Objectives

1) Identify inflammatory versus anti-inflammatory foods, herbs and supplements.

2) Understand methods for optimizing brain-derived neurotrophic factor (BDNF) through diet.

3) Plan and prep easy brain optimizing meals.
Brain Injuries...

- 1.4 million Americans each year (reported)
  - over $4 billion annually in health care costs and loss of productivity
- Treatments dependent on severity
  - Surgery
  - Medication
    - Pain
    - Anxiety, depression, anti-psychotics
    - Anticonvulsants
    - Anti-Coagulants
    - Muscle relaxants
    - Stimulants or sedatives and sleep aids
  - Relaxation
  - Rehabilitation therapies: PT, OT, Speech
• Brain insults are by nature inflammatory; nutrition plays a key role in our body’s inflammation load.
• Nutrients are the building blocks of all the ‘ticks’ in our body
• Nutrients after Brain Injury should ‘feed’ the brain
  – What does it need to function optimally?
  – Reducing inflammation & cytokine production
  – Supporting neuron recovery (and reduced dying off)
“Evidence indicates that diet and exercise assist brain-derived neurotrophic factor (BDNF)”

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2805663/

BDNF has been observed to play an important role in protecting neurons from insult and disease while supporting normal brain function and recovery events following brain insults/injuries.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3225186/
Actions of BDNF

- Sustains the viability of neurons (neuroprotection)
- Increases dendritic arborization and the number of synapses.
- BDNF gene is suppressed by stress (via cortisol).
- Decreased BDNF levels lead to neuronal atrophy and neuronal death.
- BDNF levels are low in depression, but increase with antidepressant treatment.
- Exercise increases BDNF levels.
S.A.D....
Inflammatory Foods

• High-fat sucrose (HFS) diets are a HUGE public health issue
  • Obesity, hypertension, and many other debilitating disorders.
  • Research suggests HFS diets can reduce levels of brain-derived neurotrophic factor (BDNF) leading to reductions in neuronal and behavioral plasticity.
    • http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3111862/

• Rats fed a Standard American Diet (SAD) for a period of 1-2 months performed significantly worse on the spatial learning mater maze test than rats fed a healthier diet
  • http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3225186/
Inflammatory Foods

• SAD:
  – Highly processed
    • Bags, boxes, cans, takeout
    • Sports centers are the worst
  – High amounts of processed carbohydrates
  – Low in fresh fruit/veggies (anti-oxidants and minerals/vitamins)
  – High in poly-unsaturated fats
  – Refined sugary snacks and drinks
  – Lots of added sugar
    • Average American consumes 100-130gm each day and 150-200# of sugar each year
Portions are Inflammatory

- Portions
  - Restriction of excess calories increases levels of BDNF, resulting in improved neuronal function
  
  [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3225186/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3225186/)

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Ketogenic diet (KD)

• “Based on the evidence presented, the ketogenic diet holds promise of effectiveness in improving the outcomes of TBI. There are indications that ketones may provide an alternative and readily usable energy source for the brain that might reduce its dependence on glucose metabolism, which may be impaired immediately following TBI.” [http://www.ncbi.nlm.nih.gov/books/NBK209323/]

• “The results indicated that both mRNA and protein levels were significantly elevated 72 hours after TBI and decreased by KD administration. KD administration also reduced brain edema and cellular apoptosis.” [http://www.ncbi.nlm.nih.gov/pubmed/19408168]
A typical ketogenic meal includes a 3-5 ounces of protein, usually cooked in natural fats (for example, butter, olive oil, or coconut oil) with the addition of green leafy or non starchy vegetables such as salad greens, spinach, summer squash, or kale.
The Keto Food Pyramid

- Berries & Non-green Veggies
- Cheese & Oils
- Eggs & Dairy
- Nuts & Other Protein
The branched-chain amino acids (BCAAs) (leucine, isoleucine, and valine) are nutritionally essential in that they cannot be synthesized endogenously by humans and must be supplied by diet.

“Those patients on the BCAA-enriched formula exhibited positive nitrogen balance (+1.8%), whereas those on the standard formula were in negative balance (−8.0 percent)”

http://www.ncbi.nlm.nih.gov/books/NBK209312/
Fats... Yes – I said the “F” word!

