Understanding Energy and Fatigue: Focus on Stress, Habits, and the Brain

Presented by

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Disclosure
Neither Dr. William J. Sieber, the presenting speaker, nor the activity planners of this program are aware of any actual, potential or perceived conflict of interest

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COURSE OBJECTIVES

Participants completing this new 6-hour program should be able to:

1. *Describe how stress-related fatigue affects the brain and body.*
2. *Identify how hormone imbalance can produce fatigue.*
3. *Discuss how diet, drugs and herbs affect fatigue.*
4. *Discuss how inflammation can induce fatigue and lower mood.*
5. *List several evidence-based strategies to improve sleep.*
6. *Identify key habits to optimize energy and reduce fatigue.*

Policies and Procedures

1. Questions are encouraged. However, please try to ask questions related to the topic being discussed. You may ask your question by clicking on "chat." Your questions will be communicated to the presenter during the breaks. Dr. Sieber will be providing registrants with information as to how to reach him by email for questions after the day of the live broadcast.

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6. **IMPORTANT: Your certificate of completion will be available by email, mail or fax following receipt of your fully completed evaluation form.** If you request the certificate by mail, it will be mailed within 2 business days upon receipt of your fully completed evaluation form.

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9:00 – Introductions, expectations, and assumptions

Activity log and fatigue assessment

Epidemic of Sleep Deprivation and fatigue:

- In 1960 surveys showed the average American adult slept 8.5 hours per night, in 1995 surveys showed that average had dropped to 7 hours nightly, and a survey in 2008 showed that more than 30% of American adults reported less than six hours on average. 20% report insomnia or severe sleep disturbance
- Sleep problems in developing countries is approaching those in developed nations.
- Up to 10% of primary care patients have fatigue as their primary complaint; 50% or more of these patients fail to improve within one year.

Common conditions with "fatigue" as a symptom

- Allergic rhinitis
- Anemia - the most common blood condition in the U.S. affecting about 3.5 million Americans.
- Depression – annual prevalence rates that hover around 10%
- Anxiety – recently reported as more prevalent in primary care than depression
- Food allergies/intolerance
- Heart and lung disease
- Rheumatoid arthritis, Fibromyalgia, and other types of chronic pain
- Sleep apnea
- Type 2 diabetes
- Hypothyroidism. Approximately 17% of all women will have a thyroid disorder by age 60, and most won't know it.
- Medication: analgesics, psychotropics, anti-hypertensives, anti-histamines.

The biology of fatigue

- **Mitochondria and energy production**
    - Mitochondria are highly dynamic organelles. Mitochondrial dysfunction in the brain is associated with neurodegenerative diseases such as Alzheimer's Parkinson's and ALS.
    - Mitochondrial energy metabolism: In each cell glucose is broken down to pyruvate, pyruvate enters the mitochondria of each cell, in the cell the Kreb's cycle which produces some ATP and the electron transport chain (which requires significant oxygen to operate)

regenerates ATP. So almost 30 molecules of ATP are produced per molecule of glucose and these provide the energy for living.
    - Wealth of data showing that mitochondrial dysfunction is responsible for production of reactive oxygen species (ROS; oxidation), one factor promoting aging. Oxidative stress, and telomere dependent senescence is affected by mitochrondria activity. Shortening of telomeres (ends of chromosomes) affect the senescence of cells, and thus serve as a biological clock counting the number of divisions (telomere shortening). Several studies support that the average telomere length is better maintained in conditions of low oxidative stress (or better mitochondrial function).

- **Hormones & fatigue**:
    - Cortisol: low at night with 7-fold increase in the morning;,
    - Thyroid
        - Hyperthyroidism - Up to 90% of hyperthyroidism is caused by Grave's disease (thought to be autoimmune process related to Hashimoto's), with women affected more than men from 4:1 to 10:1. Half of patients with abnormal thyroid function report fatigue and weakness.
        - Hypothyroidism – diagnosed with elevated TSH, more common with advancing age, affecting 7% of those over age 55. Hypothyroidism associated with weakness, fatigue, memory loss, slowed thinking, and depression.
    - Insulin, ghrelin and leptin

- **Organ function and fatigue**
    - **Heart**: fatigue-related warning symptoms suggestive of CVD work-up: painful breath, SOB, edema, dizziness
    - **Kidney:** fatigue related to excess creatinine and poor filtration may also be associated with fever, frequent infections, weight loss, thirst, frequent urination.
    - **Liver:** Liver function affects fatigue via glucohomeostasis and protein malnutrition

Creating Energy: Expending energy (behavior) increases the number of the energy-producing mitochondria
    - Skeletal muscles are ideal locations to assess Adenosine triphosphate (ATP) production. Decreased mitochondrial activity, and thus ATP activity, suggests a mitochondrial disorder and is most often seen in physically inactive, otherwise healthy subjects.

- Aging results in reduced mitochondrial function (and insulin sensitivity) though not clear if this is due to age or inactivity; exercise clearly increases mitochrondrial function. Vicious cycle of sedentary lifestyle leads to decreased mitochondrial function, decreasing spontaneous physical activity, further decreasing mitochondrial function to the point of fatigue and impairment.

- Sleep & Sleep cycles
  - Spousal caregivers showed more 'wake time after sleep onset' and this was associated with elevation of a marker of CVD

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MORNING BREAK

- 24 hour behaviors pattern assessment
    - Alcohol & Caffeine
    - Activity
    - Pre-bed routine
    - Alarm clocks and light
- 700 nurses with "adverse work schedules" were compared to 1000 with favorable work schedules and while both groups showed overweight/obesity at 55% those with adverse schedules to less sleep, less exercise and more often were caregivers, whereas those with favorable work schedules smoke and drank more.
- Light exposure at night for 4 weeks increases cytokines which cause inflammation. This inflammation is associated with signs of depression, yet diminishes after two weeks of return to normal light cycles.

Improving Sleep:

- Sleep hygiene, sleep restriction, and stimulus control
    - The goal is "sleep efficiency", not total sleep time
    - Developing a regular rising time, then compressing sleep time for efficiency

The "Gut Brain"

- Enteric Nervous System: The enteric nervous system (ENS) is referred as to the "second brain" because of its capability to function in the absence of

nerve inputs from the central nervous system. The ENS is found in the gut wall and extends from the esophagus to the anal sphincter.

- Gastric intestinal symptoms often seen in diabetes are due in part to diabetic neuropathy, yet neuropathy in the GI tract differs from segment to segment in the GI tract.

- **Stress-Related Eating**:
  - Hyperglycemia stimulates oxidative stress, a driving force in atherosclerosis.
  - Dr. E. Epel reported that for women only the combination of cortisol and carbohydrates increases midline weight gain, leading to inflammation and fatigue.

