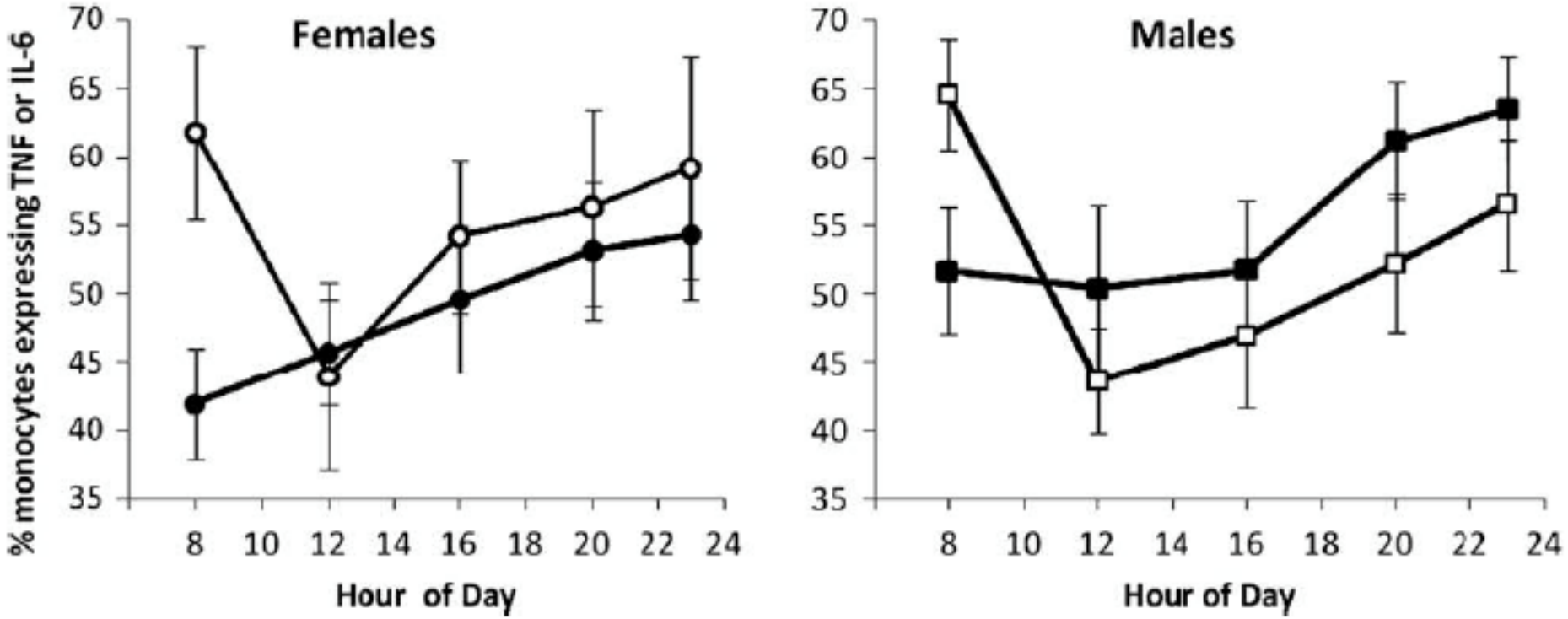
Sleep deprivation: 11 p.m. to 3 a.m.



Arch Intern Med. 2006;166:1756

Sleep loss activates cellular markers of inflammation: Sex differences





Sleep Loss Activates Cellular Inflammatory Signaling

Biological Psychiatry

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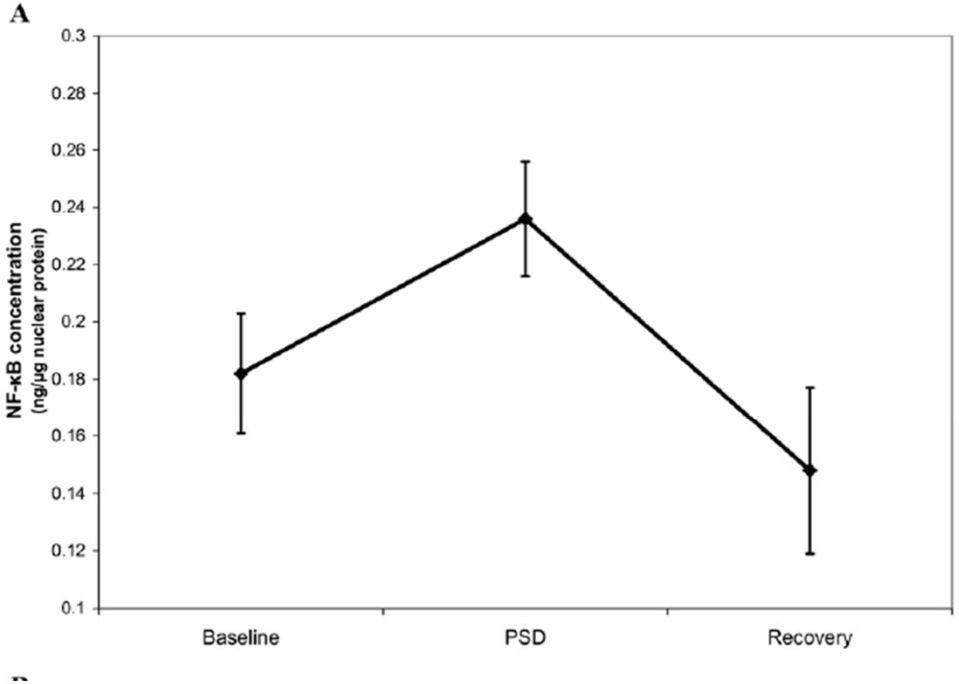
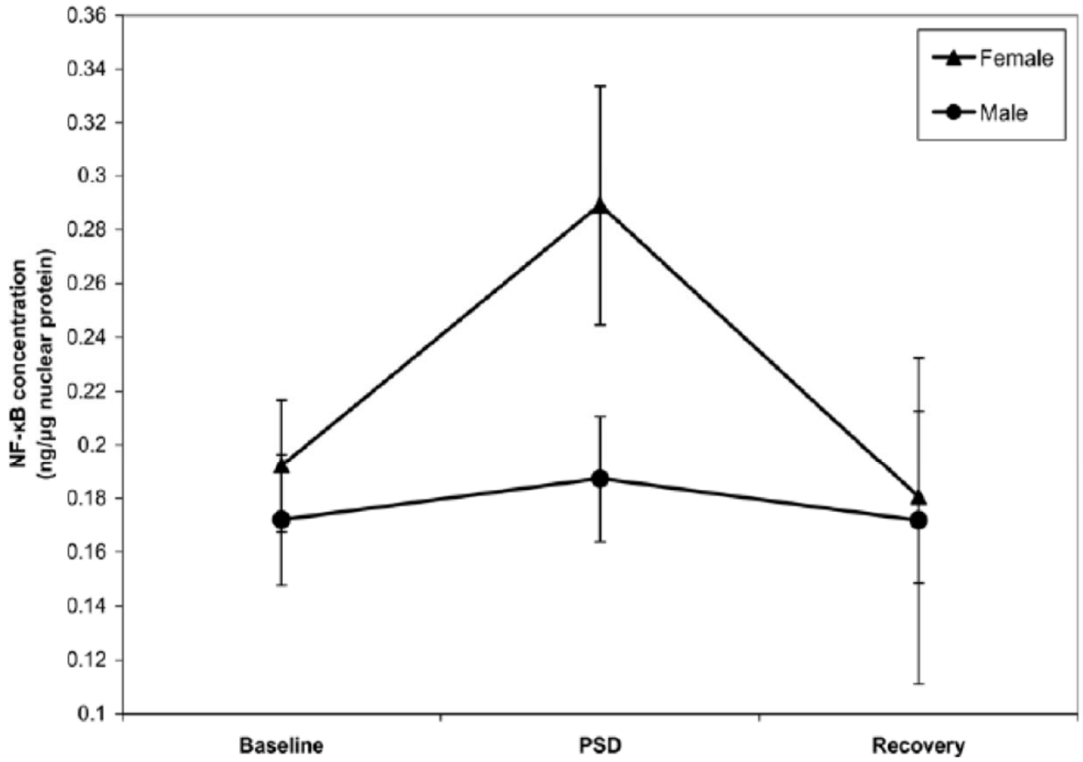




BIOL PSYCHIATRY 2008;64:538–540

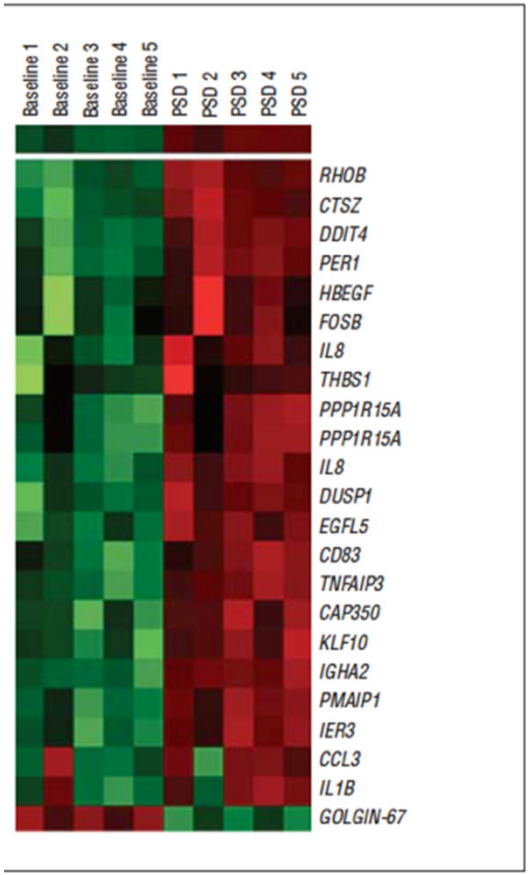
ORIGINAL INVESTIGATION

Sleep Deprivation and Activation of Morning Levels of Cellular and Genomic Markers of Inflammation

Michael R. Irwin, MD; Minge Wang, MSN; Capella O. Campomayor, MS; Alicia Collado-Hidalgo, PhD; Steve Cole, PhD

Table. Gene Transcripts Induced by Sleep Deprivation

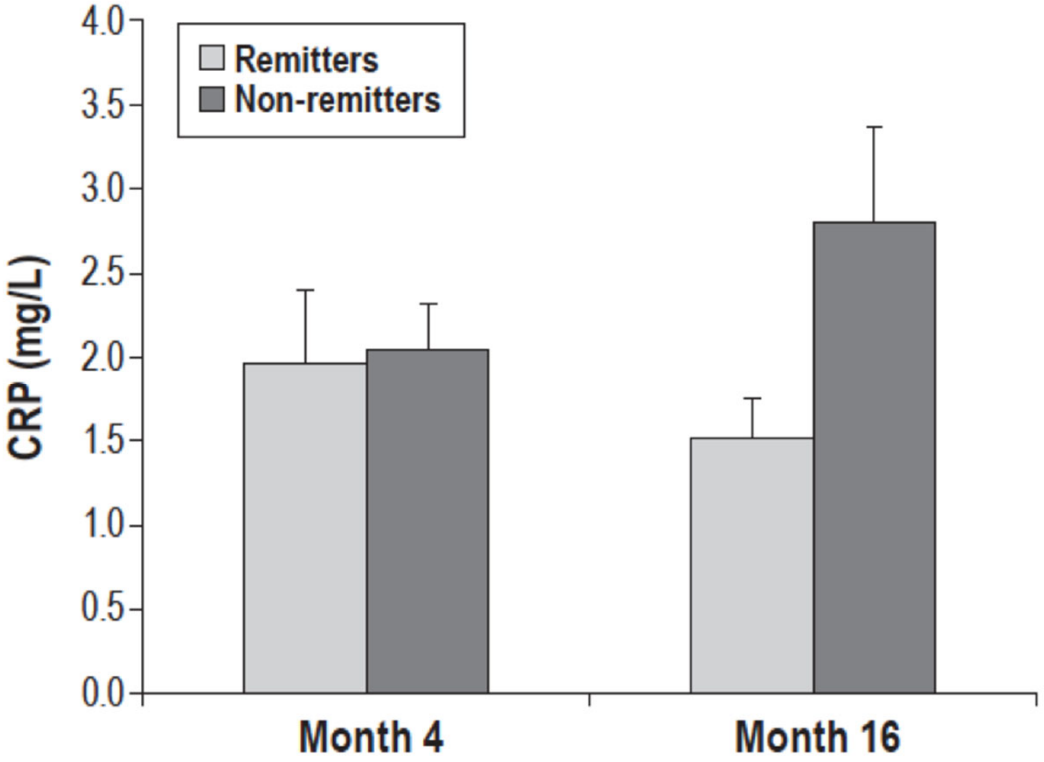
Probe Name	Gene Symbol*	Common Gene Name
202644_s_at	*TNFAIP3*	TNF-α–induced protein 3†
205067_at	*IL1B*	IL-1β†
202014_at	*PPP1R15A*	Protein phosphatase 1, regulatory (inhibitor) subunit 15A‡
210042_s_at	*CTSZ*	Cathepsin Z‡
204373_s_at	*CAP350*	Centrosome-associated protein 350‡
217022_s_at	*IGHA2 /// MGC27165*	Immunoglobulin heavy constant α 2 (A2m marker) /// hypothetical protein MGC27165‡
37028_at	*PPP1R15A*	Protein phosphatase 1, regulatory (inhibitor) subunit 15A‡
204440_at	*CD83*	CD83 antigen (activated B lymphocytes, immunoglobulin superfamily)‡
204285_s_at	*PMAIP1*	Phorbol-12-myristate-13-acetate-induced protein 1‡
201110_s_at	*THBS1*	Thrombospondin 1‡
205114_s_at	*CCL3 /// CCL3L1 /// MGC12815*	Chemokine (C-C motif) ligand 3 /// chemokine (C-C motif) ligand 3-like 1 /// chemokine (C-C motif) ligand 3-like, centromeric‡
202393_s_at	*KLF10*	Kruppel-like factor 10‡
201631_s_at	*IER3*	Immediate early response 3‡
202859_x_at	*IL8*	IL-8‡
202887_s_at	*DDIT4*	DNA damage–inducible transcript 4‡
212099_at	*RHOB*	*ras* Homologue gene family, member B‡
202768_at	*FOSB*	FBJ murine osteosarcoma viral oncogene homologue B‡
212830_at	*EGFL5*	EGF-like domain, multiple 5‡
38037_at	*HBEGF*	Heparin-binding EGF-like growth factor‡
211506_s_at	*IL8*	IL-8‡
201044_x_at	*DUSP1*	Dual-specificity phosphatase 1‡
202861_at	*PER1*	Period homologue 1 (*Drosophila*)‡