• The brain is made of nearly 60% fat [http://www.ncbi.nlm.nih.gov/pubmed/20329590]
• Fish oil - next slide
• Olive oil
  – “Findings suggest that EVOO has beneficial effects on learning and memory deficits by reversing oxidative damage in the brain, effects that are augmented with increasing concentrations of polyphenols in EVOO” [http://www.ncbi.nlm.nih.gov/pubmed/21955812]
• Coconut oil
  – Medium-chain triglycerides, constituents of coconut and palm kernel oils, are medium-chain fatty acid esters of glycerol
  – Readily cross the blood-brain barrier (BBB) & oxidized by the brain.
  – May provide both a direct and an indirect brain fuel source [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2671041/]
• Nuts
Fish-derived omega-3 fatty acids have been shown to improve cognition, plasticity, and recovery of neurons after traumatic brain injury.

- One of the most important forms of omega-3 fatty acids, docosahexaenoic acid (DHA) - Key component of neuronal membranes at sites of signal transduction at the synapse, suggesting that its action is vital to brain structure and function
- Evidence suggests DHA serves to improve neuronal function by supporting synaptic membrane fluidity and function, and regulating gene expression and cell signaling
- Sardines, salmon, oysters, mackerel, wild rainbow trout, and herring (*don’t recommend tuna, swordfish and shark due to it’s high mercury level*)
- Ensure fish oil supplements are from reliable sources that test for mercury

Look for “Actual” DHA/EPA – not the labeling on the front of a bottle

- Doses as high as 10-20,000gm/day are needed for brain recovery [http://www.sciencedirect.com/science/article/pii/S221343441300025X](http://www.sciencedirect.com/science/article/pii/S221343441300025X)
Vitamins & Recovery

• **Vitamin D**
  
  • Causes the expression of more than 1000 genes that consequently results in activation of many pathways in CNS (central nervous system). Recent studies have shown that vitamin D deficiency may intensify traumatic brain injury and reduce the effects of other therapies for TBI.
  
  • “I call vitamin D ‘God’s miracle vitamin’. It is the backbone drug supplement in treating traumatic brain injury because it works on so many levels. Vitamin D3 directly influences hundreds of human genes.”


  – “VDR (Vitamin D Receptor) signaling on immune function has been the focus of many recent studies as a link between 1,25(OH)2D3 and susceptibility to various infections and to development of a variety of inflammatory diseases has been suggested. It is also becoming increasingly clear that microbes slow down immune reactivity by dysregulating the VDR ultimately to increase their chance of survival.”

  [PubMed #PMC3684798](https://www.ncbi.nlm.nih.gov/pubmed/23918691)
Vitamin D

The body makes vitamin D when it is exposed to Ultraviolet (UV) rays from the sun.

FOOD SOURCES:

- Cheese
- Margarine
- Butter
- Fortified Milk
- Healthy Cereals
- Fatty Fish
• “These results indicated that brain injury triggered the development of circulating autoantibodies against the 38–50 kDa brain autoantigen”
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0092698

• “Deficiency in vitamin D is associated with increased autoimmunity as well as an increased susceptibility to infection. As immune cells in autoimmune diseases are responsive to the ameliorative effects of vitamin D, the beneficial effects of supplementing vitamin D deficient individuals with autoimmune disease may extend beyond the effects on bone and calcium homeostasis...The implications of vitamin D deficiency on the immune system have become clearer in recent years and in the context of vitamin D deficiency, there appears to be an increased susceptibility to infection and a diathesis, in a genetically susceptible host to autoimmunity” PubMed #PMC3166406
Autoimmunity

S100B - a well-accepted protein biomarker for traumatic brain injury

• Present in varying degrees in blood samples of the 67 football players after every game - even though none of them suffered a concussion. Demonstrates that even the most routine hits have some impact on the blood-brain barrier and possibly the brain itself

• Results showed that players with the most head hits also had the highest S100B levels and elevated levels of autoimmune antibodies. Players who often remained on the sidelines had significantly lower S100B levels. In addition, the blood samples predicted abnormalities seen in the imaging tests, and correlated with observed cognitive changes

• Researchers also showed that S100B accumulates in dendric cells, which regulate auto-immune responses. Therefore, as the blood-brain barrier repeatedly opens during the football season it might set the stage for a continuous autoimmune-type attack on the brain