- **Outsmarting the "Gut Brain" With Nutrients**:
  - Energy drinks – US estimate of $744 million spent annually on energy drinks. Doses of caffeine found in energy drinks can range from 80 to 300 mg in an 8-ounce serving. While the FDA presently regulates caffeine in soft drinks to a maximum of 65 mg per 12 ounces, energy drinks are not subjected to the same regulations. Guarana seeds contain three times more caffeine compared to coffee beans. 16 – 24 ounce drinks also contain up to 90 grams of sugar. Over 25% of adults reported using energy drinks in previous year, with 6% alcohol and energy drinks consumers – these drinkers were more often likely to be hazardous drinkers.
  - Caffeine - The combination of fluid loss from sweating during exercise with the diuretic effect of caffeine causes increased risk of dehydration. Caffeine intensifies dopamine receptors, resulting in stimulation of the cardiovascular system. Long-term caffeine consumption has also been linked to cardiovascular disease and fibrocystic breast disease.
  - The adiposity hormones, leptin and ghrelin, regulate short-term food intake to achieve long-term energy balance.
  - Some women added 3 apples or three pears or three oatmeal cookies per day for 10 weeks; results showed a significant decrease in weight for the apples and pears compared to the cookies, where intake/eating significantly decreased for the fruit groups (nearly 2 pound weight loss for the fruit group
  - Benefits of multiple small meals and slower consumption = fewer calories consumed due to absorption in the gut of 40% of meal empties into the intestine before meal termination.
  - Gastric satiation is volumetric, while intestinal satiation is nutritive. Gastric satiation signals arise primarily from mechanical distention, whereas those from the intestine derive largely from the chemical

effects of food. Cholecystokinin (CCK) from the intestine signals satiety and is secreted in response to fats and proteins.
    - Solid high-protein meals suppressed hunger 3 hours after ingestion whereas liquid high-protein resulted in satiety lasting only half as long
- **Ghrelin**
    - Ghrelin is a peptide produced by the stomach and increases food intake; circulating levels surge shortly before meals and is suppressed by ingestion of nutrients carbohydrates, then proteins, then fats, (in that order)
    - Sympathetic nervous system activation increases levels of ghrelin. Chronic ghrelin administration increases body weight via diverse, concerted actions on food intake, energy expenditure, and fuel utilization.
    - Ghrelin exerts neuroendocrine effects on energy metabolism, with glucose and crude fiber both markedly inhibiting ghrelin production; lipid ingestion leads to a smaller decline in ghrelin; estrogen leads to increase in ghrelin levels.
    - Social stress increase intake of high fats due to signaling of greater ghrelin during such stress.
    - A crossover feeding trial (n=164) compared 3 diets, each rich in a different macronutrient (carbohydrates, fats, proteins). A diet rich in protein from lean meat and vegetables reduced self-reported appetite more compared to a diet rich in carbohydrate and fat.
    - On 2 separate occasions 46 participants consumed a 380 calorie milkshake under the pretense it was either a 620-calorie "indulgence" or a 140-calorie "sensible" shake. Ghrelin was measured via blood samples at 3 time points: baseline, anticipatory (60 minutes) and post-consumption (90 minutes). The mindset of "indulgence" produced a dramatically steeper decline in ghrelin after consuming the shake. Participants' satiety was consistent with what they believed they were consuming rather than the actual nutritional value of what they consumed.

- **Foods that help or hinder the inflammation process and fatigue**
    - sources of omega-3s, anti-inflammatory spices (e.g., garlic, turmeric, curcumin), green tea, red wine and dark chocolate
    - Tyrosine
    - Obesity is pro-inflammatory, and inflammatory cytokines can lower mood.

- Inflammatory cytokines signal inflammation and alter glucose metabolism in brain centers that involve depression, namely the cingulate gyrus.
- Omega 3 & 6s have to be taken in through food ingested.
    - Omega 3 fatty acids are anti-inflammatory (linseed oil, nuts, soya beans, wheat, and cold water fish.
    - Omega 6 fatty acids are pro-inflammatory (maize, sunflower oil and sesame oil).
    - Omega 3's shown to reduce depression while Omega 6's induce feelings of social isolation, depression and increase the risk of suicide.
    - Omega 6: Omega 3 ratios most predictive of inflammation.
    - It is argued that increased rates of depression in the Western world in the past century is due in part to changing diet from fish, game and vegetables to greater use of cereal (corn, wheat) and cereal oils. However there is an association between very low cholesterol levels and depression.
    - Study of 68 medical students who received Omega-3 supplements showed a 20% reduction in anxiety symptoms and 14% reduction in inflammation

- **Additional nutritional and eating behavior tips for increased energy**:
    - Low-glycemic foods maintain stable blood sugar
    - Flaxseed increases satiety, fullness and decreased food intake
    - Tryptophan-rich (e.g., nut butters) and melatonin-rich foods help regulate the sleep-wake rhythm (walnuts, cherries, dairy products)

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LUNCH

Stress, inflammation, cardiovascular disease and fatigue:

- Stress and models for understanding the effect of stress on our lives.
- Studies of limbic structures in psychiatric disorders suggest abnormal regional cerebral blood flow (rCBF) is associated with specific emotional states related to stress such as fear and anger.
- The pathway most often studied connecting stress with negative health outcomes is the hypothalamic-pituitary-adrenal (HPA) axis. This sequence involves the hypothalamus releasing corticotropin releasing hormone (CRH) to the pituitary, which then releases adrenocorticotropin hormone (ACTH) and beta-endorphins into the circulation. ACTH activates the adrenal cortex, which responds by releasing cortisol into circulation. The hypothalamus also activates the adrenal medulla which releases catecholamines (epinephrine and norepinephrine), these in turn increasing glucose utilization and cardiovascular tone, while suppressing digestion. The hypothalamus also causes the release of enkephalins (endogenous opiods) that increase analgesia often seen as a benefit during extremely stressful events.
- Prolonged HPA activation, often the result of hyper-vigilance secondary to a traumatic event impairs sleep and reduces sleep quality. In addition, chronic stress can result in hormonal imbalances and impact thyroid function. Thyroid irregularities may also cause fatigue. A low thyroid level can cause fatigue, weakness, lethargy, weight gain, and depression; high thyroid levels can cause fatigue, though paired with weight loss, increased heart rate, and anxiety.

- The role of stress-related symptoms are vital for survival, yet the sustained nature of such symptoms cause significant distress. Cortisol in the short term improves learning and memory, suppresses digestion, increases cardiovascular tone, and increases glucose utilization. However, chronic activation leads to cardiomyopathy, digestive disorders, damage to the hippocampus resulting in cognitive/emotional impairment, and immune-mediated disorders.

    1. There are multiple direct and indirect pathways connecting stress and cardiovascular disease (CVD)
        a. Direct effects of stress on blood pressure and CVD outcomes
            i. Elevated blood pressure and family history of hypertension predict cardiovascular response to stress.
            ii. Increased testosterone, cortisol, and cholesterol.
            iii. Poor vagal tone and decreased heart rate variability predict poor CVD outcomes over time.
        b. Indirect effects of stress on behaviors that lead to CVD

i. Increases in unhealthy behaviors (e.g., eating, drinking, smoking).
ii. Chronic cynical hostility is the most important factor in the stress-CVD link, and can be self-perpetuating in that moods influence expectations that in turn influence future behavior and relationships (i.e., poor listening).