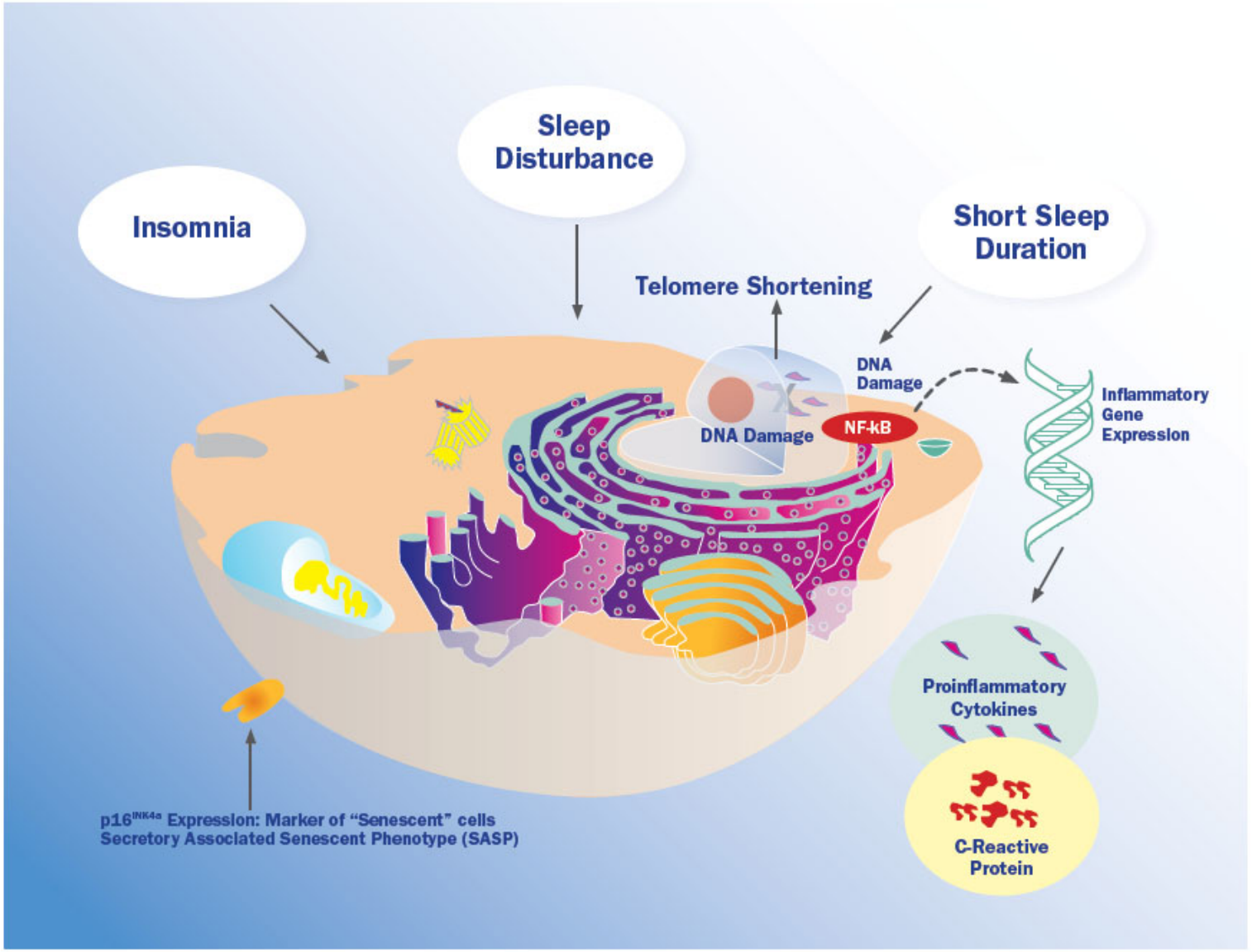
Treatment remission of insomnia reverses inflammation

CBT VS. TAI CHI FOR LATE LIFE INSOMNIA AND INFLAMMATORY RISK

Cognitive Behavioral Therapy vs. Tai Chi for Late Life Insomnia and Inflammatory Risk: A Randomized Controlled Comparative Efficacy Trial



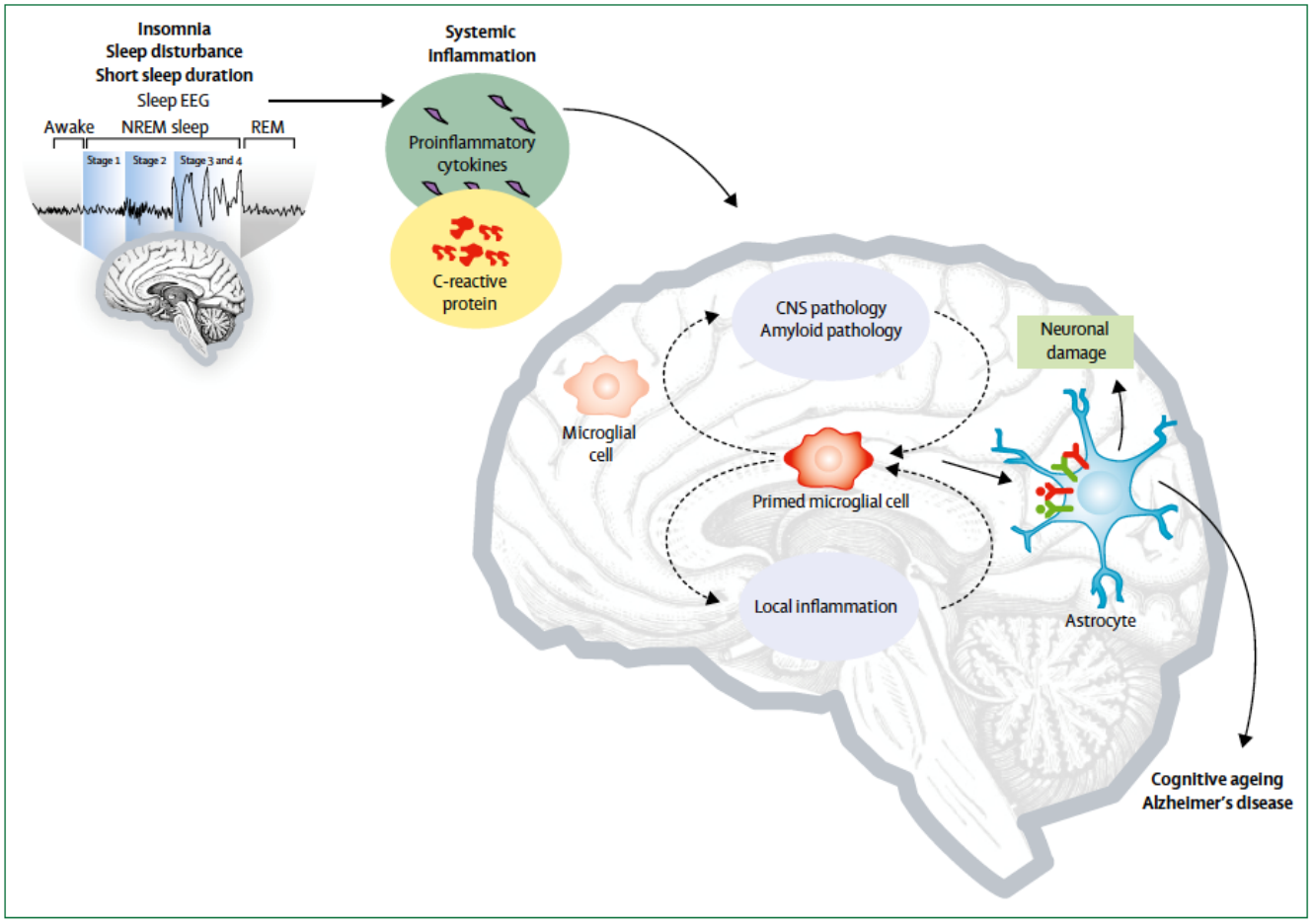
SLEEP 2014;37(9):1543-1552.

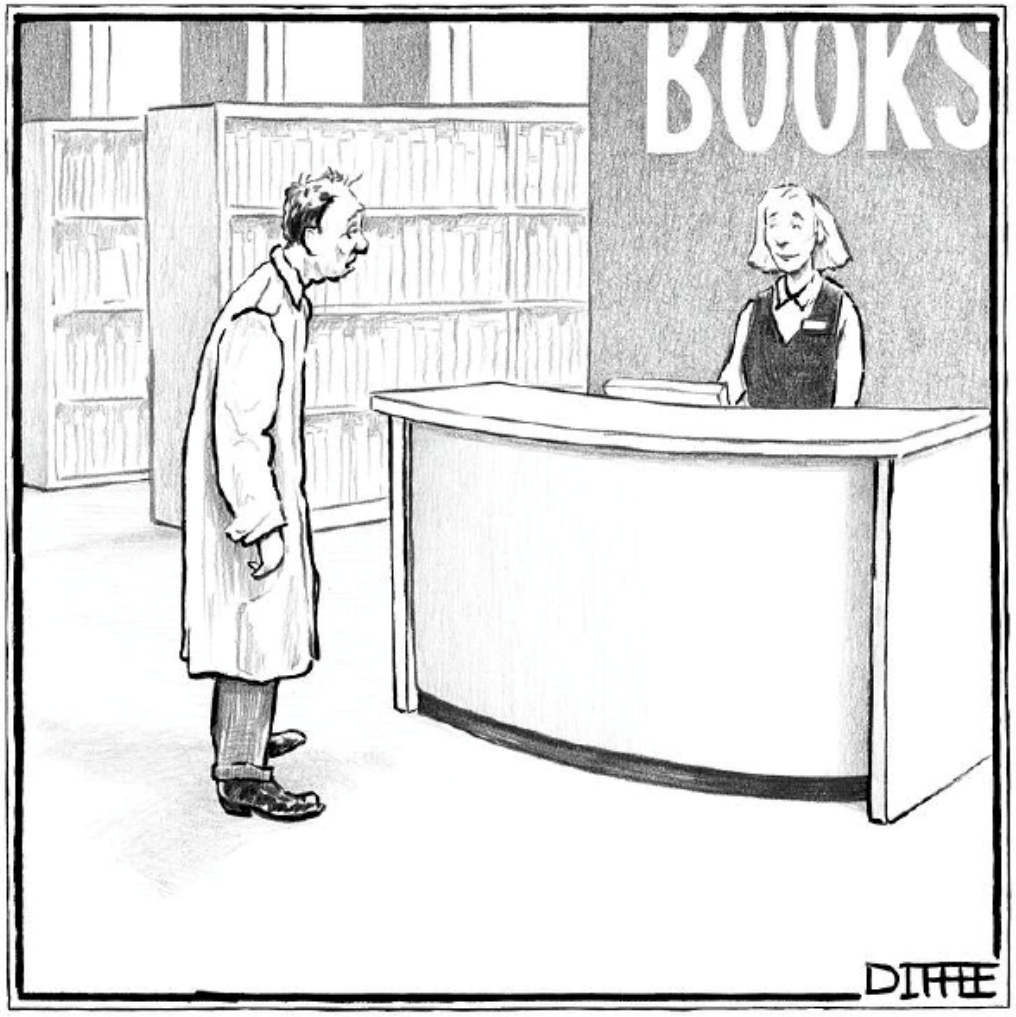

Sleep Disturbance
Insomnia
Short Sleep Duration
Telomere Shortening
DNA Damage
DNA Damage
NF-kB
Inflammatory Gene Expression
Proinflammatory Cytokines
C-Reactive Protein
p16INK4a Expression: Marker of "Senescent" cells
Secretory Associated Senescent Phenotype (SASP)

Implications of sleep disturbance and inflammation for Alzheimer's disease dementia

