Seven Scientifically Proven Anti-Inflammatory Strategies for Today’s Modern Mental Health Practice

A Brief Introduction

What’s so bad about inflammation?

What Do We Mean by Increased Inflammation in Psychiatric Conditions?

The “Truth” about Depression as an Inflammatory Condition

What’s So Bad about Mildly Increased Inflammation When Chronic?

Chronic mild inflammation today increases the risk of the following in the future:

- Major depression
- Posttraumatic stress disorder (PTSD)
- Premature aging
- Cardiovascular disease
- Stroke
- Diabetes
- Cancer
- Dementia

Anti-inflammatory Strategy #1

Probiotics

Probiotics and MDD: Quite the Buzz

MDD = major depressive disorder.

Brave Mice and Timid Mice

NIH Swiss = “bold”

Transfer of Microbiota Transfers Behavior between Mouse Strains

BDNF = brain-derived neurotrophic factor.

Depression May Be (Partly) a Matter of “Gut Feelings”

The gut microbiotas of 58 medically-healthy depressed individuals were compared with those of 63 matched controls. Depression was associated with increased Actinobacteria and decreased Bacteroidetes, and increased and decreased operational taxonomic units within Firmicutes. Transplantation of microbiota from depressed individuals to germ-free mice produced depressive- and anxiety-like behavior compared to transplantation of microbiota from control participants.

Probiotics Reduced Negative Emotionality in Normal Volunteers

In 55 medically-healthy volunteers a probiotic formulation of Lactobacillus helveticus and Bifidobacterium longum R0175 taken for 30 days reduced depression, anxiety, and other negative emotions when compared to placebo. But note that baseline scores on these items were low and differences between groups were modest.
Probiotics May Reduce Anxiety But Not Depression in Chronic Fatigue Syndrome

In 39 participants with chronic fatigue syndrome randomized to L. casei strain Shirota vs placebo, 8 weeks of probiotic treatment increased stool samples of beneficial bacteria and was associated with a reduction in anxiety but not depressive symptoms.

BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory.


Probiotics May Improve Symptoms in MDD

40 participants with major depressive disorder randomized to 8 weeks of a probiotic formulation (L. acidophilus, L. casei, B. bifidum) vs placebo. Outcomes included depressive symptoms, CRP, insulin sensitivity, and antioxidant capacity.

HOMA = homeostatic model assessment; IR = insulin resistance; hs-CRP = high-sensitivity C-reactive protein; GSH = glutathione.


Birth by C-Section: An Anti-probiotic Strategy Par Excellence

Birth by C-Section produces a profound change in the infant microbiota, characterized by reduced maternal vaginal flora and increased skin flora.

Birth by C-Section is associated with an increased risk of asthma, allergic rhinitis, childhood obesity, systemic connective tissue disorders, juvenile arthritis, inflammatory bowel disease, immune deficiencies, leukemia and type 1 diabetes.


Exposure to Maternal Vaginal Fluid Normalizes Microbiota of C-Section Babies


Anti-inflammatory Strategy #2

Calorie Restriction/Intermittent Fasting

Web Site for Probiotic Formulations

http://usprobioticguide.com/
### Methods of Eating Less

<table>
<thead>
<tr>
<th>Type of fasting</th>
<th>Characteristic</th>
<th>Main effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified therapeutic fasting</td>
<td>Caloric intake 200–500 kcal/day by formula or liquid meal</td>
<td>Rapid weight loss, strong anorectic response</td>
</tr>
<tr>
<td>Very low-calorie diet</td>
<td>Caloric intake 500–800 kcal/day by formula liquid meals, protein supplements</td>
<td>Rapid weight loss</td>
</tr>
<tr>
<td>Caloric restriction</td>
<td>Experimental models; long-term adaptation to undernutrition</td>
<td>Increasing levels of leptin, reduced energy expenditure, improved functional indices</td>
</tr>
<tr>
<td>Continuous caloric restriction</td>
<td>30–40% daily reduction in calorie intake</td>
<td>Increase in levels of leptin, reduced energy expenditure, improved functional indices</td>
</tr>
<tr>
<td>Intermittent fasting</td>
<td>Alternate-day fasting (24 h)</td>
<td>Increase in levels of leptin, reduced energy expenditure, improved functional indices</td>
</tr>
<tr>
<td>Total fasting</td>
<td>4% caloric intake; water and tea ad libitum</td>
<td>Rapid weight loss, pronounced protein catabolism; numerous adverse effects</td>
</tr>
</tbody>
</table>