2. Minimizing the impact of stress on cardiovascular disease
    a. Reduce hostility. Research suggests multiple skills provide cool relief from the heat of anger. Understanding how to "use" anger and shorten its 'life cycle' is critical to minimizing the impact of stress-related anger on heart health.
    b. Practice the AAA model. Starting with **A**wareness one must decide to **A**ct if there are options to exert primary control, or **A**ccept if secondary control is all that's available. Studies consistently show positive health outcomes for those who not only enjoy high levels of perceived control, but who can quickly engage in cognitive strategies to maintain perceived control.
    c. Create and maintain an optimistic attitude. Studies show that beyond lowering anger, anxiety, and depression, people who maintain a positive outlook have fewer cardiac events than those with more pessimistic attitudes.
    d. "Listen" to your health behaviors & enjoy healthy pleasures. Small changes over time predict better health than any single factor or attempts to make significant changes in one's life. "**Moments of separation"** between stressful events, utilizing SMART goal-setting, and cognitive flexibility all play critical roles maintaining heart health. Sometimes self-assessment is sufficient to initiate healthful change.
    e. "Connect" inside and out. Social support has been identified as a primary factor in healthy aging, just as being self-aware and self-assured predicts health throughout our lifespan.

- **Stress and the Brain**:
    - fMRI studies have shown how stress hormones hydrocortisone and noradrenaline shut down activity in prefrontal cortex and thus goal-directed behavior, impairs the hippocampus, amygdala and prefrontal cortex, resulting in poor memory, sleep and mood.

Inflammation

- **Common Sources of Chronic Inflammation**:
    - amyloid, arterial, and dental plaque

- chronic infections
- abdominal fat

- **Chronic Inflammation and Depression**: inflammation from stress-related midline fat lowers mood in 2 ways: reduction of serotonin synthesis in the gut, and immune system cytokines that affect the prefrontal cortex and limbic system.

- **Inflammation and Chronic Fatigue Syndrome:**

  - Chronic fatigue syndrome is characterized by a state of constant fatigue, as well as exhaustion after completion of simple tasks. Symptoms include: fatigue for >6 months, dull headaches, joint and muscle aches, fever and chills, sleep disturbances, tender lymph glands, and depression. Course often includes acute infection followed by exhaustion and chronic fatigue. Immune and endocrine abnormalities have been reported. Women account for 65-80% of CFS.
    - Stressful events and CFS. One hypothesis is that metabolism of CFS patients is normal and symptoms are due to psychological factors, yet mental fatigue is considered lack of motivation yet the brain is major consumer of resting cellular energy.
    - Parental physical abuse, childhood GI symptoms, and parental reports of many colds each had ORs > 1.6 for patients with CFS.
    - CFS is characterized by severe and disabling fatigue for more than six months that cannot be explained medically. There is very poor stamina and delayed post-exertional fatigue, both physical and mental fatigue.
    - Differential diagnosis and the role of chronic stress. Large study of over 18,000 patients diagnosed with fatigue symptoms between 1988 & 2011 found those diagnosed with myalgic encephalomyelitis had significantly poorer prognosis than those with CFS .
    - In response to peripheral infection, innate immune cells produce pro-inflammatory cytokines that act on the brain to cause sickness behavior. When activation of the peripheral immune system continues unabated, such as during systemic infections, cancer or autoimmune disorders, the ensuing immune signaling to the brain can lead to exacerbation of depression. This may be why depressive symptoms such as fatigue, reduced interest, and low mood are more prevalent in physically ill people. Inflammation is an important risk factor for depressive disorders.
    - Prolonged stress elevations paired with compromised compensatory recovery systems can result in autoimmunity.

When gluccocorticoids are released as part of short term stress they destroy weaker (older) lymphocytes, whereas prolonged stress elevations lead to indiscriminate destruction of lymphocytes. Repeated cycles of prolonged severe stress thus tend to increase the baseline immune response (i.e., recovery to baseline is rarely accomplished) increasing the likelihood of autoimmune disorders such as rheumatoid arthritis and lupus.

- CFS patients with post-infective fatigue had gene expression profiles of "altered host response" compared to those who recovered quickly (Non-CFS patients), with most of these genes affecting mitochondrial functions. It remains unclear whether post-infective fatigue reflects chronic effects of persistent Epstein Barr Virus (EBV) or whether acute EBV infection functions as a stressor that triggers an altered host response to the virus leading to ongoing symptoms. The subjects in one study who did not recover from mononucleosis had altered gene expression during early phase EBV infection that led to changes in mitochondrial abnormalities in fatty acid metabolism.
- EBV and other viral proteins release pro-inflammatory cytokines that contribute to fatigue, fever, aching, sleep disturbance and inactivity. Acute viral infections stimulate T cell development, chronic infections may lead to immune exhaustion particularly of CD8 T cells; reduced CD8 T cells and NK cytotoxicity was lower in patients with CFS
- Xenotropic retrovirus is NOT linked to CFS as the assays used to measure this connection are unreliable
- Interventions usually incorporate a program in which level of activity is gradually increased, while dysfunctional beliefs are challenged. Outcomes are predicted by a decrease in 'perceived problems with activity' and increase in sense of control over fatigue. Patients with CFS tend to perceive substantial problems with activity independent of their own objective performance and see CFS as uncontrollable. A change in perceived problems with activity challenges this and leads to some symptom relief.
- Patients may have negative symptom beliefs that exacerbate symptoms, resulting in exacerbation of fatigue due to energy wasting by stress, anxiety and tension. An alternative hypothesis is that there is a metabolic dysfunction in which not enough energy is produced. Main source of energy comes from oxidation of glucose in food. If there is a problem with the digestive system then glucose and fatty acids and amino acids are not produced. This insufficient energy production then leads to fatigue. When the digestive system is operating properly glucose and lipids are fed

into the blood stream, where with erythrocytes (red blood cells) they are transported to every cell in the blood.

- Inside the cell glucose is broken down into pyruvate, which enter the mitochondria; cardiac and skeletal muscle cells and liver and brain cells contain the highest number of mitochondria per cell. The mitochondria generate energy by oxidative metabolism (in the form of ATP), which then releases energy for muscle contractions and nerve impulses. Thus mitochondrial dysfunction will result in fatigue and produce other symptoms of CFS. Impaired recycling of ATP in the mitochondria is found in CFS patients.
- Ample evidence now shows that multi-faceted management programs are effective for both fibromyalgia and CFS. Effective relief and improved functioning is seen when the following elements are offered to patients: stepped stretching and activity, pool-based exercise, education, CBT strategies for stress management, antidepressant medication, dietary monitoring and modification (e.g., small meals), daily mid-day power naps, and sleep hygiene.
- Study published July 9, 2012 in Proceedings of the National Academy of Sciences demonstrating that arrhythmic circadian clock leads to constant expression of inflammatory proteins and causes low-grade, chronic inflammation. Exercise reduces chronic systemic inflammation by increasing anti-inflammatory proteins.

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AFTERNOON BREAK

Feeling tired or tired of feeling?

- Study in Britain of 68,000 adults showed even low levels of psychological distress raises risk of death, even after accounting for weight, exercise, smoking and alcohol consumption.
- **Brain Centers That Can Keep Us Awake**:
    - pain and the precentral gyrus;
    - anxiety, threat, hypervigilance and the amygdala
        - Insula-amygdala resting-state functional connectivity has high potential to serve as a biomarker for anxiety.