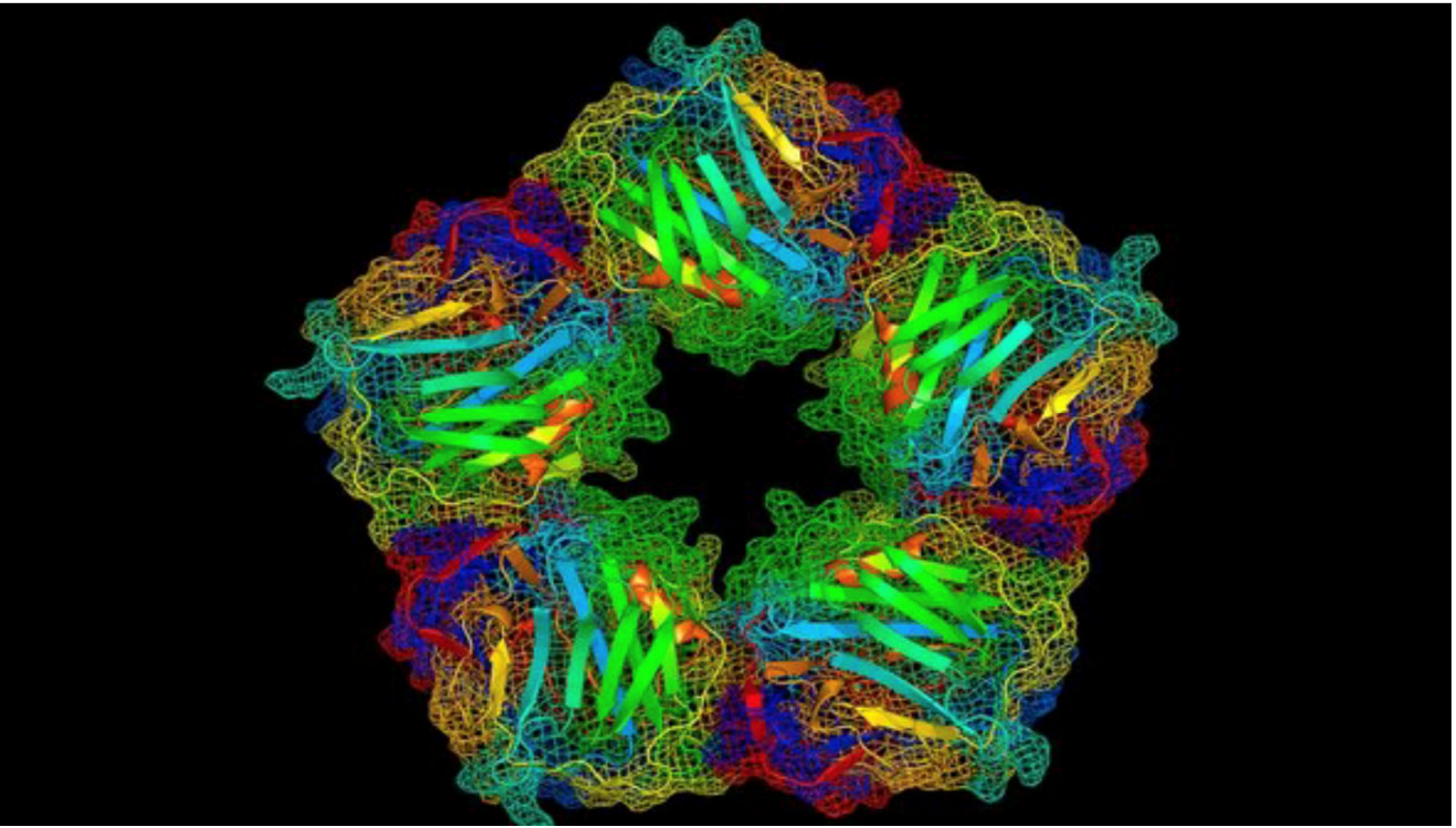
Michael R Irwin, Michael V Vitiello

THE LANCET
Neurology
Volume 18 · Issue 3 · March 2019



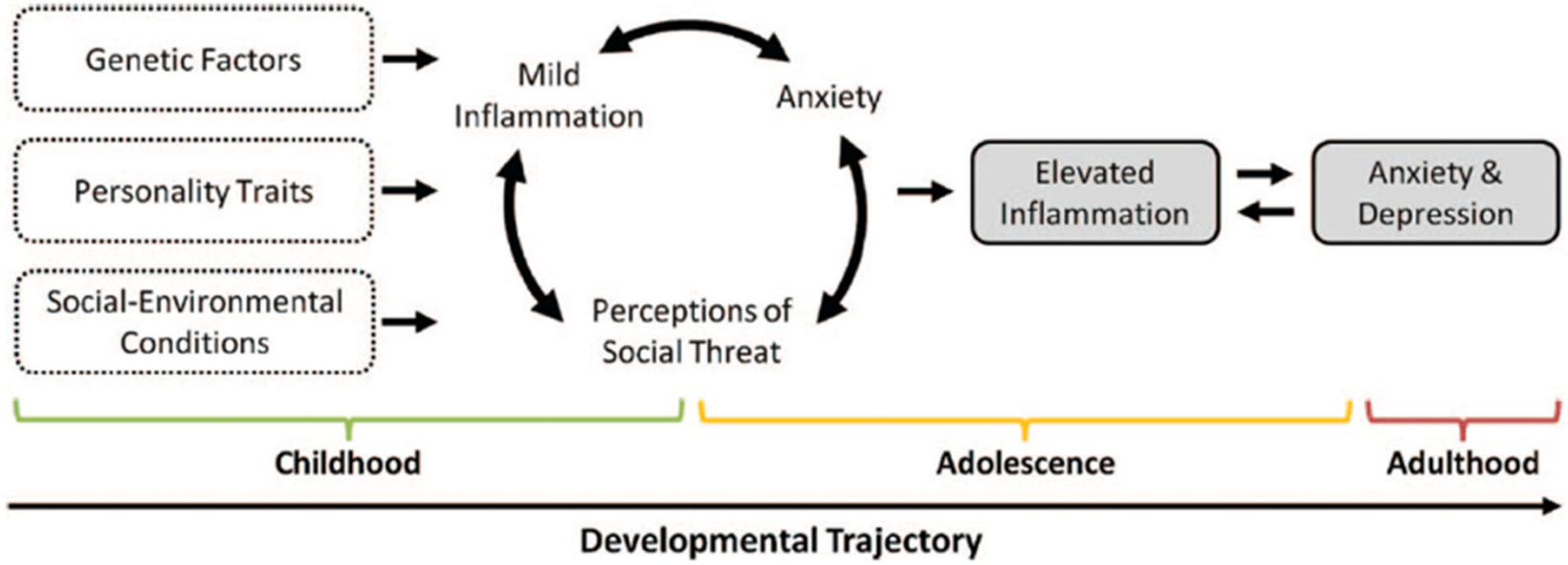


"Do you have any why-to books?"



From Stress to Inflammation and Major Depressive Disorder: A Social Signal Transduction Theory of Depression

George M. Slavich and Michael R. Irwin



Psychol Bull. 2014 May;140(3):774-815

Link between inflammation and depression

- Elevated levels of inflammatory cytokines are found in depressed patients
- Inflammation alters neurotransmitter systems involved in regulation of mood and behavior
- Inflammation induces depressive symptoms and prospectively predicts depression
- Inflammatory markers predict depression treatment response*
- Anti-inflammatory strategies show potential in depression treatment

PNI COUSINS CENTER

Experimentally examining the inflammatory biotype of depression to define mechanisms of vulnerability and to refine treatments

Human Endotoxin Administration as an Experimental Model in Drug Development

AF Suffredini[1] and RJ Noveck[2]

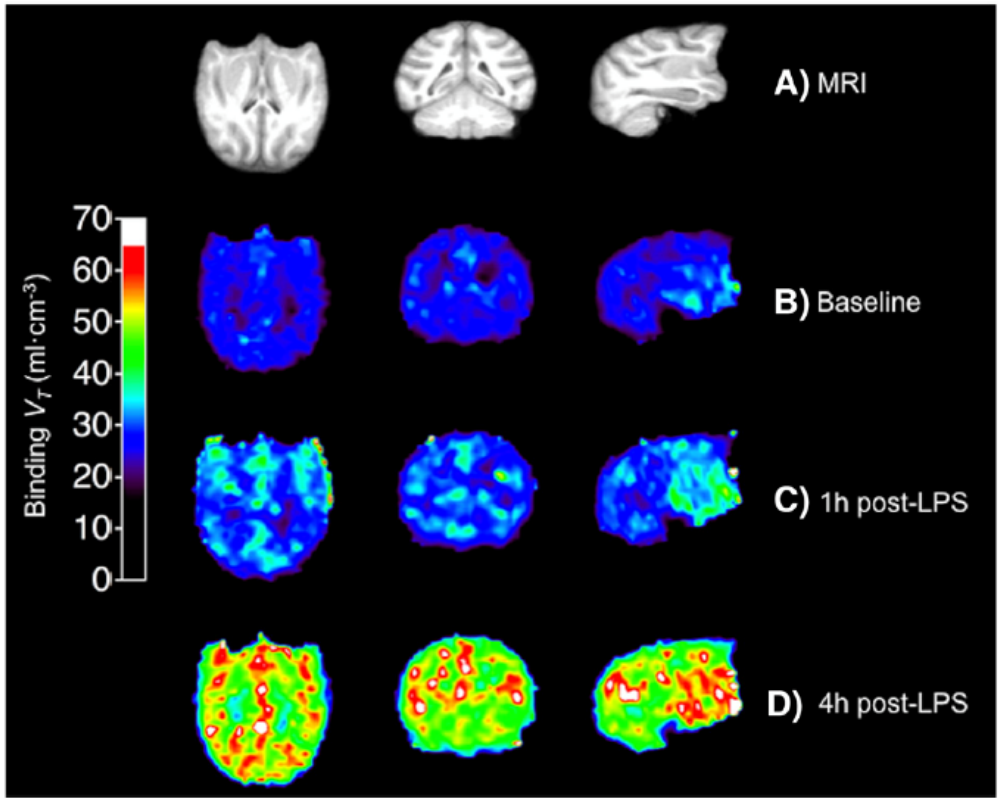
Linking human physiology to inflammatory mechanisms discovered *in vitro* or in animal models is essential to determine their importance. Innate immunity underlies many of these inflammatory responses in health and disease. Bacterial endotoxin is the quintessential trigger of innate immune responses. When administered to humans, endotoxin has been an important means of demonstrating key inflammatory mechanisms *in vivo*. Furthermore, endotoxin challenges have provided opportunities to test the effects of novel inflammation-modifying agents in humans.

Contents lists available at ScienceDirect

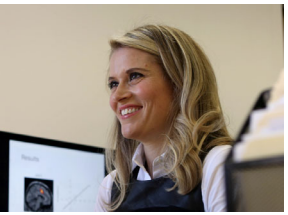
NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

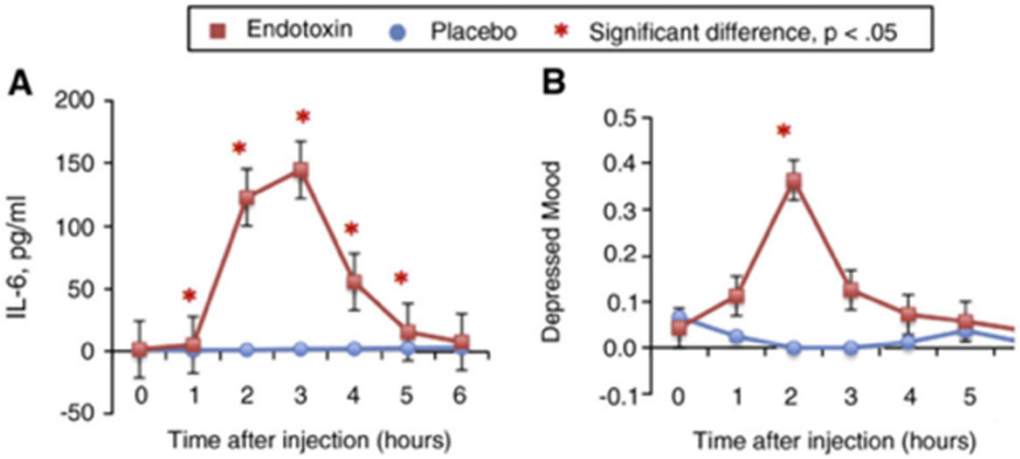
Endotoxin-induced systemic inflammation activates microglia: [^{11}C]PBR28 positron emission tomography in nonhuman primates



Inflammation is a molecular signal to induce depressed mood



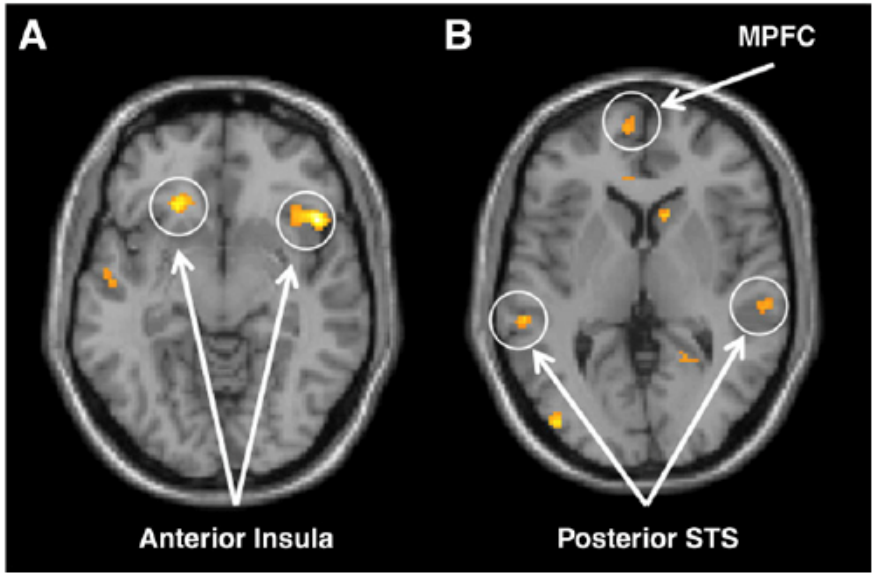
An fMRI study of cytokine-induced depressed mood and social pain: The role of sex differences



