Practices to Tame the Flame

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FOODS
INFLAMMATION

Physical (In)Activity
Stress/ Stress Relief
Stress and Inflammation

- Psychological stress may be a trigger of inflammation
- Inflammation may be a key biological mediator linking stress and health
- Regular practice of stress reduction techniques may reduce inflammation and improve management of inflammation-related chronic diseases

Stress, Hematopoiesis and Cardiovascular Disease

Acute Stress and Cytokines

- Following laboratory-induced psychological stress, there is a modest increase in circulating inflammatory markers, esp. IL-6 and IL-1β
- Increases of these markers appear to occur after a delay
- The time course of responses has not been established


Brain and Stress-related Increase in Inflammation

- Greater amygdala activity in response to a stressor and tighter coupling between the amygdala and dorsomedial prefrontal cortex (DMPFC) are associated with greater increases in inflammatory activity

Muscatell KA et al., *Brain Behav Immun*. 2014
Mediators of Stress Response


Use of CAM in the U.S.

<table>
<thead>
<tr>
<th>Type of Therapy</th>
<th>1990</th>
<th>1997</th>
<th>2002</th>
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<tr>
<td>Relaxation Techniques</td>
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<td>16.3</td>
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<td>Yoga</td>
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</tbody>
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In 2012 8.7% Prevalence of Yoga use “aspirational yogis”

Eisenberg et al., *JAMA*, 280:1569-1575, 1998
Relaxation Response

- O₂ consumption
- Respiratory rate
- Heart rate
- Blood pressure
- Muscle tension
- Alpha waves

The Inflammatory Reflex

- The nervous system reflexively regulates the inflammatory response in real time, just as it controls heart rate, GI tract motility and secretion, pancreatic endo- & exocrine secretions, hepatic glucose production, and other vital functions

Involuntary Nervous System and Inflammation

Inhibition of synthesis of TNF, IL-1, IL-18 and other pro-inflammatory cytokines


The Inflammatory Reflex

- Afferent vagus nerve fibers sense peripheral inflammatory molecules and convey signals to the brain
- Efferent vagus nerve cholinergic neurons inhibit acute inflammation
  - Indirectly via splenic T cells
  - Directly by releasing acetylcholine

The Inflammatory Reflex

- Implicated in the suppression of inflammation in:
  - septic and hemorrhagic shock
  - inflammatory bowel disease
  - autoimmune myocarditis
  - and other inflammatory and autoimmune conditions
- Many of these disorders are associated with autonomic dysfunction and decreased vagus nerve tone
- Enhancement of vagus nerve output could have therapeutic potential in these settings

Increased Vagal Tone by Calming Practices?

- All Heart Rate Variability (HRV) components are predominantly under vagal control

Reyes del Paso GA et al., *Psychophysiology*. 2013 May;50(5):477-87
Relaxation Training Increases Parasympathetic Tone

- High frequency component of heart rate variability increased during autogenic training compared with quiet rest
- It indicates enhanced cardiac parasympathetic tone


Relaxation Response and Genomic Counter-Stress Changes

- **M**_Long-term relaxation response (RR) practice_
- **N1**_Novices with no prior RR experience_
- **N2**_Novice after 8 weeks of RR training_
  - a 20-minute elicitation of the RR
  - 8 weekly individual RR-training sessions
    1. diaphragmatic breathing
    2. body scan
    3. mantra and mindfulness meditation

Metabolic Pathways Modulated by Relaxation

Highly significant enrichment in gene sets related to various cellular stressors/stress responses and metabolism
- decreased oxidative stress
- decreased inflammation pathways


Gene Expression Changes by Relaxation Response

- After a single RR practice session - enhanced expression of genes associated with:
  - energy metabolism
  - mitochondrial function (mitochondrial ATP synthase)
  - insulin secretion
  - telomere maintenance
- RR practice reduced expression of genes linked to:
  - inflammatory response (NF-κB pathway genes)
  - stress-related pathways

Compassion Meditation May Calm Mind and Inflammation

- RCT, 63 healthy adults, 6 weeks of training
- Increased meditation practice was correlated with decreased stress-induced IL-6 and POMS distress scores


Mindfulness Meditation May Reduce Neurogenic Inflammation

49 healthy non-meditators were randomized to:

- **Mindfulness-Based Stress Reduction (MBSR)**
  - 8 weekly 2.5 hr sessions and one full day session
  - Daily at home practice 45 to 60 min

- **Control_ Health Enhancement Program (HEP)**
  - Walking
  - Balance, agility, core strength
  - Nutritional education
  - Music therapy

Mindfulness Meditation May Reduce Neurogenic Inflammation

- Successful induction of both stress and inflammation
- At post-training, compared with control participants, those randomized to mindfulness meditation group showed:
  - a smaller potentiation of the flare response
  - a steeper diurnal cortisol slope
  - lower blister fluid cytokine (TNF-α, IL-8) levels with greater time spent practicing mindfulness

Rosenkranz MA et al., Brain Behav Immun, 27 (2013) 174-184
Therapeutic Yoga

Improved Musculoskeletal and Cardiopulmonary Functions by Yoga

- Improved muscular strength and flexibility and overall physical fitness
- Reduced pain due to:
  - Osteoarthritis of the hands and carpal tunnel syndrome
  - Low back pain
  - Neck pain

Raub JA: J Altern Complement Med, 8:797-812, 2002
Yoga for Low Back Pain

- 313 adults with chronic or recurrent LBP
- 12 yoga classes over 3 months
- Scores on Roland–Morris Disability Questionnaire (RMDQ)
- Control group got education booklet and usual care
- It is cost effective intervention