---

### Fasting/Calorie Restriction May Improve Mood and Reduce Anxiety


### Similar Physiological Benefits for Exercise and Intermittent Fasting


### 24-Hour Fast Decreases NLRP3 Inflammasome Activity


### Specific Suggestions on Utilizing this Anti-inflammatory Strategy

<table>
<thead>
<tr>
<th>Chronic Calorie Restriction</th>
<th>Fasting</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Set realistic goals</td>
<td>• Experiment with brief fasting periods first (i.e., 12 hours)</td>
</tr>
<tr>
<td>• Attempt to reduce daily calorie intake by 10% initially, if successful consider increasing to 25% depending on food intake at baseline</td>
<td>• Restricting intake to 300 to 500 calories on fasting days quite effective</td>
</tr>
<tr>
<td>• Hydrate aggressively</td>
<td>• If successful consider up to 24 hours of fasting with nothing but water</td>
</tr>
<tr>
<td>• Time the calorie content of your meals to match natural hunger cycles</td>
<td>• Try fasting at least 2 days per week</td>
</tr>
<tr>
<td>• Do not over-restrict</td>
<td></td>
</tr>
</tbody>
</table>

---

**Anti-inflammatory Strategy #3**

Sleep Away Your Inflammation
IL-6 May Be Elevated in Insomnia Patients: A Preliminary Finding

Induced cytokine levels (ng/mL) before the strike (left dot of each line) and after it (right dot) in 10 anesthesiologists. Presented are IL-6 in which significant decline was evident.

Study examined the interplay of social engagement, sleep quality, and plasma levels of IL-6 in a sample of aging women (N = 74; aged 67–90 years, mean age = 73.4). Sleep was assessed by using the NightCap in-home sleep monitoring system. The interaction significantly predicted plasma IL-6 levels (β = 1.19, P < .05).

**Sleep Deprivation and Inflammatory Marker CRP – Reason for Concern**

**Good Sleep Benefits Inflammatory Response**

**Shift Work May Impact Inflammatory Response**

**Autonomic, Endocrine, and Immune Imbalance in Insomnia**

Associations between environmental stress, life events, and insomnia, activation of peripheral inflammation, and increases in central inflammatory signaling, which together are thought to contribute the occurrence of somatic symptoms of pain or hyperalgesia, sleep disturbance, and fatigue.
Sleep and Social Support Interact to Modulate Inflammation

PSQI global scores predicting IL-6 and CRP. The statistical interaction between PSQI and social support is shown here using mean social support and low social support modeled at 1 SD below the mean of the sample. Participants were 67 sedentary men (n = 37) and women (n = 30).

PSQI = Pittsburgh Sleep Quality Index.

Good Sleep May Mitigate the Pro-inflammatory Effect of Poor Relationships?

Top ("high relations") and bottom ("low relations") tertiles of scores from the positive relations scale.


CBT for Insomnia May Provide an Enduring Anti-inflammatory Benefit

As compared with sleep seminar education active control condition. CBT-I reduced levels of CRP (months 4 and 16, P < .05), monocyte production of pro-inflammatory cytokines (month 2 only, P < .05). 123 older adults with insomnia were randomly assigned to CBT-I, TCC, or sleep seminar education active control condition for 2-hour sessions weekly over 4 months with follow-up at 7 and 16 months.


Conclusions

• Sleep disorders and sleep deprivation may be associated with increased inflammatory signaling
• Sleep disorders should be assessed along with other medical and psychiatric disorders at diagnosis and treated simultaneously
• Sleep of adequate quantity and quality may help ameliorate excessive inflammatory tone
• Preliminary evidence suggests that CBT-I may provide a sustained anti-inflammatory benefit

Anti-inflammatory Strategy #4

You Cannot Run Away from Inflammation, or Can You?