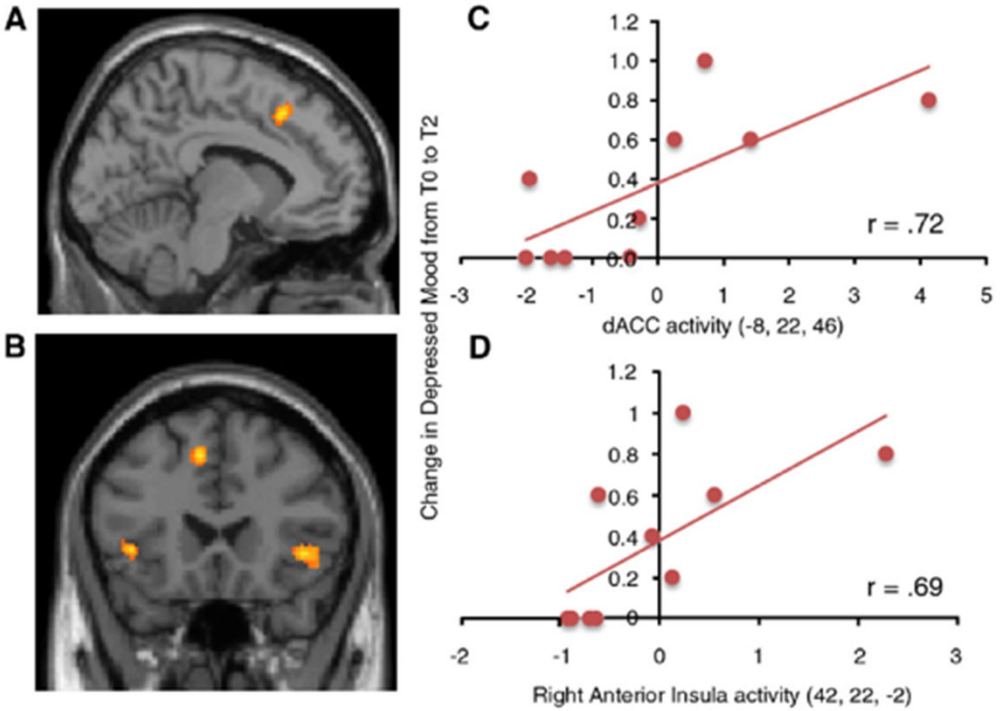
- Adults (n=39; females, n=20)
- Double-blind, placebo-controlled randomized controlled trial of low dose endotoxin
- Behavioral measures of social distress and depressed mood
- Neuroimaging session to assess reactivity to social exclusion

Eisenberger et al, Neuroimage 2009

Inflammation: a molecular signal that induces depressed mood



Increases in IL-6 correlated with activation of anterior Insula, medial prefrontal cortex, and posterior superior temporal sulcus

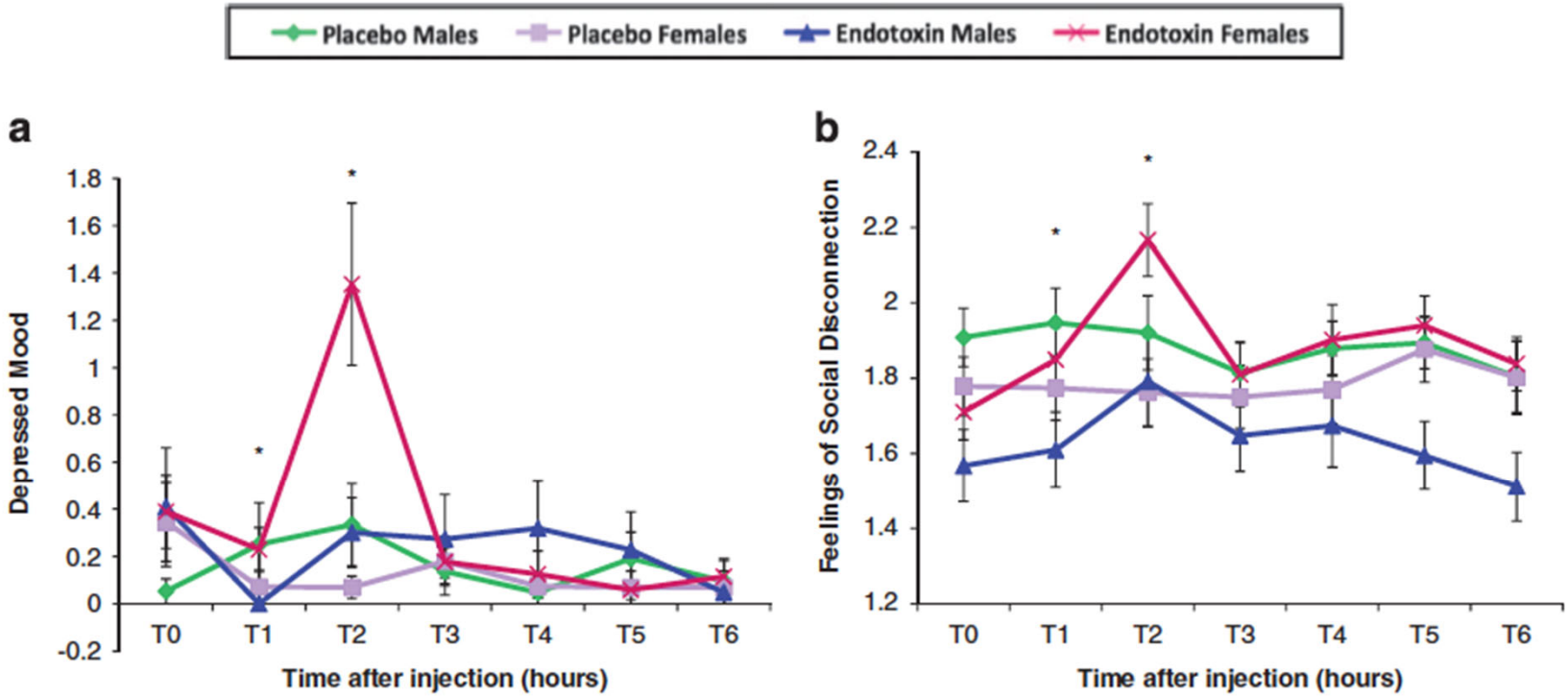


Only in females, IL-6 correlated with activity in the dACC and anterior insula, which correlated with depressed mood

Eisenberger et al, Neuroimage 2009

Sex Differences in Depressive and Socioemotional Responses to an Inflammatory Challenge: Implications for Sex Differences in Depression

Adults: N=115
Females: N=69
Males: N=46

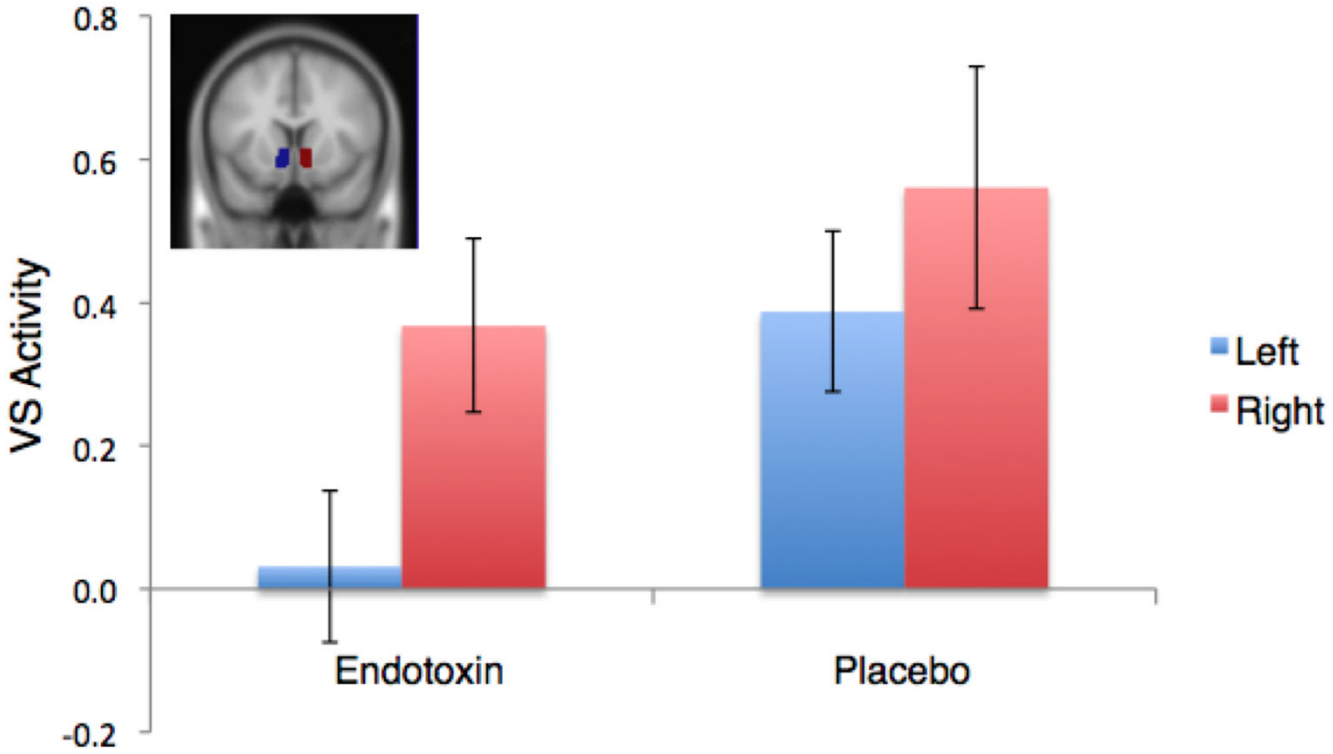


Neuropsychopharmacology (2015), 1–8

www.neuropsychopharmacology.org

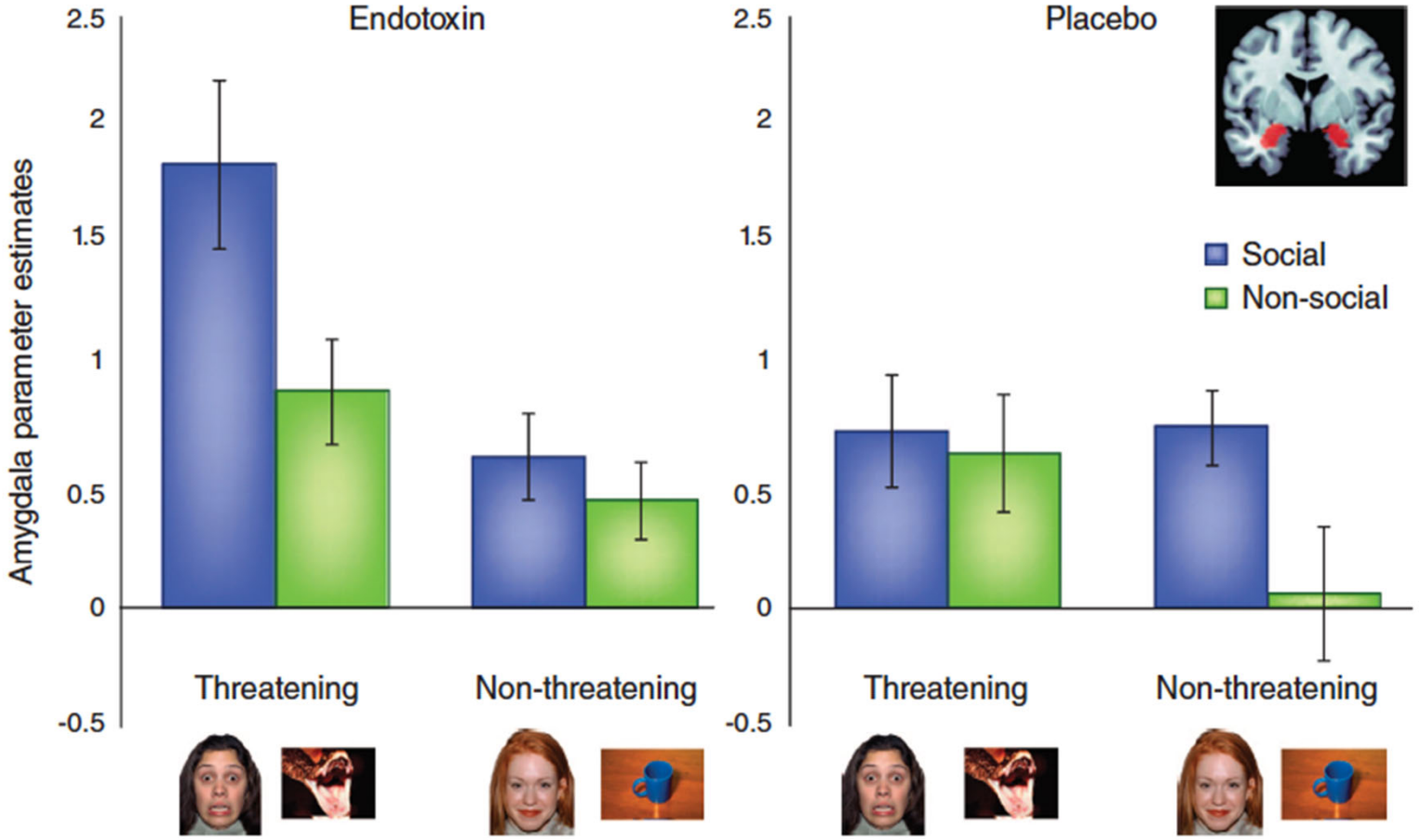
Inflammation-Induced Anhedonia: Endotoxin Reduces Ventral Striatum Responses to Reward