Yoga Practice May Decrease Inflammation

- Novice (n=25) vs Yoga experts (n=25)
  - Yoga experts had 41% lower IL-6 levels than novices
  - Yoga experts produced less LPS-stimulated IL-6 in response to stressor than novices
  - The odds of a novice having detectable hs-CRP were 4.7 times as high as that of an expert
**Yoga Practice and Cortisol**

- **Decrease in Cortisol when aberrantly elevated** (Breast Cancer Survivors)

- **Increase in Cortisol when aberrantly decreased** (Fibromyalgia Patients)

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**Yoga and Melatonin**

Yoga practice increases night time melatonin levels and positively correlates with well-being

- **Control Group**
  - Army exercise (1 hr)
  - Played games (1 hr)

- **Yoga Group**
  - Postures (45 min)
  - Breathing (15 min)
  - Postures (15 min)
  - Breathing (15 min)
  - Meditation (30 min)

- **Duration of 3 months**

Harinath K et al., *J Altern Compl Med*, 2004, 10:261-8
Tooley GA et al., *Biol Psychol*, 2000 May;53:69-78
Reduced Inflammation and Fatigue by Yoga Practice

- RCT of 200 breast cancer survivors
- Yoga practice 90 min/twice per week x 12 weeks
- Wait-list control


Intensive Cardiac Rehabilitation Program
Dr. Ornish’s Program for Reversing Heart Disease
Paid For By Medicare & Medicare Advantage For Patients With Coronary Artery Disease & Soon For Men With Prostate Cancer On Active Surveillance And Diabetics

18 Visits of 4 hrs
- Monitored Exercise (as in standard phase 2 Cardiac Rehab)
- Nutrition Education with Lunch (Low-fat Vegetarian Diet)
- Stress Management (Yoga-based Stress Reduction)
- Support Group
Yoga and Overweight/Obesity

Enhancing Behavioral Changes

**Meditation/Yoga practice:**

- Reduces cognitive rigidity, that is, narrowing of perceived options
  - Less resistance to change in beliefs, habits, attitudes
- Enhances acceptance of emotional states → better executive control → more likely to overcome impulses and override automatic behaviors


“The only way to keep your health is to eat what you don't want, drink what you don't like, and do what you'd rather not.”

Mark Twain
*Following the Equator: A Journey Around the World*

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**Stress And Lifestyle**

![Graph showing experienced stress in past month]

Stress Less

• Eliminate the causes

• Change perception of the stress
  - Stress is often based in emotional memories and responses
  - We can modulate our responses to stressors

Brain Changes with Meditation

• Neuropathways change with practice

• Increased brain structure and function
  - Improved memory scores
  - Modulation of chronic pain
  - Decreased symptoms of stress, anxiety and depression

Hanson R and Mendius R: *Buddha’s Brain*, 2009
Emotions Reported in Meditative State

- Physical Relaxation
- Mental Quiet
- Strength and Awareness
- Joy
- Love and Thankfulness
- Timeless, Boundless, Infinite

Where Do We Go From Here?

- Prediction is very difficult, especially about the future.

Robert Storm Petersen
Niels Bohr
Mark Twain
Yogi Berra
What About Microbiome?

The Microbiota-Gut-Brain Axis

- Functional HPA axis
- Normal behaviour
- Normal nociception
- Well-being
- Dysfunctional HPA axis
- Altered behaviour
- Increased pain perception

- Balanced microbiota
- Normal gut function
- Balanced immune system
- Normal gut morphology
- Dysbiosis → Catecholamines or other neurotransmitters (e.g., GABA)
- Gut dysfunction
- Low-grade or overt inflammation
- Tissue damage

The Microbiota-Gut-Brain Axis: Communication Pathways


Calming Practices for You and Your Patients

- Experiment with:
  - Meditation
  - Guided Imagery
  - Yoga
  - Autogenic Training
  - Tai Chi
  - Biofeedback

- Evolution vs. Revolution

- Take classes - Center for Lifestyle Medicine
  877-331-9355 or Lifestylemed@ccf.org
Redefine Your Lifestyle
A WEEKEND RETREAT

Enhance Your Life — Experience the Joy of Health!

Join Cleveland Clinic Center for Lifestyle Medicine experts for an exclusive weekend retreat: Redefine Your Lifestyle.

The focus will be on you as we help you improve your health. You’ll leave feeling better — inside and out.

Over the three-day weekend, you’ll experience firsthand our unique approach to lifestyle change ... and learn how to do it on your own!

We promise the weekend will positively enhance your lifestyle.

To register, call 877.331.WELL (9355) or email lifestylemed@ccf.org.

StressFreeNow

Stress Free Now is a clinically-based online program developed by experts at the world-renowned Cleveland Clinic. This six-week program is based on mindfulness practice, which is what research shows is most effective in mitigating the impact of stress on your quality of life. It contains the tools you need to reduce stress, reduce your risk of developing stress-related diseases, and improve your well-being and your health.

Findings from the 2010 Stress in America survey show that the majority of Americans are living with moderate or high levels of stress. Isn’t it time you took control of your stress? Or take control of your stress - today.

By following this program, you will become more in control of your stress, reduce your risk of developing stress-related diseases and live a happier, more fulfilling life.

A healthy you is just a click away
Your FREE Gift! Sign up and get a FREE Stress Free Now CD ($19.99 value)

http://www.clevelandclinicwellness.com

Summary

• Communication between the brain and immune system is vital for controlling inflammation

• Yoga, meditation, biofeedback, autogenic training and other practices that elicit relaxation response may have anti-inflammatory effects

• These calming practices are safe, easy to learn and do not interfere with other treatments of patients with chronic inflammation-related diseases
"You must first be the change you wish to see in the world."

*Mahatma Gandhi*