Neurobiology of Exercise: A Complex Cascade That Also Involves Neurotransmitters and Receptors

ANS = autonomic nervous system; CNS = central nervous system; CREB = cyclic adenosine monophosphate response element-binding protein; CVD = cardiovascular disease; DA = dopamine; ERK = extracellular signal-regulated kinase; 5-HT = serotonin; ROS = reactive oxygen species; TrkB = tyrosine residue kinase receptor-type 2; VTA = ventral tegmental area; WAT = white adipose tissue.

**Anti-inflammatory and Cardiovascular Benefits of Exercise**

EC = endothelium; NO = nitric oxide; PAI = plasminogen activator inhibitor; PLT = platelet; RBC = red blood cell; sCD40L = soluble CD40 ligand; TF = tissue factor; tPA = tissue plasminogen activator.


**Exercise: Effects on Immune System, Skeletal System, Adipose Tissue, and Brain**

**Exercise and Cytokines: A Complex Relationship**

FFA = free fatty acids; ROS = reactive oxygen species.


**Physical Exercise: A Modulator of Inflammatory Cytokines**


**Not So Fast? Anti-inflammatories May Interfere with Exercise Induced Muscle Protein Synthesis**

*Significantly different (P < .05) from PLA. PGs have been shown to modulate skeletal muscle protein metabolism as well as inflammation and pain. Ibuprofen and acetaminophen inhibit the normal increase in skeletal muscle protein synthesis after high intensity eccentric-resistance exercise. 24 males (25 ± 3 yr) were assigned to 3 groups that received IBU (1200 mg/day), ACET (4000 mg/day), or a placebo after 10 to 14 sets of 10 eccentric repetitions at 120% of concentric 1 repetition maximum using the knee extensors.


**Exercise May Mitigate Inflammatory Signaling in MDD**

107 participants, aged ≥ 40 years

Participation in moderate-intensity physical activity may buffer the risk of higher inflammation often associated with higher levels of depressive symptoms

Conclusions and Recommendations

- Exercise has an established anti-inflammatory effect thereby promoting general health and well-being, while ameliorating symptoms of psychiatric disorders
- For general health, adults should achieve a minimum of 30 minutes/day, of at least moderate intensity, on ≥ 5 days of the week

Anti-inflammatory Strategy #5
Increasing Socialization

Association between Childhood Social Isolation and Inflammation in Adulthood

Study used multiply-imputed data on 7462 participants of the National Child Development Study in the United Kingdom

Socially isolated children had higher levels of CRP in mid-life.

Volunteering and Lower Inflammation

Representative survey of adults aged 57–85 years from the National Social Life, Health, and Aging Project (N = 1790). Study investigates whether productive activities by older adults reduce bodily inflammation.

Productive activities—and frequent volunteering in particular—may protect individuals from inflammation.

Social Network Ties and Inflammation

Lower SNI (Social Network Index) scores showed significantly greater inflammation marked by CRP and Fibrinogen.
Specific Suggestions on Utilizing This Anti-inflammatory Strategy

"Macro" Socialization
- Increase Quality and Quantity of Social Connections
- Create / Nurture – Meaningful, supportive, stimulating relationships
- Increase (not decrease) macro socialization when early stress is detected

"Micro" Socialization
- Text and e-mail connectedness (not to replace macro socialization, but to augment it)
- Do more “chit-chatting” with strangers and people you bump into in a variety of everyday situations
- Smile (a lot!)

Specific Suggestions on Utilizing This Anti-inflammatory Strategy

Tools:
Here are some tools you could utilize –

Want to measure Social Connectedness?

Want to educate patients about the importance of Social Connectedness?

Access Patient Educational booklet on Social Connectedness here – www.wildresources.com
Password: wellnessmatters

We Indeed are What We Eat: Impact of Our Diets on Inflammation

Summary:
Dietary practices that are more Mediterranean-like may be associated with lower levels of systemic inflammation.