Biological Psychiatry

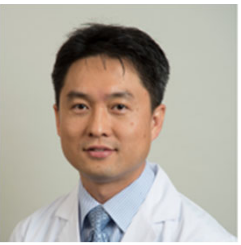


Eisenberger et al, Biol Psychiatry 2010

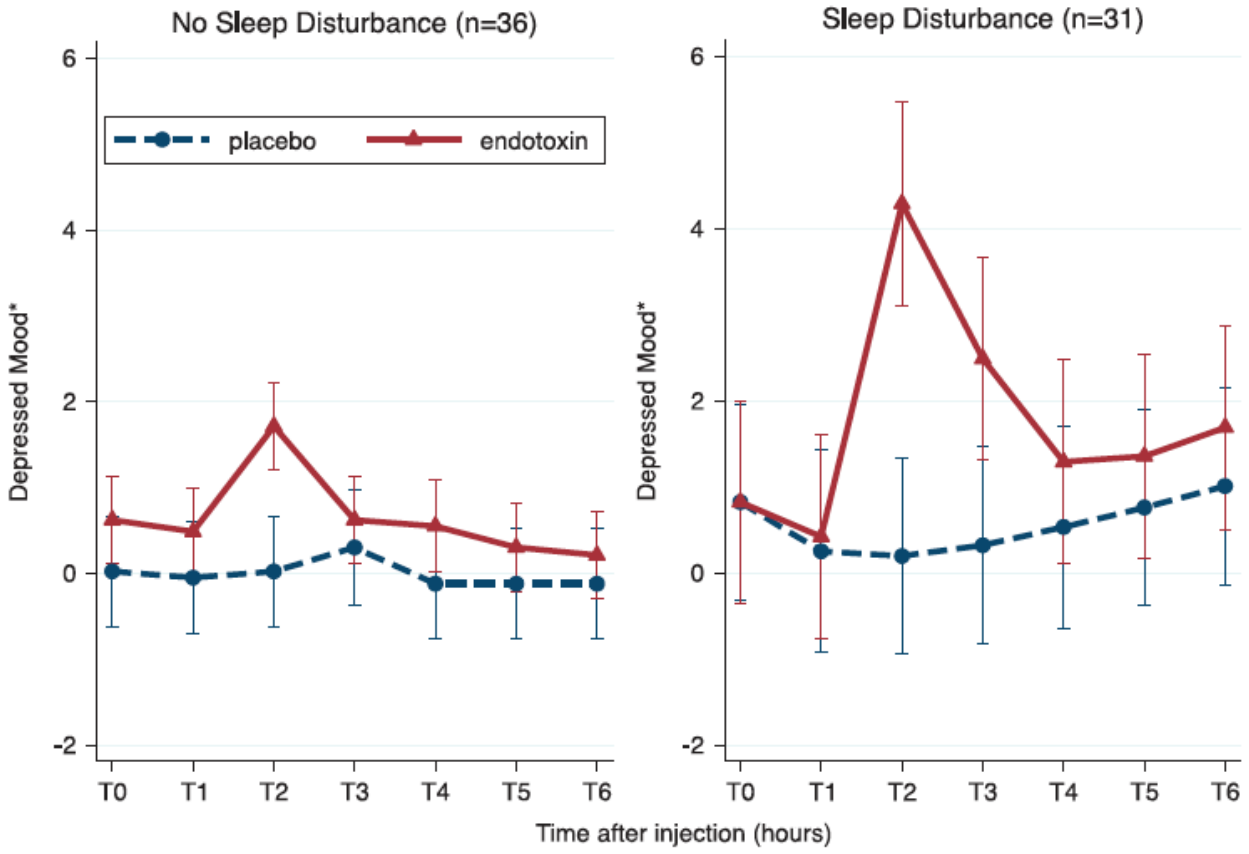
Inflammation selectively enhances amygdala activity to socially threatening images



T.K. Inagaki et al. / NeuroImage 59 (2012) 3222–3226



Preexisting mild sleep disturbance as a vulnerability factor for inflammation-induced depressed mood: a human experimental study



Transl Psychiatry (2016) **6**, e750; doi:10.1038/tp.2016.23

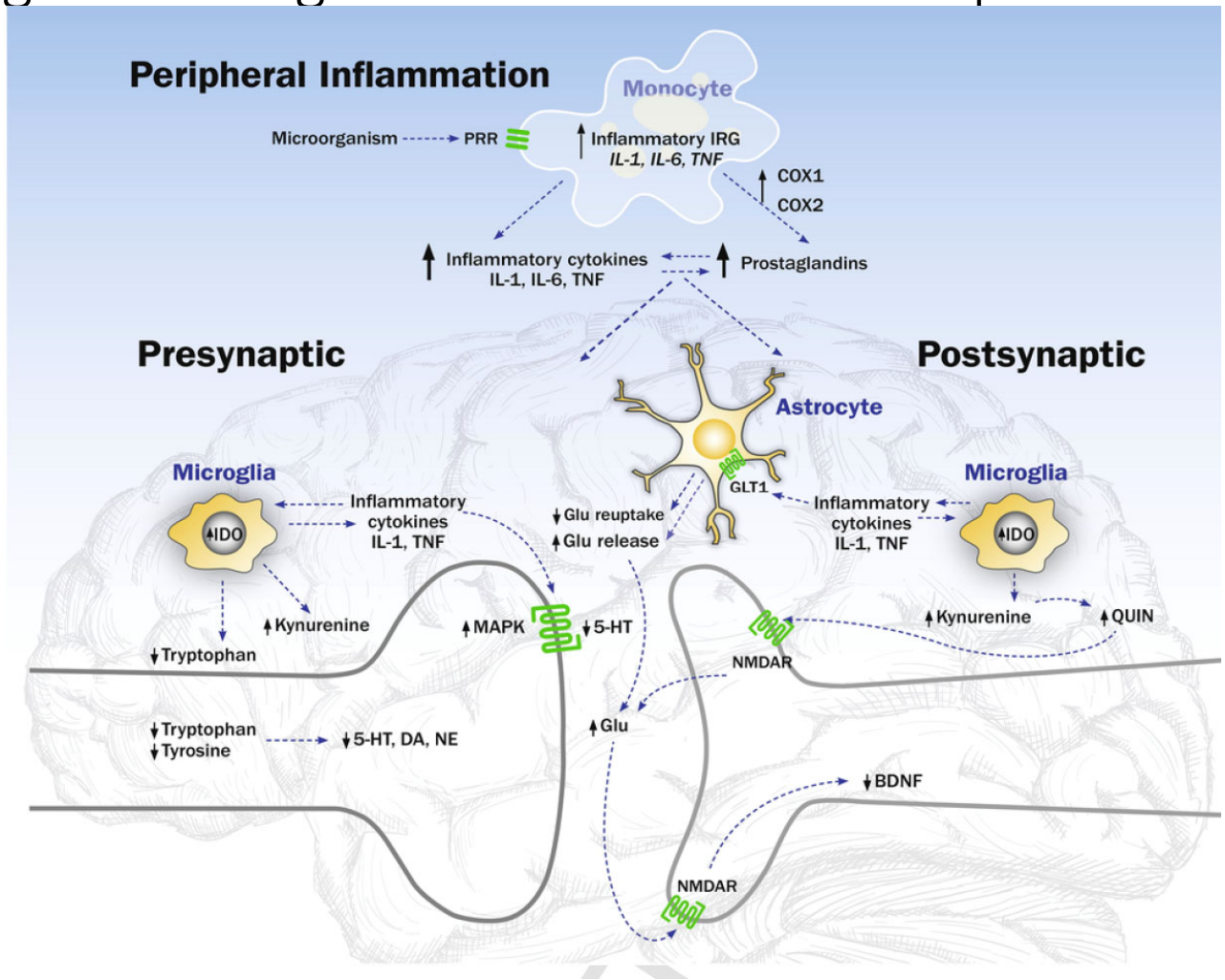
"You should relax less."

Building an evidence base to accelerate sleep-health

in the community by treating insomnia,

reducing depression risk, and reversing inflammation

Peripheral and CNS inflammatory signaling alters monoamine and glutaminergic neurotransmission implicated in depression



Might anti-inflammatory treatments improve depressive symptoms, or mitigate prodromal symptoms and risk of depression?

Roman & Irwin: Brain Behav Immun, 2019

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Novel neuroimmunologic therapeutics in depression: A clinical perspective on what we know so far

Michael Roman[a], Michael R. Irwin[b,*]

Neuroimmunologic therapeutics examined:

- Nonsteroidal anti-inflammatory pathways (i.e., aspirin, celecoxib)
- Cytokine antagonism (i.e., etanercept, infliximab)
- N-methyl-D-aspartate receptor (NMDA) receptor antagonism (i.e., ketamine)
- Modulation of kynurenine pathways (i.e., minocycline)

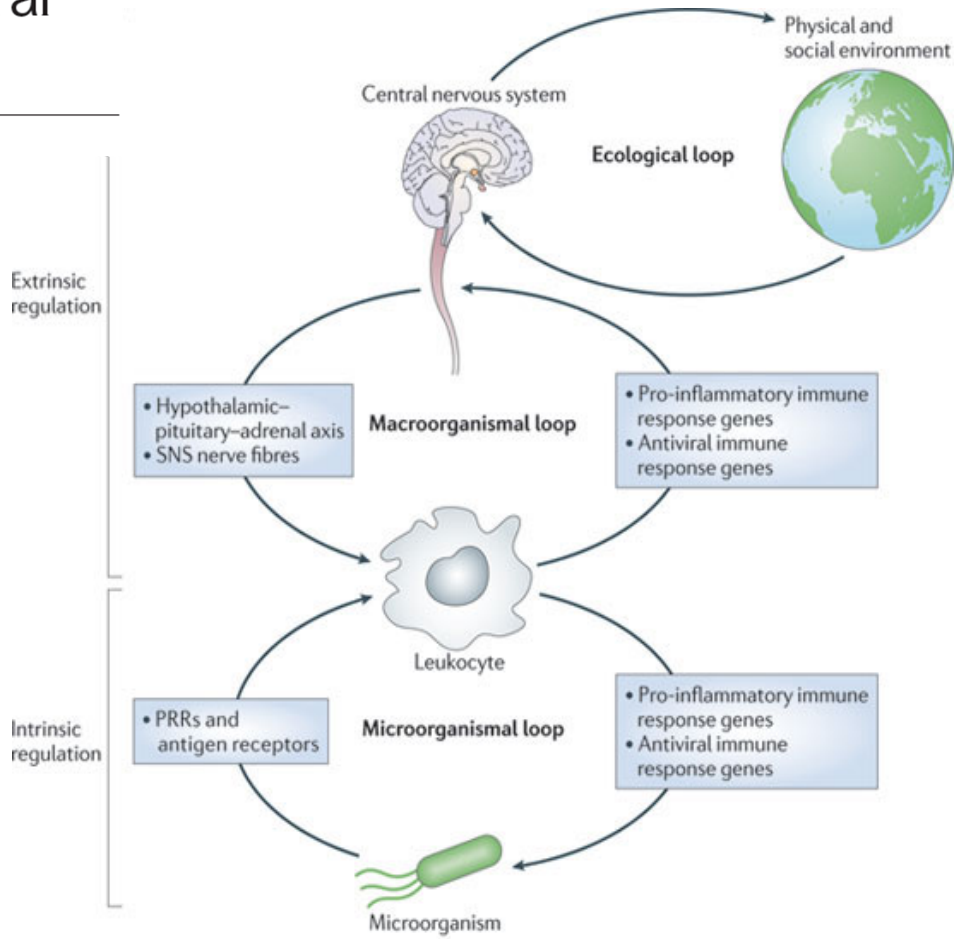
Conclusions:

- Strategies that target neuroimmune mechanisms show limited efficacy in the treatment of depression, and related depressive symptoms.
- Are there other innovative approaches?

SCIENCE AND SOCIETY

Reciprocal regulation of the neural and innate immune systems

Michael R. Irwin and Steven W. Cole



Nature Reviews | Immunology

Annals of Internal Medicine

EDITORIAL

Cognitive Behavioral Therapy for Chronic Insomnia: State of the Science Versus Current Clinical Practices

- CBT-I: ”Gold standard” treatment of Choice for chronic insomnia: Amercian Academy of Sleep Medicine, and the American College of Physicians

- CBT-I is as effective as pharmacotherapy in the treatment of insomnia, and more durable than pharmacotherapy

- Limitations:
  - Access to treatment is limited;
  - Few mental health professionals are trained in the delivery of CBT-I
  - Expensive

OXFORD

EDITORIAL

Innovation in the Treatment of Insomnia in Breast Cancer Survivors

Michael R. Irwin

- Mindfulness meditation and other practices that embrace contemplative traditions, are thought to attune our perceptions to quiet the mind and body. Mindful awareness is a systematic practice of attending to moment-by-moment experiences, thoughts, and emotions from a nonjudgmental perspective

Efficacy of mind-body treatments

- ❖ Mindfulness Meditation
- ❖ Tai Chi

What is Mindfulness Meditation?

Mindfulness: A state of consciousness characterized by attention to the present moment.

Mindful awareness: A systematic practice of attending to moment-by-moment experiences, thoughts, and emotions from a nonjudgmental perspective

What is Tai Chi?