Leaky Gut Syndrome

Triggers Causing Intestinal Damage:
- Dietary Proteins
- Low HCL and Enzymes
- Antibiotics
- Infections
- Blood Sugar Issues
- Antibodies
- Pregnancy
- Stress
- Menopause
- Toxins
- Food Allergies

Intestinal Mucosal Cells:
- Normal tight junction
- Leaky and Inflamed

Blood Stream:
- Circulating Immune Complex

Consequences:
- Blood Brain Barrier Breach
- Inflammation
- Autoimmunity
- Malabsorption & nutrient deficiency
Leaky gut – Intestinal Permeability

- “TBI caused a significant increase in intestinal permeability compared to sham (surgical placebo) after 6 hours”
  [Link](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2989839/)

- “This study demonstrates that Vitamin D is an important mediator of intestinal epithelial defenses against infectious agents. Vitamin D deficiency predisposes to a more severe intestinal injury”
  [Link](http://www.ncbi.nlm.nih.gov/pubmed/24755435)

- “Traumatic brain injury (TBI) can lead to several physiologic complications including gastrointestinal dysfunction. Specifically, TBI can induce an increase in intestinal permeability, which may lead to bacterial translocation, sepsis, and eventually multi-system organ failure.”
  [Link](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2989839/)
Healing Leaky Gut

• Remove inflammatory foods
  – High Glycemic (avoid sugar substitutes)
  – Processed foods

• Vitamin D (aim at serum levels of 55-75)

• Add in gut healers
  – Bone Broth
  – Curcumin
  – L-Glutamine
  – DGL (Deglycyrrhizinated Licorice)
  – Aloe
  – NAC (N-Acetyl Cysteine)
Vitamins & Recovery

• Vitamin E
  – “It has been shown that after a mild TBI, rats showed increased protein carbonylation, another marker of oxidative stress. This event correlated with poor performance accompanied by decrease in the levels of the neurotrophic factor BDNF”
  http://nnr.sagepub.com/content/early/2009/10/19/1545968309348318.abstract
  – “Diet with 500 IU/kg of vitamin E for 4 weeks “Results suggest that vitamin E dietary supplementation can protect the brain against the effects of mild TBI on synaptic plasticity and cognition, using molecular systems associated with the maintenance of long-term plasticity, such as BDNF and Sir2”
  http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2824788/

• Vit E Rich foods:
  – Vitamin E- A fat soluble vitamin present in nuts (almonds & hazelnuts), seeds, vegetable and fish oils, and apricots.
Oxidative Stress

- Appears to be a primary driver of TBI pathophysiology
- “Evidence strongly suggests that oxidative stress is a cornerstone event leading to and propagating secondary injury mechanisms such as excitotoxicity, mitochondrial dysfunction, apoptosis, autophagy, brain edema, and inflammation” http://www.ncbi.nlm.nih.gov/pubmed/24532027
- “The protective role of endogenous antioxidant enzymes in ischemic brain injury has been well established in the literature” http://stroke.ahajournals.org/content/27/6/1124.short
- “Trauma not only interferes with the regulation of antioxidant mechanisms but may also convert these mechanisms into prooxidative ones through its ability to disrupt cell compartmentalization” http://www.karger.com/Article/Abstract/94168
- “Oxidative damage to DNA is also an early event in TBI. In animal models, the oxidative marker of DNA damage is increased within the first 15 minutes after trauma” http://journals.lww.com/jtrauma/Abstract/2004/06000/Oxidative_DNA_Lesions_in_a_Rodent_Trauma_Model_of.pdf
Antioxidants

Think “A.C.E.”