    - Several neuro-imaging studies underlined the importance of the amygdala and prefrontal brain structures (e.g. dorsolateral prefrontal cortex [DLPFC]) for the processing of emotional stimuli and for emotional regulation. fMRI studies show those with subclinical levels of anxiety or depression had stronger amygdala-prefrontal activation and coupling while exposed to negative words.
    - rumination, indecision and lateral prefrontal cortex
        - Even a single night of total sleep deprivation (SD) altered the valuation process in the ventromedial prefrontal cortex (VMPFC) suggesting that the ability to discriminate the values between choices is impaired from poor sleep, independent of the effects of SD on attention and vigilance.

Disorders of Anxiety and Mood:

- Differential impact of anxiety and depression on sleep
    - If stress produces primary feelings of anxiety and worry an individual will likely experience sleep onset insomnia, have poor quality/depth of sleep, and may wake frequently throughout the night with limited ability to return to sleep.
    - If an individual experiences primarily feelings of depression secondary to stress then sleep onset may present little problem though early awakening occurs more often (compared to anxiety) with little if any ability to maintain sleep for more than 4 hours.
- anxiety and difficulty initiating and maintaining sleep
    - The neurobiology of the disorder is thought to involve a wide cortical and subcortical network that includes but is not limited to the amygdala and the bed nucleus of the stria terminalis (BNST). These two regions have been hypothesized to play different roles in stress and anxiety; the amygdala is thought to regulate responses to brief emotional stimuli while the BNST is thought to be involved in more chronic regulation of sustained anxiety. Medication-free GAD patients as well as non-anxious controls were exposed to a gambling game intended to elicit a stressful response and sustained anxiety. fMRI scans showed that GAD patients demonstrated decreased activity in the amygdala and increased activity in the BNST. GAD patients disengaged the amygdala and its response to acute stress earlier than non-anxious controls, making way for the BNST to maintain a more sustained response - anxiety.
- depression
    - Depression affects 9.4% of American adults annually, whereas a survey reported in 2012 of nearly 1200 hospital-employed nurses showed prevalence of depression to be at 18%.

Lifestyle Habits to Increase Energy

- **Taming the Physical Environment**:
    - Reducing clutter and messes
    - How to combat energy-draining inertia.
    - Creating a more restful environment
    - Higher loneliness scores were significantly linked to higher levels of fragmented sleep, not total sleep but number of awakenings
    - Creating boundaries with fatigue-inducing people (e.g., narcissists, borderline personalities, manipulators).

- **Emotional Management**:
    - Interpersonal issues produce cumulative toxic emotions including anxiety, anger, and depression primarily through the attributions we make as to the cause of such events and conflict.
    - In addition to cognitive flexibility, compartmentalization is a key coping strategy to minimize the impact of stress on our energy and health overall. Thought stopping and attention-grabbing tasks are effective if part of a diverse array of responses.
    - **Mindfulness & acceptance**: "The root of mindfulness practice is experiencing the itch as well as the urge to scratch and then not acting it out." (Pema Chodron).
        - Researchers found that a form of mindfulness meditation created changes in the anterior cingulate cortex after 4-wk training, a part of the brain network related to self-regulation.
        - One study compared experienced meditators performing two types of meditation, a "focused-based" practice and a "breath-based" practice. fMRI showed that the frontal regions, anterior cingulate, limbic system and parietal lobes were affected during meditation and that there were different patterns of cerebral blood flow between the two meditation types.

    - Tai Chi is a traditional Chinese form of conditioning exercise derived from martial arts and rooted in eastern philosophy and Chinese Medicine. An RCT of 102 adults compared those in 6 months Tai chi training to a control group. Participants in the Tai chi group reported significant improvement in sleep quality and executive function. Improvements have often been reported in health functioning, physical and emotional health, reducing falls, fear of falling and risk of falls, and possibly enhancing cardiovascular functioning in older adults although the effects on bone density, cognitive and immunological functioning are less clear.

Professional Fitness:

- Emotional exhaustion, fatigue and professional burnout
    - Health care providers work in some of the highest risk professions.
    - Models of professional burnout as a variant of the stress response include job strain, caregiver burden, and traumatic response.
    - Remedies for professional burnout parallel stress management skills including self-care, cognitive reframing, and soul-searching.

- **Maintaining Energy-Enhancing Habits**: training your brain to adopt healthful habits that are sustaining rather than draining.
    - Learn to highly value behaviors that promote wellness and devalue behaviors that lead to poor health
    - Enrich your life by taming immediate gratification
    - Enhance resiliency
    - Make healthy habits habitual
    - Make flexible decisions

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Understanding Fatigue: Facts, Fiction, & Fixes

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Inner Solutions for Success

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Alphabet soup

- ATP = Adenosine Triphosphate
- HPA = hypothylamic pituitary adrenal
- PNI = psychoneuroimmunology
- CPAP = continuous positive airway pressure
- CRF = corticotropin releasing factor
- CFS = Chronic fatigue Syndrome
- CDC = Centers for Disease Control
- OR = Odds Ratio
- ACT = Acceptance and Commitment Therapy

Stress in America

(StressinAmerica.org)

- 22% of Americans report stress at 8 or higher on 10-point scale
- 92 % believe stress negatively impacts health; only 31% believe stress negatively affects ***their*** health
- Nearly half state they're poor at preventing or managing stress
- Money (75%) and work (70%) are tops stressors; Time is biggest barrier
- Top symptoms of stress: irritability (42%), anxious (39%), and fatigue (37%), feeling sad (37%), and low energy (35%)
- One-third of caregivers do so 40+ hours/wk; median age = 49

Stress in America

(StressinAmerica.org)

- Importance to well-being? Good family/friend relationships (76%), managing stress (61%), getting enough sleep (60%), eating well & exercising (54%)
- Willpower (27%) and not enough time (26%) are main reasons preventing healthy lifestyle changes
- 32% of adults report not getting enough sleep, 42% of caregivers report the same. 58% of adults report trying to get more sleep in the past 5 years
- 44% report in past month "lay awake at night" (60% of caregivers)

Stress in America: Age, gender, and region

- Those under 40 were more likely to report that stress decreases their libido, leads to nervousness, and increases fatigue than those over age of 60.
- Adults on the east coast report most stress (e.g., money, relationships, job stability), while those in the West report being the healthiest and least likely to have physical symptoms of stress.
- Westerners report socializing more to manage stress while Easterners drink more alcohol.
- Poor diet: 12% East, 6% South, 3% Midwest, 2% West.
- Daily vigorous exercise: 24% in West, 19% South, 15% Midwest, 12% East.

Fatigue in context

- Population prevalence: 6% – 7.5 % of adults in U.S. report "feeling fatigue often"
- 21% to 33% of primary care patients report significant fatigue, resulting in approx. 7 million office visits annually
- Age/context may be under-appreciated:
  - Teens with circadian rhythms are asked to be at class at 7:00 am
  - College years: partying and cramming
  - New parents are asked to keep schedules despite their newborns haven't gotten the memo
  - Menopause depends on appreciation by the culture
  - Another loss of aging is sleep
  - Is fatigue a symptom that something larger is wrong? Do we try to 'solve' it so we don't see the larger problem?

What is the problem?