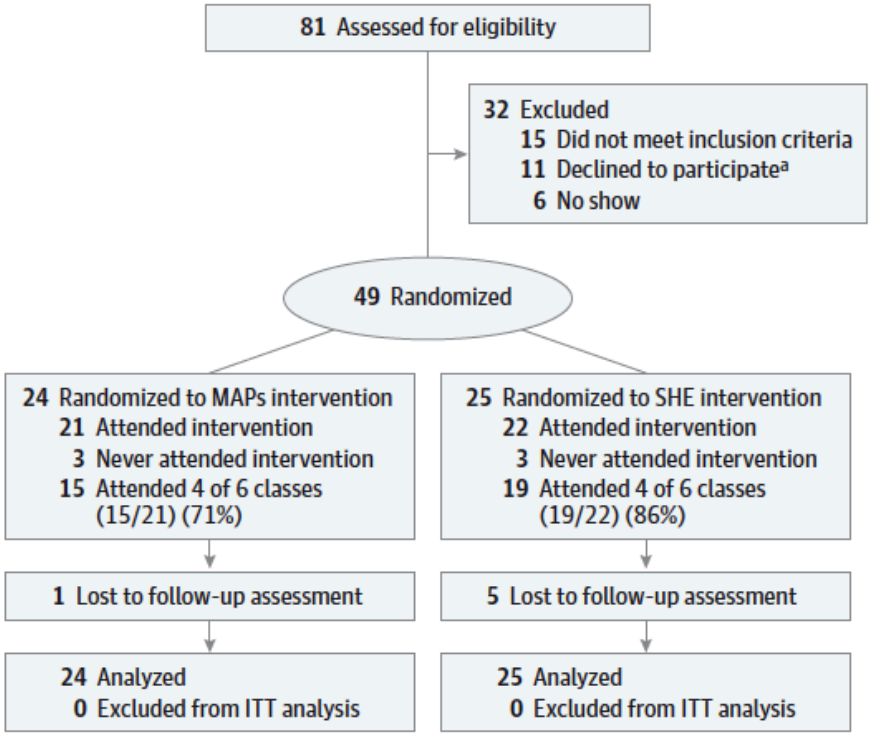
Tai Chi: A moving meditation, incorporating elements of mindfulness, balance, and physical movement

Tai Chi Chih: 20 standardized exercises taught as a research curriculum

Original Investigation

Mindfulness Meditation and Improvement in Sleep Quality and Daytime Impairment Among Older Adults

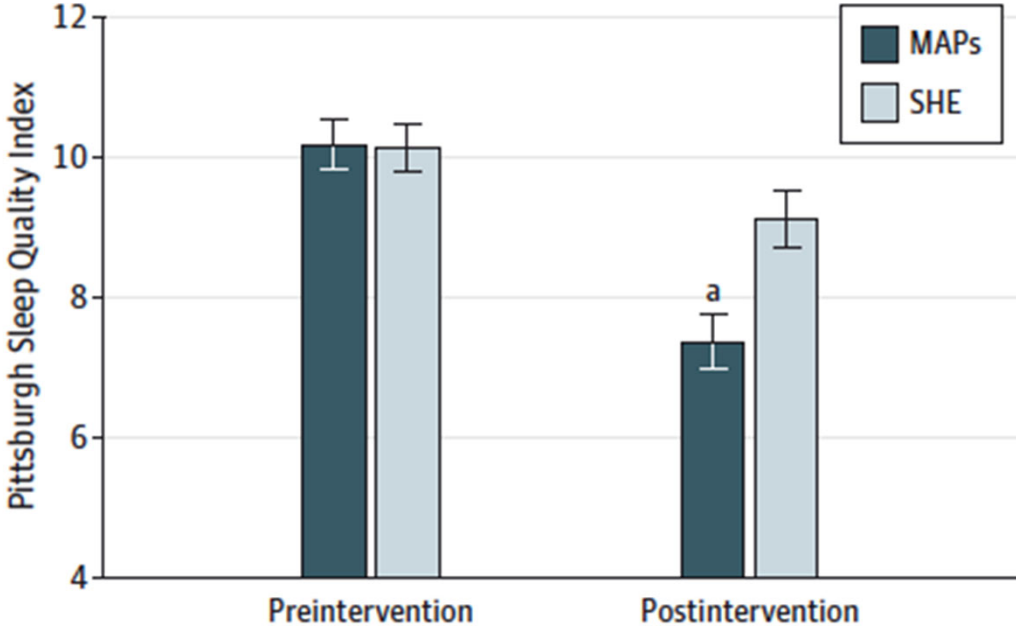
Figure 1. Consolidated Standards of Reporting Trials Flow Diagram of the Single-Site, Parallel-Group Randomized Clinical Trial of MAPs Compared With SHE for Sleep Problems in Older Adults

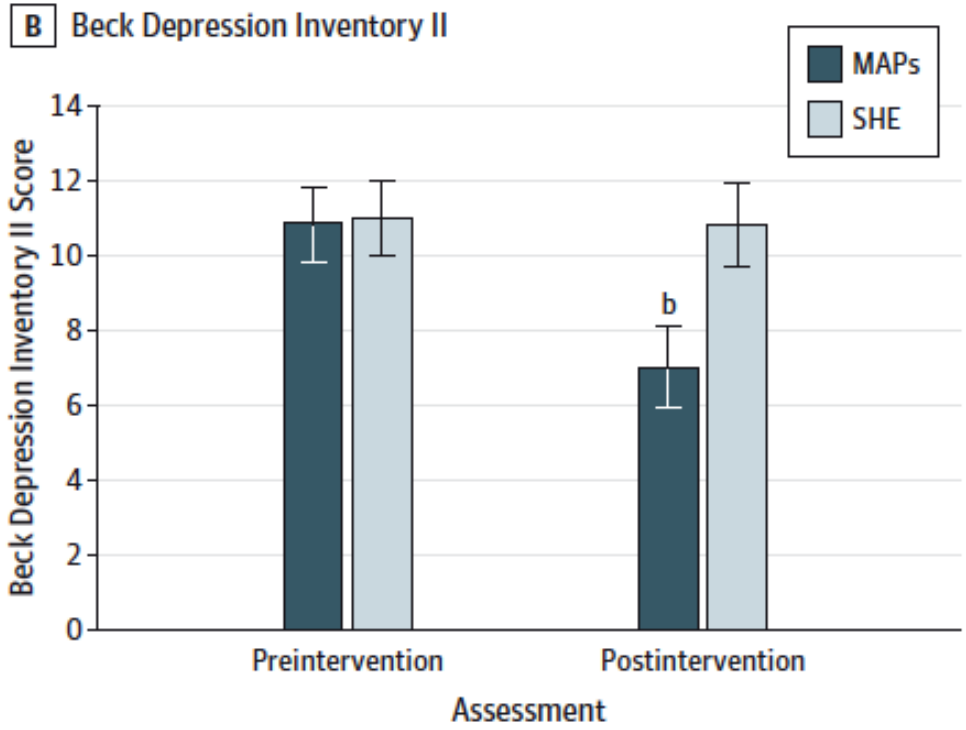


JAMA Intern Med. 2015;175(4):494-501.

Original Investigation

Mindfulness Meditation and Improvement in Sleep Quality and Daytime Impairment Among Older Adults



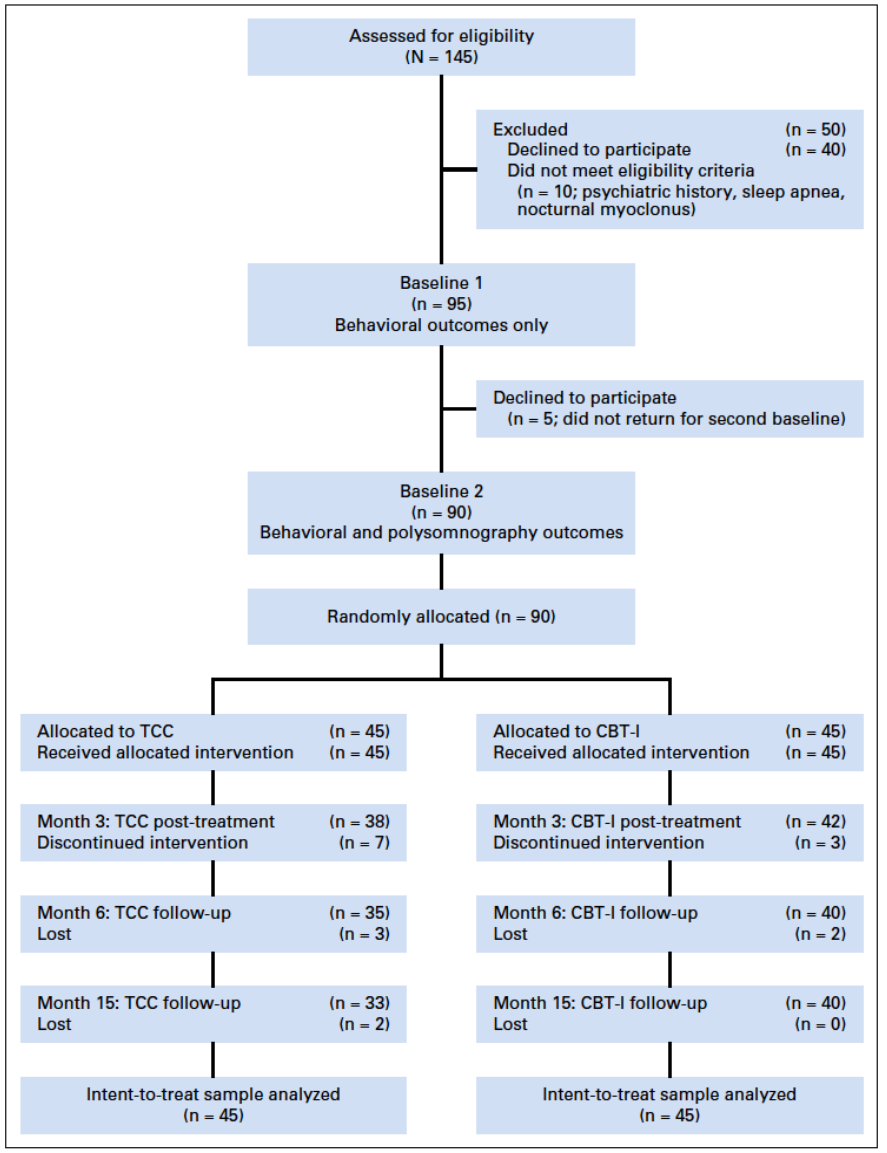


JAMA Intern Med. 2015;175(4):494-501.

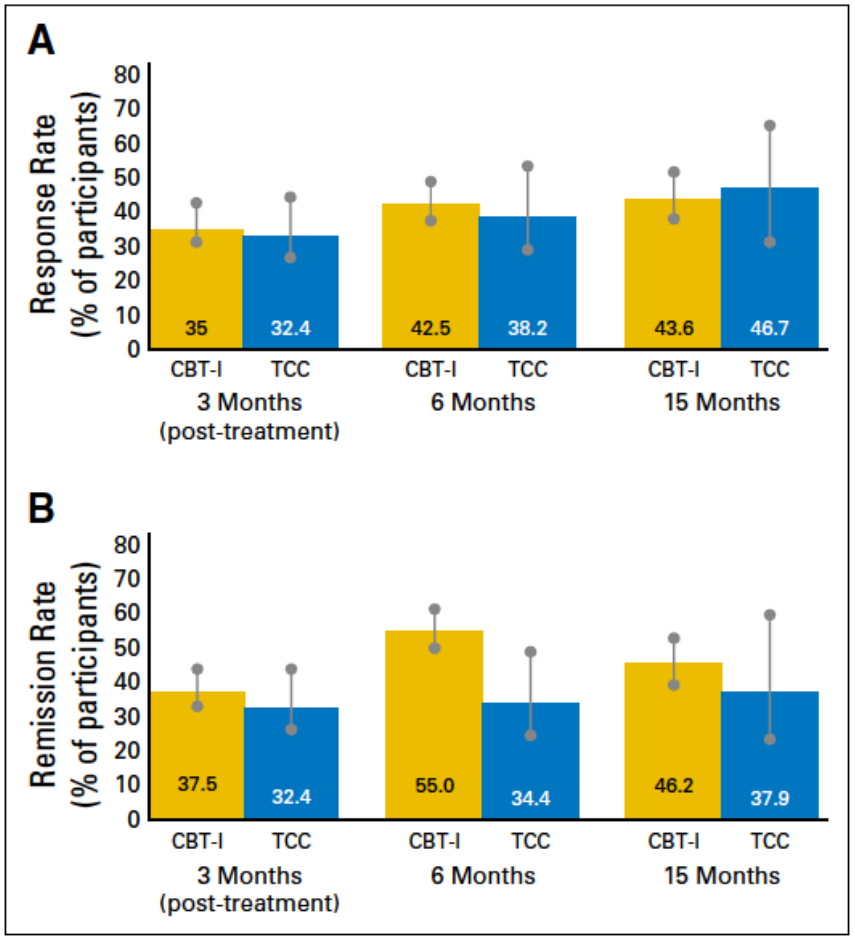
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

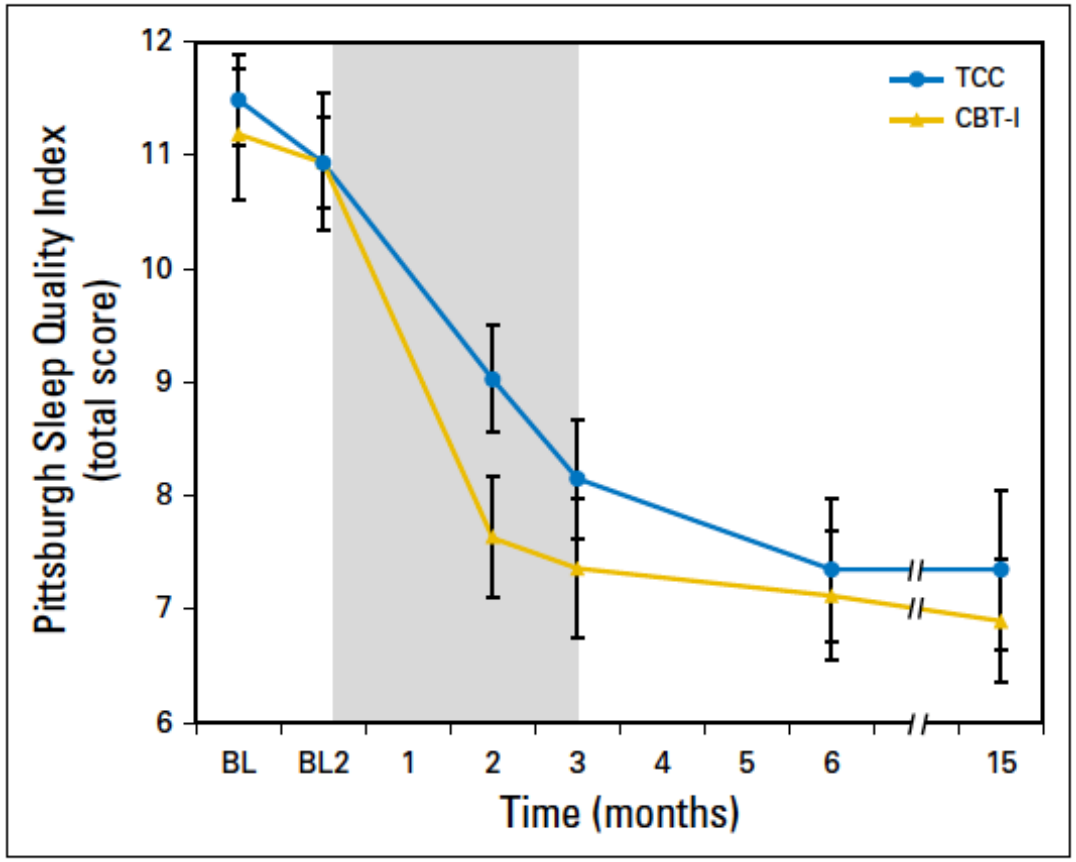
Tai Chi Chih Compared With Cognitive Behavioral Therapy for the Treatment of Insomnia in Survivors of Breast Cancer: A Randomized, Partially Blinded, Noninferiority Trial