Are We What We Eat? Emerging Scientific Data on Nutrition and Health (Risks/Benefits)

Review of 304 studies examining the link between nutrition and chronic diseases (mental health, obesity, skeletal health, cardiovascular disease, cancers)

Radar plots for food groups and beverages vs number of references (percentages from 0% to 100% shown on concentric circles) showing protective (solid green lines), neutral (dashed yellow lines), or deleterious (dotted red lines) effects towards all diet-related chronic diseases.


Specific Suggestions on Utilizing This Anti-inflammatory Strategy

"Macro" Nutritional Changes
- Sugars/Simple carbs = OUT
- ↑ Vegetables! By a lot
- ↑ Nuts! By a lot
- ↑ Fish! By a lot
- Moderate red meats

"Micro" Nutritional Changes
- Data supports following micro-nutrients as antidepressants and as anti-inflammatoriey
  - Vitamin D
  - L-methylfolate
  - SAMe
  - Omega-3 fatty acids
Tools to Incorporate This Anti-inflammatory Intervention into Your Practice

### Meditative Practice & Therapeutic Benefits in Inflammatory Situations

Both Psychological and Physical Stressors

- AA = alpha-amylase; LTM = long-term meditators; MNP = meditation-naive participants; TSST = Trier Social Stress Test.


<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>TSST</th>
<th>Perceived Stress</th>
<th>Cortisol</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTM</td>
<td>1.2</td>
<td>1.0</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>MNP</td>
<td>1.3</td>
<td>1.1</td>
<td>1.5</td>
<td>1.6</td>
</tr>
</tbody>
</table>

**RESULTS:**
- LTM had lower TSST-evoked cortisol ($P < .05$) and perceived stress ($P < .01$).
- Smaller neurogenic inflammatory response ($P < .05$).
- LTM reported higher levels of psychological factors associated with well-being and resilience.
- LTM practice may reduce stress reactivity and be of therapeutic benefit in chronic inflammatory conditions characterized by neurogenic inflammation.

---

### Mindfulness: Acts as an Anti-inflammatory Agent with Exposure to Stressors


<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>TSST</th>
<th>Cortisol</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBSR</td>
<td>1.4</td>
<td>1.3</td>
<td>1.1</td>
</tr>
<tr>
<td>HEP</td>
<td>1.5</td>
<td>1.4</td>
<td>1.2</td>
</tr>
</tbody>
</table>

**RESULTS:** MBSR resulted in a significantly smaller post-stress inflammatory response compared to HEP, despite equivalent levels of stress hormones.

---

### Specific Suggestions on Utilizing This Anti-inflammatory Strategy

**Initiate Practice**
- Teach this – there is no perfect way to practice mindful meditation. Teach – “You can’t do it ‘imperfectly.’”
- Offer an app / CD
- Recommend daily practice
- Amount – short! As little as 8 to 15 minutes a day is a great start

**Maintain Practice**
- Do not just recommend and run! At regular intervals check to see if mindfulness practice is being maintained.
- Be a gentle coach. Remind them of the Biological and Clinical studies demonstrating Mindfulness’ benefits.
- Recommend increasing practice with early sign of stress.

---

### Tools

Access Patient Educational booklet on Mindfulness and Audio Files of all the Mindfulness practices here – www.wild5resources.com.
Password: wellnessmatters.

---

**Anti-inflammatory Strategy #7**

**Mindfulness**
Mindfulness Meditations

WILD 5 Wellness Program


CD OR DOWNLOAD

Disc One: Tracks 1 through 6:
1. Five-Minute Breathing Space (6:45)
2. Mindful Breathing (15:09)
3. Body Scan (13:56)
4. A Moment of Gratitude (9:58)
5. Happiness Meditation (11:37)
6. Pain Meditation (13:35)

Disc Two: Tracks 1 through 3:
1. Introduction to Mindful Meal Meditation (5:19)
2. Mindful Meal Meditation (23:31)
3. Mindful Moment With A Raisin (5:17)

In Conclusion:

1. For most of our patients (and ourselves) learning to eat less is one of the most powerful anti-inflammatory strategies available
2. Optimized sleep and physical exercise have both demonstrated anti-inflammatory effects and incorporating them into daily practice is critical
3. Practical, actionable recommendations on each of these 7 anti-inflammatory can, and should be offered to our patients. All 7 of these recommendations work through various pathways to improve outcomes