- ***Weakness*** is a lack of physical strength and feeling that extra effort is required to move. Possible causes: thyroid dysregulation, Guillain-Barre syndrome, myasthenia gravis, or low levels of potassium or sodium.
- ***Fatigue*** is a feeling of tiredness or exhaustion or a need to rest due to lack of energy. Possible causes: thyroid dysregulation, low hemoglobin, CAD, metabolic disorder, anxiety, depression, kidney or liver disease, stress, medications, alcohol, or caffeine
- **Fatigue consist of 3 components:**
  - **inability to initiate activity**
  - **reduced capacity to maintain activity**
  - **difficulty with concentration, memory and emotional stability.**
- **Three categories are used in referring to fatigue based on duration:**
  - **Recent - < 1 month**
  - **Prolonged - > 1 month**
  - **Chronic - > 6 months**

What models do we use?

- Symptoms as pathology – DSM-IV criteria for somatoform disorders (chronic fatigue, insomnia, depression)
- Dualism or integration?
  - Psychological or physical
  - Holistic, multi-factorial model of inter-connectivity (e.g., allostatic load)
- Direct mind-body connection (HPA axis)
- Behavioral response to stress (smoking, alcohol, caffeine, nutrition, social connectivity, physical activity)

Causes of fatigue

- **Not enough sleep**
- **Sleep apnea**
- **Caffeine overload**
- **UTI**
- **Thyroid dysregulation**
- **Kidney disease**
- **Immune abnormalities**
- **Medications**
- **Heart disease**
- **shift work/sleep disorders**
- **Hormone dysfunction**
- **CFS/Fibromyalgia**
- **Not enough fuel/food**
- **Anemia/low hemoglobin**
- **Dehydration**
- **Diabetes**

The cellular biology of fatigue

- Mitochondria are highly dynamic organelles. Mitochondrial dysfunction in the brain is associated with neurodegenerative diseases
- Kreb's cycle and ATP are vital functions in creating cell energy and take place in each cell mitochondria
- Expending energy (behavior) increases the number of the energy-producing mitochondria
  - Decreased mitochondrial activity is most often seen in physically inactive, otherwise healthy subjects.
  - Exercise clearly increases mitochrondrial function.
  - Vicious cycle of sedentary lifestyle leads to decreased mitochondrial function, decreasing spontaneous physical activity, further decreasing mitochondrial function to the point of fatigue and impairment.

The cellular biology of fatigue

- Wealth of data showing that mitochondrial dysfunction is responsible for oxidation, one factor promoting aging.
- Aging results in reduced mitochondrial function (and insulin sensitivity) though not clear if this is due to age or inactivity.
- Telomere dependent senescence is affected by mitochrondria activity

Hormones & fatigue

- Cortisol: low at night with 7-fold increase in the morning
- Stress induced cortisol elevations stimulate the pituitary to release TSH. Chronic cortisol elevations lead to immune suppression, increased rate of infections, which lead to lower thyroid function.
- Lower levels of estrogen and progesterone, seen in menopause and ageing, are associated with fatigue.
- Testosterone was more effective in reducing fatigue in HIV+ men than antidepressants.
- Thyroid hormone levels affect fatigue, weakness, cognitive processes, and mood
- Estimated 30% of women 55 & older have hypothyroidism.

Hormones & fatigue

- National Academy of Hypothyroidism www.nahypothyroidism.org
- Not just serum levels (T3 & T4) but cellular levels (not affected by diffusion, but by cellular energy/mitochondrial function) which creates a very recursive/cyclical loop !
- TSH levels is a poor indicator of thyroid's impact on fatigue as pituitary thyroid levels are not indicative of levels in other body tissues. Synthroid (T4) is relatively ineffective in improving cellular thyroid hormone levels.
- Abnormal thyroid transport will not show in low T4 levels because less in the cell, then ***more*** found in serum. High reverse T3 levels are best markers of reduced transport of thyroid hormones.
- Abnormal thyroid transport found in diabetes, obesity, anxiety, depression, aging, CFS, fibromyalgia, and stress –conditions associated with mitochondrial dysfunction and low cellular energy!

Thyroid & fatigue

- Anxiolytics (Ativan, Xanax) lower T3 into cells
- Stress lowers T3 & T4 into cells by as much as 50% with wide individual variation and differences between various body tissues.
- Chronic and/or yo-yo dieting reduces cellular T4 uptake by 25 – 50%.
- Nutritional supplements for thyroid function: Vitamins A, B & C; Flaxseed, zinc, selenium, iodine, tyrosine, protein, yogurt, seeds, dark greens.

Measures of sleep and fatigue

- Pittsburgh Sleep Quality Index (19 items: quality, latency, duration, etc.)
- Epworth Sleepiness Scale (8 items)
- Insomnia Severity Index (7 items: DSM criteria)
- Functional Outcome of Sleep Questionnaire -10 (10 items: activity, vigilance, intimacy, productivity, social)
- The Fatigue Scale (14 items: mental & physical)
- Piper Fatigue Scale (22 items: behavioral/severity, affective, sensory, and cognitive)

Consensus Sleep Diary-Core

Date	8/19/12	8/20/12	8/21/12	8/22/12
Time into bed	10:30 pm			
Time tried to sleep	11:35 pm			
Time to sleep onset	55 min.			
# awakened	3			
Total awakened time	75 min			
Final awakening	6:40 am			
Time out of bed	7:00 am			
Sleep quality (1-5)	2 (poor)			
Comments	Wine w/dinner; Olympics			

Sleep efficiency for 8/19 = 58%

Fatigue – Sleep deprivation?

- Opportunity versus ability
- Shift work
- Sleep apnea
- Menopause and thermal dysregulation
- Sleep needs change as we age

Effects of sleep deprivation

- Two studies using fMRI showed sleep restriction ⇧amygdala activation (and subjective emotional intensity) and lessens connectivity between amygdala and medial-prefrontal cortex (controller of amygdala) when exposed to 150 'affective' pictures. (van der Helm E, Yao J, et al, (2011) Current Biology; Yoo SS, Gujar N, Hu P, Jolesz FA, Walker MP (2011) Current Biology)
- Cross sectional survey in Japan showed < 6 hours sleep had OR 1.42 for diabetes than those with 8+ hours average (Kobayashi, Takahashi et al, 2010, Internal Medicine)
- Improved sleep for 3 months (via CPAP crossover design) in patients with metabolic syndrome results in lower blood pressure, cholesterol, and A1c (Sharma, Agrawal et al 2011, NEJM)

Sleep problems

- "Sleep state misperception"
- Obstructive Sleep Apnea
  - > 10 sec
    - Apnea = cessation of airflow
    - Hypopnea = decreased airflow → 4%+ desaturation
  - Followed by loud snoring & gasping when breathing starts
  - Results in brief awakenings
  - Excessive daytime sleepiness
- Prevalence of AHI > 10/hour
  - Under age 60: men = 15%, women 5%
  - Over age 65: Men = 70%, women = 56%

Sleep problems

- Risk factors: age, males, obesity, smoking, alcohol before sleep, family history, nasal obstruction
- Consequences:
  - Daytime sleepiness
  - Inflammation: Cardiovascular & immunologic effects (Cohen, 2009, < 6 hrs/night more susceptible to flu)
  - < 6 hours/night = higher breast cancer recurrence, post-menopausal only
  - Mortality (OR 1.97)
  - Depression
  - Impaired cognitive function (accuracy, attention, executive function)

Sleep restriction

- NIH Consensus Panel concluded sleep restriction, sleep hygiene and stimulus control are most effective treatment for Onset insomnia; terminal insomnia (SSRIs)
- Physical activity (vigorous, no closer than 3 hours)
- Set wake time
- No naps
- Bed when sleepy; 30 minute maximum per attempt

Sleep hygiene and stimulus control

- All activity outside bedroom
- darkness/no electronics 60 minutes prior to bedtime
- cool temperature to mimic lowered body temp at night
- no clock visible
- list of concerns outside bedroom (60 min pre, night-stand)
- pets in their place (53% of pet owners report disrupted sleep every night)
- Caffeine, alcohol, tryptophan (complex carbs w/ some protein and calcium)
- What will be different next week?
- What can you make a habit?