J Clin Oncol 35:2656-2665



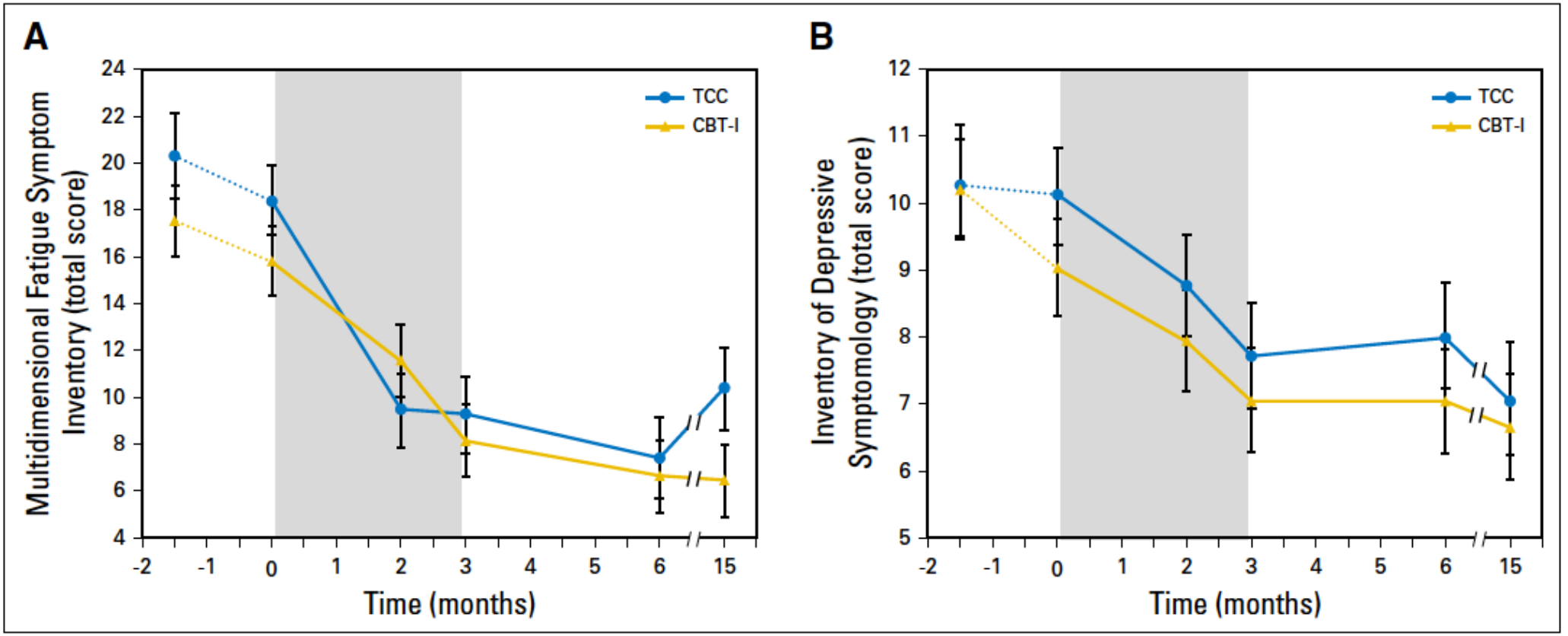
Tai Chi Chih Compared With Cognitive Behavioral Therapy for the Treatment of Insomnia in Survivors of Breast Cancer: A Randomized, Partially Blinded, Noninferiority Trial





J Clin Oncol 35:2656-2665.

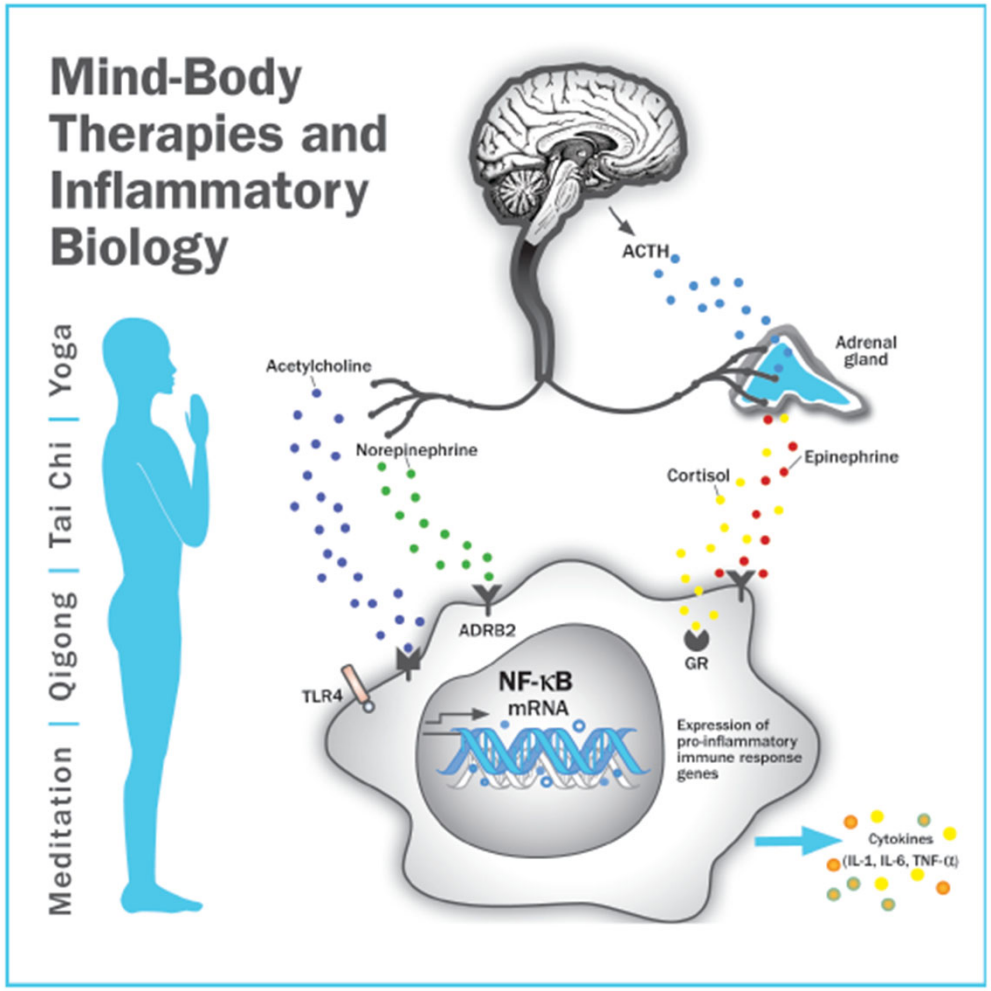
Tai Chi Chih Compared With Cognitive Behavioral Therapy for the Treatment of Insomnia in Survivors of Breast Cancer: A Randomized, Partially Blinded, Noninferiority Trial



J Clin Oncol 35:2656-2665.

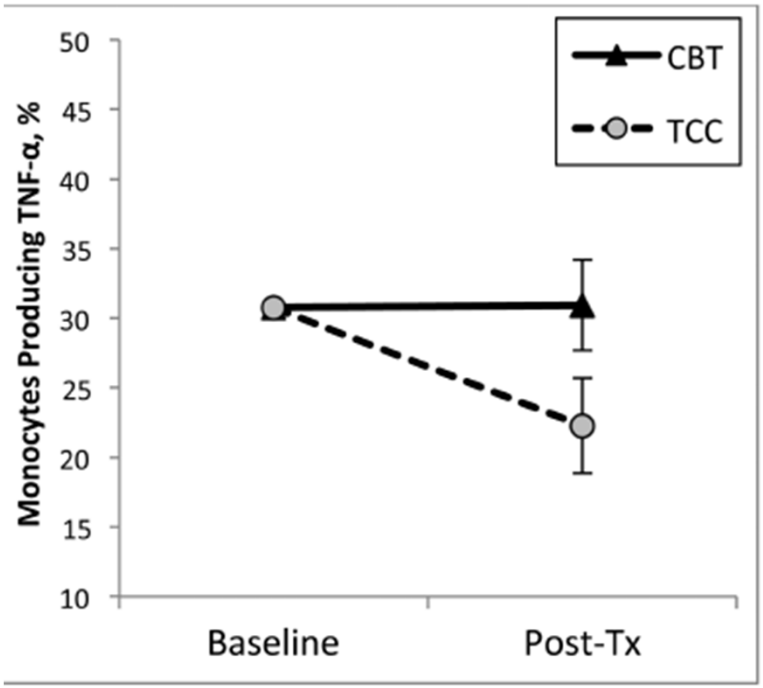
Invited Review

Mind–body therapies and control of inflammatory biology: A descriptive review



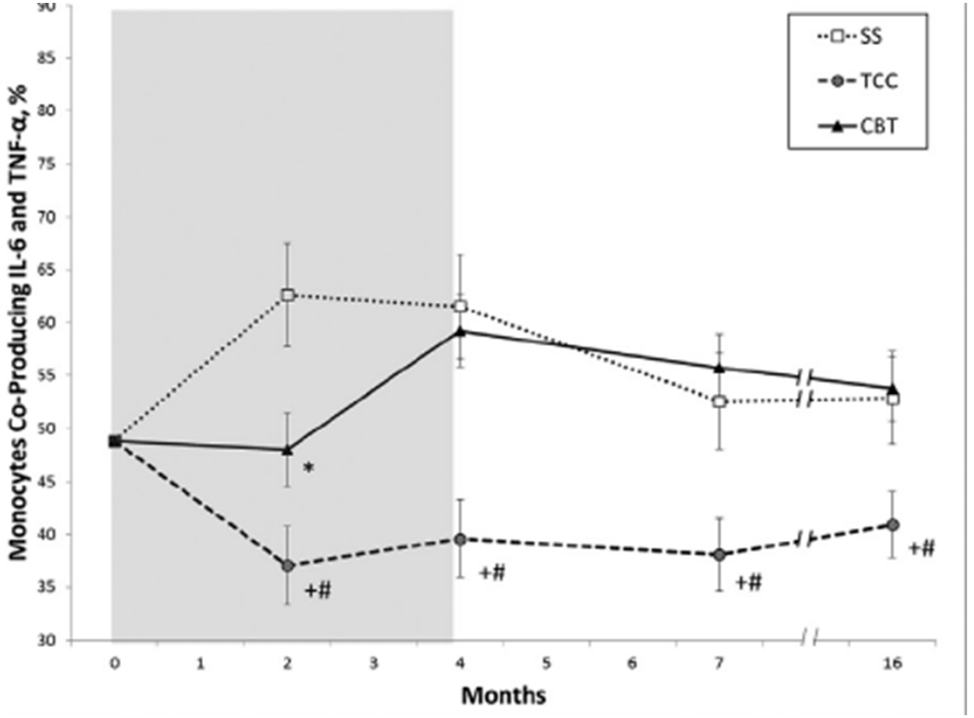
Brain, Behavior, and Immunity 51 (2016) 1–11

Mindfulness practice, Tai Chi, is more effective at reducing cellular inflammation than CBT-I in insomnia patients



Breast survivors with insomnia (n=90)

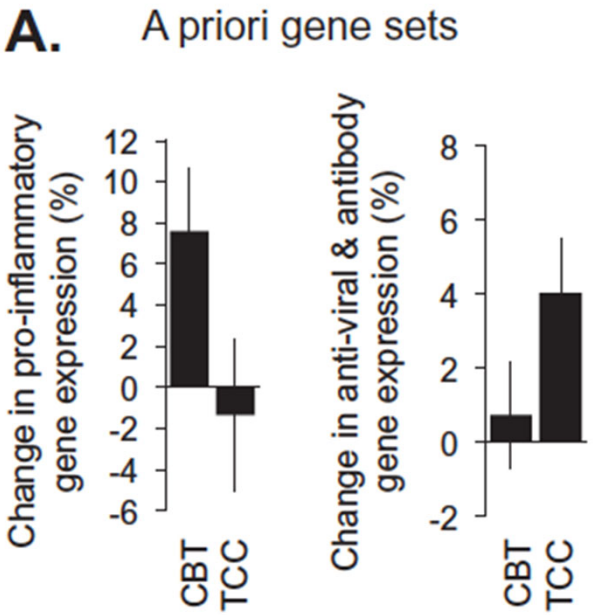
Irwin et al. J Nat Cancer Inst 2014



Older adults with insomnia (n=123)