Cathy H.

- 56 y.o. female, entertainment publisher, unknown work hours
- Adult son & family 'in transition'
- GAD-7 = 16, sleep diary, cognitive log (re: work)
- Intervention: bed only for sleep, no alcohol past 7 pm, sleep restriction, worry pad, 60 minute pre-bed routine, mid-day walk, daily planner, assertiveness training, plan for dedicated work space at home, unifying principles to guide work decisions, biofeedback (MyCalmBeat.com)

"Failing to exercise when you feel bad is like explicitly not taking an aspirin when your head hurts." – Michael Otto

"Exercise is what healthy people do, it is not punishment." Client S.T.

The "Gut Brain"

- Importance of the enteric nervous system (ENS) and its relevance to energy and fatigue.
- Regulating energy via intake
  - Caffeine and energy drinks
  - Appetite regulating hormones: Leptin & ghrelin
  - Omega 3, Omega 6, and inflammation
  - Outsmarting your gut brain
- Stress and the habits that optimize food as energy

The "Gut Brain"

- **The enteric nervous system (ENS) is referred as to the "second brain" because of its capability to function in the absence of nerve inputs from the central nervous system.**
- **GI symptoms in diabetes are due in part to diabetic neuropathy, yet neuropathy in the GI tract differs from segment to segment.**

The "Gut Brain" - caffeine

- **Most often used psychoactive substance on earth; improves attention and concentration yet impairs short-term memory when eliminated**
- **Caffeine intensifies dopamine receptors, resulting in stimulation of the cardiovascular system. May lower risk of Alzheimer disease.**
- **Chronic use increases risk of dehydration, which can lead to a variety of symptoms including fatigue.**
- **Long-term caffeine consumption has been linked to fibrocystic breast disease &cardiovascular disease** (DBP 3 pts.).
- **Now often combined with sweeteners, and thus affecting the cycling of energy, fat storage, and chronic fatigue.**

The "Gut Brain" – energy drinks

- **$744 million spent annually in U.S. on energy drinks.**
- **Caffeine found in energy drinks can range from 80 to 300 mg in an 8-ounce serving (unregulated, unlike soda).**
- **Guarana seeds contain 3x caffeine as coffee beans. up to 30 grams of sugar per 8 ounces**
- **Contains B6 & B12 (found in meat and dairy products).**
  - **3 RCTs, 5 prospective cohorts, and a Cochrane review show oral B12 effective in treatment of B12 deficiency & ↓ homocysteine.**
- **1 of 4 Americans age 13+ have used in past year**
- **6% combine alcohol & energy drinks ➔↑ "hazardous" drinking.**

"Gut Brain" - Ghrelin

- **Adiposity hormones, leptin and ghrelin, regulate short-term food intake to achieve long-term energy balance.**
  - **Leptin signals satiety, down regulates food intake**
  - **Ghrelin increase appetite and is at peak during first bites**
  - **Ghrelin is a peptide produced by the stomach and increases food intake; circulating levels surge shortly before meals. Social stress and estrogen increase ghrelin levels.**
  - **Sympathetic nervous system activation increases levels of ghrelin. Chronic ghrelin administration increases body weight via diverse, concerted actions on food intake, energy expenditure, and fuel utilization.**
  - **Ghrelin is most suppressed by ingestion of carbohydrates. Proteins and then fats suppress ghrelin to a lesser degree. Crude fiber also lowers ghrelin production.**

The "Gut Brain" - inflammation

- **Obesity is pro-inflammatory. Cytokines signal inflammation and alter glucose metabolism in brain centers that involve depression (cingulate gyrus). Saturated fats encourage bacterial growth, and if present chronically tend to promote inflammation. Increased rates of depression may be due in part to changing diet from fish & vegetables to pro-inflammatory cereals (corn, wheat).**
- **Omega 3 fatty acids are anti-inflammatory (garlic, tumeric, linseed oil, nuts, soya beans, and cold water fish). Increases storage of carbs as glycogen rather than as fat, and reduce depression.**
- **Study of medical students who received Omega-3 supplements showed a 20% ↓ in anxiety and 14% ↓ in inflammation.**
- **Omega 6 fatty acids are pro-inflammatory (maize, sunflower oil and sesame oil); increase feelings of social isolation, depression and thoughts of suicide. Omega 6: Omega 3 ratios most predictive of inflammation.**

Outsmarting your "Gut Brain"

- Gastric satiation is volumetric, while intestinal satiation is nutritive. Gastric satiation signals arise primarily from mechanical distention, whereas those from the intestine derive largely from the chemical effects of food. Cholecystokinin (CCK) from the intestine signals satiety and is secreted in response to fats and proteins.
- Increasing satiety:
  - Solid high-protein meals suppress hunger for 3 hours whereas liquid high-protein resulted in satiety lasting only half as long
  - Flaxseed increases satiety, fullness and decreased food intake
  - Small meals & slower consumption = fewer calories due in part to 40% of meal is in the intestine before meal's end, thus absorption in the gut can trigger satiety signals

Outsmarting your "Gut Brain"

- Stabilizing energy levels:
  - Having breakfast lowers cortisol spike mid-morning
  - Fiber, like protein, slows metabolism of carbs.
  - Low-glycemic foods maintain stable blood sugar (Neurology, 2012: 10% of hippocampal volume)
  - Tryptophan-rich (e.g., nut butters) and melatonin-rich foods (walnuts, cherries, dairy products) help regulate the sleep-wake rhythm
  - Ribose (fundamental component of ATP) and CoQ10 are two supplements that have emerging evidence to support their use in addressing fatigue.
  - Mild dehydration causes blood thickening ➔ fatigue

Outsmarting your "Gut Brain"

- A crossover feeding trial (n=164) compared 3 diets, each rich in a different macronutrient (carbs, fats, proteins). Protein from lean meat and vegetables reduced appetite more than diet rich in carbohydrate and fat. Proteins trigger glucose synthesis in the intestines and this glucose sends appetite suppressing signal to the brain.
- Some women added 3 apples or 3pears or 3 oatmeal cookies per day for 10 weeks. Significant decrease in weight (2 lbs.) for the apple group and the pear group compared to the cookie group.

Outsmarting your "Gut Brain"

- 380 calorie milkshake under the pretense it was either a 620-calorie "indulgence" or a 140-calorie "sensible" shake. Ghrelin was measured via blood samples at 3 time points. The mindset of "indulgence" produced a dramatically steeper decline in ghrelin after consuming the shake. Participants' satiety was consistent with what they believed they were consuming rather than the actual nutritional value of what they consumed.