Biological Psychiatry November 15, 2015; 78:721–729

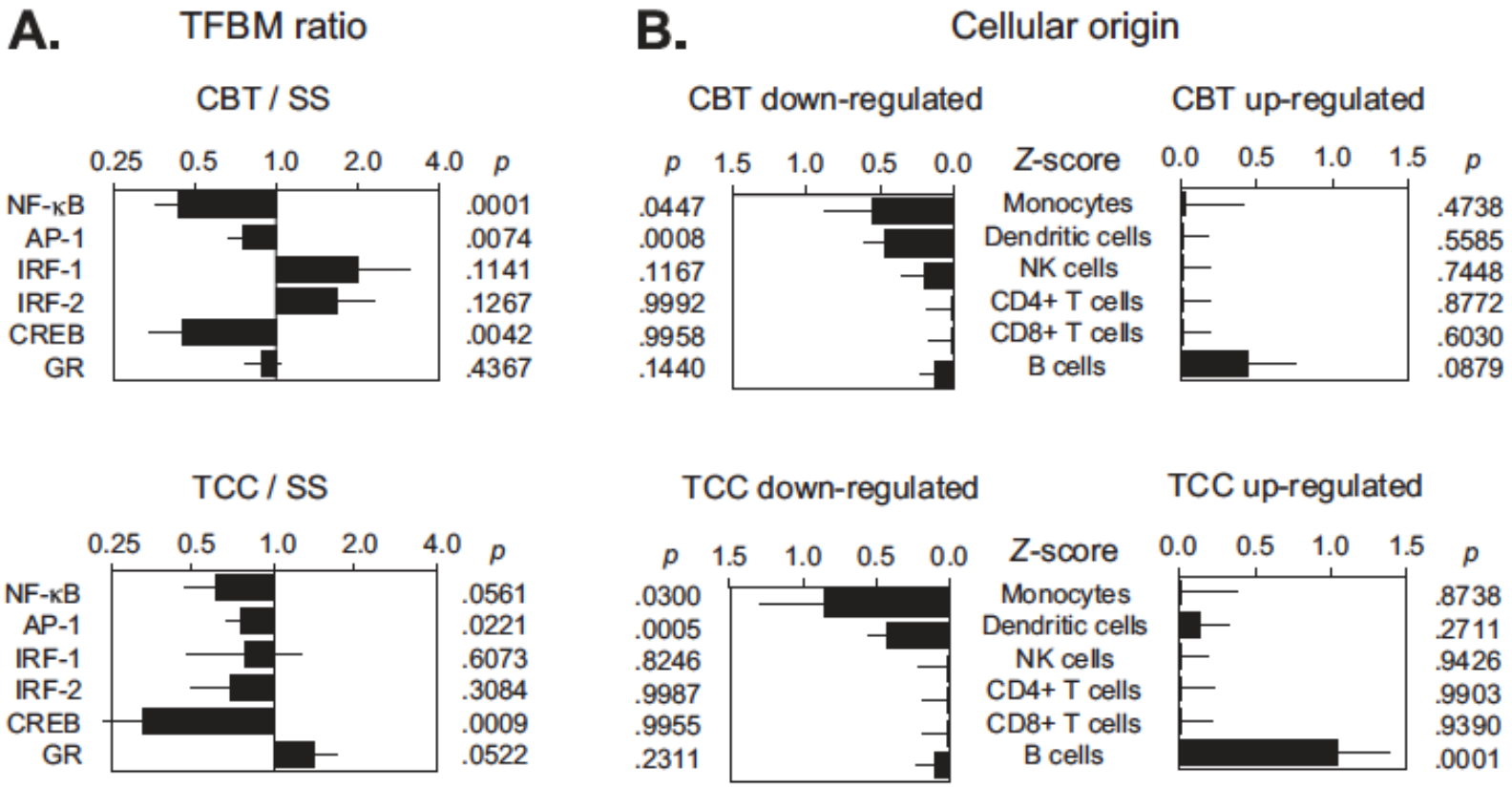
Mindfulness practice, Tai Chi, is more effective at reducing inflammatory transcriptional profiles in breast cancer survivors with insomnia…….



Breast survivors with insomnia (n=90)

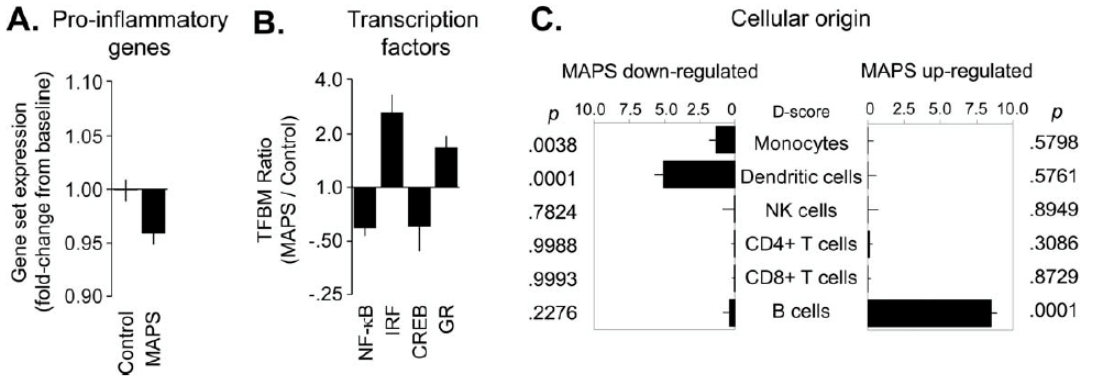
Irwin et al. J Nat Cancer Inst 2014

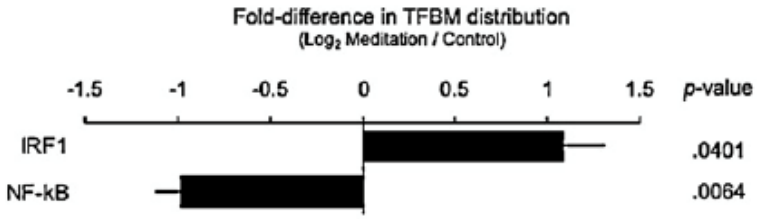
.....yet, as compared to control, both Tai Chi and CBT-I, reduce inflammatory transcriptional profiles in older adults with insomnia



Biological Psychiatry November 15, 2015; 78:721–729

Diverse mindfulness practices reduce inflammatory transcriptional profiles in other sample populations

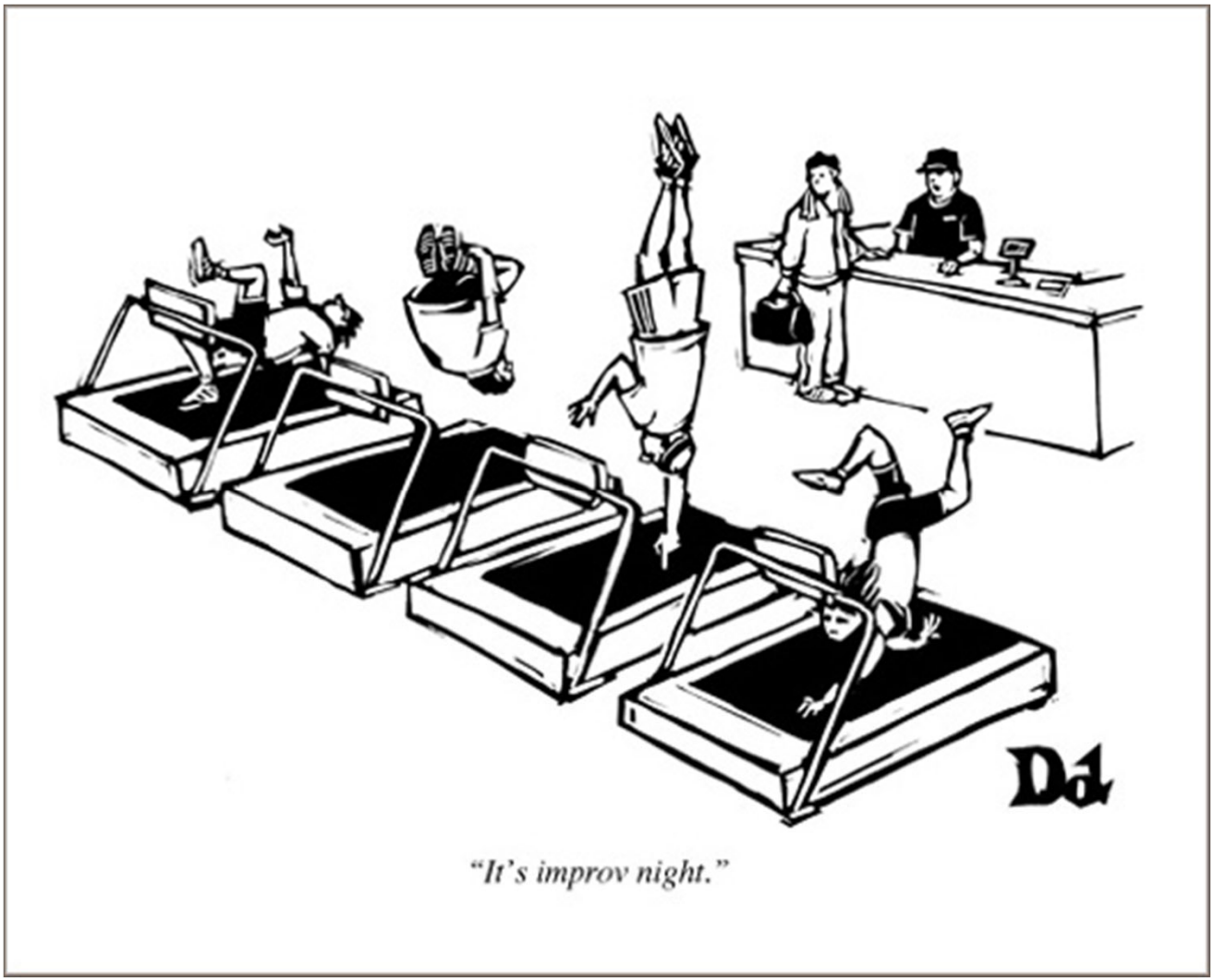




Breast cancer survivors (n=71)
MAPs
Cancer 2015;121:1231-40

Dementia caregivers (n=39)
Mantra meditation
Psychoneuroendocrinology (2013) 38, 348—355

Lonely older adults (n=40)
MBSR
Brain, Behavior, and Immunity 26 (2012) 1095–1101



"It's improv night."

COUSINS CENTER

Summary and Clinical Perspective

Sleep disturbance is a robust risk factor for depression, and this risk is amplified in association with inflammation by inducing exaggerated dysregulation of reward motivation and emotion sensitivity.

> *Actions:* Persons with sleep disturbance should be monitored for increased risk of depression, especially if sleep disturbance is persistent and/or co-morbid with an inflammatory disorder.

Sleep disturbance induces inflammation similar as the adverse effects of other lifestyle factors such as poor diet, sedentary activity, and obesity.

> *Actions:* Treatments that target sleep behaviors reduce inflammation, and could possibly mitigate risk of inflammatory disorders such as depression, dementia, or heart disease.

Summary and Clinical Perspective

Inflammation induces depressive symptoms and anhedonia, and the magnitude of the depression is shaped multiple factors including female sex, anxiety, sensitivity to social rejection, and sleep disturbance.

Action: Persons who have pre-existing sleep disturbance and experience an inflammatory challenge such as an infection should be prioritized for depression monitoring and early treatment, including therapeutic approaches that enhance reward motivation and regulate emotion.

Summary and Clinical Perspective

Mindfulness treatments are efficacious in treating insomnia and reducing depressive symptoms, with the added benefit of reversing age-related inflammation.

Action: Given that mindfulness intervention are scalable, and can be delivered at low cost with broad access, community-based programs are needed to mitigate risk of syndromal insomnia and depression, with the potential to offset adversity for chronic diseases of aging.

Acknowledgments

Awards, current and past (last 10 years) to Irwin

- NIA
  - R01 AG026364; R01AG051944; R01 AG056424; R01 HL095799; P30AG028748; R01 AG034588; R01 AG026364
- NCI
  - R01 CA160245; R01CA207130; R01CA203930; R01 CA 119159
- NHLBI
  - R01 HL095799; R01 HL079955
- NIDA
  - T32 MH19925
- NIMH
  - T32 MH19925
  - R01 DA032922
- Cousins Center for Psychoneuroimmunology

“When you run alone, you run fast.

When you run together, you run far.”

Zambian Proverb

Collaborators last 10 years

* Indicates past or current mentee

David Black* (USC)
Elizabeth Breen
Jin Cho*
Steve Cole
Patrick Finan (JHU)
Michael Hoyt* (Hunter)
Kate Kuhlman* (UCI)
David Miklowitz
Kelly Muscatell* (UNC)
Richard Olmstead
Perry Nicassio
Jonathan Savitz* (Laureate)
Michael Smith (JHU)
Chenchen Wang (Tufts)

M Bjurstrom* (Karolinska)
Emil Cocarro (U Chicago)
David Creswell* (CMU)
Cindy Ehler (Scripps)
Andrew Fuligni
Tristan Inagaki*(Pittsburgh)
Mark Laudenslager (U Co)
Mona Moieni*
Perry Nicassio
Michael Oxman (UCSD)
Christian Florey* (U Zurich)
George Slavich*
April Thames*(USC)
Karen Weihs (U Arizona)

Julienne Bower
Judith Carroll*
Mary Davis (ASU)
Naomi Eisenberger*
Patricia Ganz
Jennifer Kruse
Puja Mehta* (Emory)
Sarosh Motivala*
MF O’Connor*(U Arizona)
D Piber* (UCLA/Charite)
Kamala Thomas* (Pitzer)
Teresa Seeman
Sean Youngstedt (ASU)
Alex Zautra (ASU)

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