Stress-related eating leads to fatigue

- CRF ↓ appetite, yet CRF ↑ pituitary → ↑ gluccocorticoids → ↑ appetite
- Intense stress ↓ appetite ; repeated moderate stress ↑ appetite
- Stress → ↓ sleep quality → ↓ leptin's down-regulation capacity
- Stress-related eating is more often simple carbohydrates as this increases dopamine fastest, yet hyperglycemia stimulates oxidative stress, a driving force in atherosclerosis.
- Cortisol & carbs ↑ inflammation and waist-hip ratios in women only (E. Epel)
- Mindless eating and ***what will be different next week***?

The mind-body connection

- Maladaptive thought patterns & controlling the frontal lobe (social/emotional intelligence) → lowers prolonged distress, inflammation and fatigue
- rCBF studies show ↓amygdala response when affect was labeled (intellectualized) vs. when affect stayed 'perceptual' – self-awareness/self-assessment IS executive functioning
- Hypothalamus → CRH → pituitary → beta-endorphins & adrenocorticotropin hormone (ACTH) → adrenal → cortisol, gluccocorticoids, and pro-inflammatory cytokines → down regulate system elements upstream

Type A's, anxiety, depression, and anger: factors in CVD

- Health Professionals F/U study: OR of 2.5
- Nurses Health Study: OR of 3.8
- Normative Aging Study: OR of 4.5
- Framingham: OR of 7.1 (homemakers only)
- Collaborative Psychiatric Epi Survey (IED)

Pathways: stress to CVD

- Anxiety & hostility ↑ risk, depression → recovery
- Elevated blood pressure (esp. w/ + fam. Hx)
- Testosterone, cortisol, and cholesterol
- Vagal tone/heart rate variability, fatigue, & inflammation
- Unhealthy behaviors
- Chronicity of anger (cynicism)
- Social consequences
  - Connection to others (social support)
  - Loneliness ↑ BP w/o ↑ cardiac output

Anger management

- Separation between the stressors
  - Vacations and timeouts
- "Chilling out" and visualization
  - External versus internal images
- AAA model
- "Fallacy of Fairness" and "mind-reading"

Psychoneuroimmunology

- **Clinical relevance of research**
  - In-lab immunosuppression ≠ immuno-enhancement in immuno-compromised patients/conditions
  - Subject selection
  - Singular outcome focus
  - Important outcomes - frequent or fatal
- **Factors that determine response**
  - Controllability
  - Emotional expression
  - Phasic nature/temporal sensitivity

Chronic fatigue syndrome

Definition / criteria (CDC); Women account for 65-80% of CFS.

A. **Chronic fatigue for >6 months that doesn't resolve with bedrest & impairs function by 50% or more**
B. **Exhaustion after completion of simple tasks.**
C. **7 or more of the following: (main symptom having abrupt onset)**
   1. **Mild fever and chills**
   2. **Sore throat**
   3. **Painful lymph nodes**
   4. **Generalized muscle weakness**
   5. **Myalgias**
   6. **Post-exertional fatigue/malaise**
   7. **Headaches**
   8. **Joint aches**
   9. **Neuropsych complaints**
   10. **Sleep disturbances**
   11. **Non-productive congestion**

CFS – Stress syndrome

- **Metabolism of CFS patients is normal and symptoms are due to psychological factors, with mental fatigue considered a lack of motivation (the brain is major consumer of resting cellular energy!)**
- **Parental physical abuse, childhood GI symptoms, and parental reports of many colds each had ORs > 1.6 for patients with CFS.**
- ***Outcomes are predicted by ↓ in 'perceived problems with activity' and an ↑ in sense of control over fatigue.*** **Patients with CFS tend to perceive problems with activity independent of their own objective performance and see CFS as uncontrollable, itself resulting in chronic anxiety and fatigue.**
- **When gluccocorticoids are released as part of short term stress they destroy weaker/older lymphocytes; prolonged stress leads to indiscriminate destruction of lymphocytes. Prolonged stress elevations and compromised compensatory recovery systems can result in autoimmunity.**

CFS – Immune dysfunction

- CFS patients have less seasonal variation in symptoms than patients with depression.
- CFS patients also have subtle cognitive/information acquisition deficits (CNS changes?).
- Findings have consistently shown adrenal insufficiency/low cortisol especially during typical morning surge.
- Pro-inflammatory cytokines act on the brain to cause sickness behavior. When inflammation continues unabated, such as during systemic infections, cancer or autoimmune disorders, the ensuing immune signaling to the brain can lead to exacerbation of depression. This may be why depressive symptoms such as fatigue, reduced interest, and low mood is more prevalent with immune dysfunction.

CFS – Immune dysfunction

- EBV and other viral proteins release pro-inflammatory cytokines that contribute to fatigue, fever, aching, sleep disturbance and inactivity. Acute viral infections stimulate T cell development, chronic infections may lead to immune exhaustion particularly of CD8 T cells; reduced CD8 T cells and NK cytotoxicity is lower in patients with CFS.
- As compared to non-CFS patients, CFS patients with post-infective (mononucleosis) fatigue had gene expression profiles of "altered host response", with most of these genes affecting mitochondrial functions. It remains unclear whether this fatigue reflects chronic effects of persistent Epstein Barr Virus (EBV) or if the EBV triggers an chronically altered host response to various virus. CFS subjects who did not recover from mononucleosis had altered gene expression during early phase EBV that led to changes in mitochondrial abnormalities in fatty acid metabolism.
- Xenotropic retrovirus is NOT linked to CFS as the assays used to measure this connection are unreliable

CFS – Immune dysfunction

- When the digestive system is operating properly glucose and lipids are fed into the blood stream, where with erythrocytes (red blood cells) they are transported to every cell in the blood. If there is a problem with the digestive system, then glucose and fatty acids and amino acids are not produced. This insufficient energy production then leads to fatigue.
- Inside the cell glucose is broken down into pyruvate, which enter the mitochondria. Mitochondrial dysfunction will result in fatigue and produce other symptoms of CFS. Impaired recycling of ATP in the mitochondria is found in CFS patients.

CFS – Immune dysfunction

- Study published July 9, 2012 in Proceedings of the National Academy of Sciences demonstrating that arrhythmic circadian clock (delayed phase sleep disorder, shift work) leads to constant expression of inflammatory proteins and causes low-grade, chronic inflammation. Exercise reduces chronic systemic inflammation by increasing anti-inflammatory proteins.
- CFS patients have dysfunction in endogenous nocioceptive inhibition during exercise and thus show decrease rather than increased pain threshold post-exercise; related is that cortisol and CRF affect pain sensitivity and the low cortisol seen in CFS patients may foster pathological immune activation, since cortisol has strong pain inhibiting capacity.

Chronic fatigue syndrome

"There is generally consensus among clinicians and academics, with only a very small but vocal minority giving the impression of polarization within the field. Unfortunately, we know from the 'vaccination-autism' saga, that polarization makes for better media coeverage. While immune dysfunction is associated with CFS we do not know if this plays an etiological role or is simply confounded with low cortisol levels or sleep dysfunction, both of which are common in CFS and both of which are associated with immune activation. Cross sectional studies that compare CFS to other medical conditions have shown that the proportion of these patients with co-morbid psychological disorders is too high to simply be a reaction to having the illness but is compatible with the idea that this co-morbidity might reflect a shared underlying CNS dysfunction." – Simon Wessely, CFS expert

Chronic fatigue syndrome

"CFS has multiple causes and to call it a single disease greatly underestimates the complexity of the problem. Thus to look for "the cause" of CFS is a self-defeating exercise. There is accumulating evidence for a wide variety of abnormalities in CFS, including altered adaptive immunity, disordered pain perception, endocrine abnormalities, sleep disorders, and cardiovascular dysfunction. However, one is left with a strong sense that post-viral events are a common trigger in CFS, but how they lead to chronic disease remains unresolved." – Stephen Hilgate, CFS expert

EBBM for CFS

- Ample evidence now shows that multi-faceted management programs are effective
  - Stepped activity including pool-based exercise
  - Education and CBT / stress management
  - Antidepressant medication
  - dietary monitoring and modification (e.g., small meals)
  - daily mid-day power naps
  - sleep restriction & hygiene, stimulus control

Shannon B.

- **54 y.o. married female health care provider**
- **BMI = 34.8, hypertensive Rx**
- **Fibromyalgia, CFS, migraines**
- **Adult child with disabilities**
- **FT employed with husband intermittently employed**
- **Plan: Fibromyalgia EBBM, sleep restriction & hygiene (work), Omegas, late-night snacks and Jamba juice**

Self-assessment – mental health

- In past two weeks have you felt for several days:
- PHQ-2
  - little interest or pleasure in doing things?
  - down, depressed, or hopeless?
- GAD-2
  - Nervous, anxious or on edge?
  - Not able to sleep or control worrying?
- Anger/stress
  - Irritable, cranky or edgy?
  - Quickly frustrated or critical?

Emotional management

- Anxious individuals show greater amygdala activation when shown negative words than non-anxious adults
- 20 minutes in 20 seconds
- Biofeedback
- Framing CBT (tolerance and reduction, full tool box)
  - Thought-stopping/attention grabbing tasks
  - Worry box/compartmentalizing
  - Scheduling and problem-solving
  - Cognitive distortions/expectations/assumptions

Attributional style

- Personal? (internal . . . . . external)
- Pervasive? (global . . . . . specific)
- Permanent? (stable . . . . . temporary)

Post Traumatic Stress Disorder

- DSM-IV-R Criteria
  - Traumatic event
  - Symptoms
    - Re-experiencing
    - Persistent avoidance
    - Hyper-arousal
  - Impairment in functioning, one month or more duration
- Evidence Based Behavioral Medicine
  - EMDR
  - Emotional regulation & prolonged exposure

Mindfulness

- Meditation is not a means to an end. It is both means and the end. *- J. Krishnamurti*
- If you're not happy here & now, you never will be.*-Taisen Deshimaru*
- What lies behind us and before us are tiny matters compared to what lies within us. *- Oliver Wendell Holmes*
- The ordinary man looks outward – *Zen saying*
- **Live vertically, not horizontally.** *– W. Sieber*
- Cognitive flexibility & non-judgmental focus on the present.
- Focus on empty space between thoughts. Don't hold on and don't push away. Observe.
- *Five Good Minutes – Jeff Brantley*

Meditation

- **Neuroplasticity**
  - **Focused attention activates (results in higher CBF) the prefrontal cortex, anterior cingulate, and other executive function areas of brain, whereas 'open monitoring' decreases activation (Manna, Raffone, 2010)**
  - **Mindful meditation > relaxation training for anterior cingulate** (Tang, Lu, Fan Yang, Posner, 2012, Proc Natl Acad Sci; Xue, Tang, Posner, 2011, Neuroreprot)
  - **Compassion changes the anterior cingulate (Richard Davidson: www.investigatinghealthyminds.org)**
- **Davidson, R. J., & Begley, S. (2012).** ***The emotional life of your brain: How its unique patterns affect the way you think, feel, and live -- and how you can change them*****. New York, NY: Hudson Street Press.**

ACT:
Acceptance & Commitment Therapy

- Mindfulness: moments, control is the problem, self-awareness, 'healthy dissociation' (i.e., cognitive diffusion)
- Acceptance: % 'unfixable', "If I were more willing to be anxious, I may not be so anxious", 'river flowing through me', what if fatigue is not something to be **fixed** but a signal to rest?
- Values-based living, priorities honored?
  - What's important? "I won't let that determine my day." "Where am I headed, and how is this very relevant to my journey?"
  - Engaging in a meaningful life; fatigue is not an issue when there is passion

Minding the body, mending the mind

- Social connections more important than cholesterol
  - You socialize more or less when fatigued?
  - You feel more tired when spending more time alone (introvert v. extrovert)
  - ⇧ cytokines (inflammation) lead to social withdrawal
- Strengthening boundaries with fatigue-inducing people (e.g., narcissists, borderline personalities, manipulators)
- Tai Chi: 6 months of Tai Chi resulted in improved sleep quality, and better executive functioning (Nguyen MH, Kruse A, 2012, Clinical Interventions in Aging)
- Tailoring a lifetime program for optimal quality of life
  - Biospsychosocialspiritual

Burnout & emotional fatigue

- ***Emotional exhaustion, cynicism, inefficacy, fatigue***
- ***Job strain***
  - "fit" and "role ambiguity" v. intrinsic motivation
  - High emotional demands X low decisional latitude = burnout
- ***Caregiver burden***
  - Depletion of personal investment
- ***Traumatic response***
  - Emotional numbing from prolonged re-experiencing, vigilance & hyperstartle

Burnout: Intervention options

- Time management
  - Good decisions are more important than working faster
- Self-care & self-complexity
  - separation/time-outs, spirituality, exercise
- Cognitive reframing
- Soul searching

Caroline P.

- 34 y.o. female ICU nurse with unscheduled shift work
- Relocated to San Diego from Chicago with little social support; fatigue, weepiness, anxiety
- "former" in-line skater, "former" painter
- Strategies:
  - identify fatigue, weepiness and anxiety as burnout
  - externalize cause of sadness and anxiety
  - attentional focus training
  - self-care including diet, activity and joy
  - examination of 'productivity'
  - reassessment of career with emphasis on non-linearity

How (else) can you increase dopamine?

- When dopamine is low in the limbic system then immediate rewards (simple decision) wins out. When sufficient dopamine is present, then prefrontal cortex (complexity, delayed gratification) will win out.
- Memory, based in hippocampus, tends to lower firing of dopamine neurons with expectation of a familiar non-gratifying activity, more firing of dopamine neurons with a familiar pleasurable activity, whereas greater firing of dopamine neurons occur when 'opportunity' for pleasure is novel (encouraging exploration).
- Gratitude journal ("the body follows....")
- Self-care, massage, dance, play, novelty

Where's your motivation?

- Often people attempt to live their lives backwards: they try to ***have*** more things or more money, in order to ***do*** more of what they want, so they will ***be*** happier. The way it actually works is the reverse. You must first ***be*** who you really are, then ***do*** what you need to do, in order to ***have*** what you want – Margaret Young
- What is your goal, what would change if less fatigued?
- List 3 behaviors that most interfere with energy level
  - Mood Sleep Activity Nutrition
- For each behavior state intention/plan for next week.
- ***What will be different next week?***