– Vitamins A, C & E ... And Beta Carotene (BC)
– Vitamin A – Beta Carotene is a precursor to vitamin A (retinol) and is present in liver, egg yolk, milk, butter, spinach, carrots, squash, broccoli, yams, tomato, cantaloupe, peaches, and grains. (Vitamin A can be toxic in high doses, therefore we recommend food sources of BC for conversion)

• Vitamin C
– Ascorbic acid: Observed a significant stabilization of the perilesional edema in severely head-injured patients receiving highdose vitamin C. Our data also showed a reduction of hospital mortality (at the expense of more patients in a vegetative state) and an improvement in long-term outcome for patients receiving vitamin E.
  • [http://journals.lww.com/neurosurgery/Citation/2010/08000/Beneficial_Effects_of_Vitamin_C_and_Vitamin_E.96.aspx](http://journals.lww.com/neurosurgery/Citation/2010/08000/Beneficial_Effects_of_Vitamin_C_and_Vitamin_E.96.aspx)
  • Citrus fruits and juices, green peppers, cabbage, spinach, broccoli, kale, cantaloupe, kiwi, and strawberries.
Antioxidant Rich Foods

• Greens (Not Iceberg) – Think Collard Green, Spinach, Kale,
  – Try for 3 doses each day – tons of A, BC & C – (see prior slide)
  – Minerals like lutein, lycopine and zeaxanthin
  – The vitamin E found in green leafy vegetables works with vitamin
• The smaller and darker- the more Antioxidant packed
  – Blueberries, grapes, raspberries
• Orange veggies
  – Carrots, butternut, acorn squash, sweet potatoes
• Selenium rich foods
  – Brazil nuts (also great source of healthy fats)
Antioxidant Rich Foods

• Curcumin (Turmeric)
  – Curcumin enhances recovery events after brain trauma. It was found to protect the brain from lipid peroxidation and nitric oxide-based radicals
  – Supplementation of curcumin into the diets of rats reduced the effects of experimental concussive injury on cognitive function tasks

• Caffeine
  – A new study shows chronic treatment with caffeine protects the brain against injury by increasing glutamate release and inflammatory cytokine production
  – Green Tea
    • Phytochemicals: anthocyanin and pro anthocyanin
    • Both are antioxidants that help fight inflammation
    • Epigallocatechin gallate (EGCG), which is a catachin is a particularly potent antioxidant
Antioxidant Brain Fruit

- **Avocado**: Promote brain health & contributes healthy blood flow.
- **Pomegranate**: Protect the brain from damage of free radicals.
- **Blueberries**: Improve learning & motor skill on brain.
- **Cherries**: Help nervous system on brain.
- **Cherries**: Helps prevent dementia.
- **Carrot**: Reduce age-related memory deficits and inflammation in the brain.
- **Nuts, Seeds**: Help stimulate brain activity, increase blood flow in the brain.
- **Watermelon**: Target brain function.
- **Kiwi**: Increases bone mass.
Other Studies- Supplement possibilities

• Recent research has shown that nutritionally based therapies are critically important in terms of TBI outcome.
  
  – Iron
    • Research points to abnormal iron as potential source of secondary injury following mTBI. There is a small body of evidence that non-heme iron (ferritin and transferrin) as well as free iron is increased after mTBI. Patients who have sustained multiple mTBIs, evidence of significant non-heme iron deposition similar to that seen in AD. [Link](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3922137/)

  – B complex
    • Therapeutic administration of nicotinamide (Vitamin B₃) following TBI shown to be effective at improving behavioral and histological outcome in various models of TBI. Other nutrient compounds administered following injury, such as riboflavin (Vitamin B₂) & pyridoxine (Vitamin B₆) improve outcomes. [Link](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2942865/)

  – Choline
    • Choline treatment resulted in significant cortical tissue sparing, reduced brain inflammation, and normalized some TBI-induced deficits in neuronal nicotinic cholinergic receptor expression. [Link](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2946871/)
Herbs

• Curcumin as mentioned
• Rosemary
  – Performance on cognitive tasks is significantly related to concentration of absorbed 1,8-cineole following exposure to rosemary aroma, with improved performance at higher concentrations. http://tpp.sagepub.com/content/early/2012/02/24/2045125312436573.abstract
Pulling it all together

More of this!
Pulling it all together...

- PLAN – SHOP – PREP
  - Make a menu
- 3-4 veggies/day
  - At least 3 greens
- 3-4 fruits/day
  - Darker and smaller
  - Try for low glycemic
- Smoothies
  - Avoid juice (high glycemic), dairy (can increase leaky gut)
  - ½ veggies, ½ fruit
  - Add in protein (BCAA)
- Juicing
- Veggies in Egg muffins or grain free breads and muffins
- Soups
Eating on your own...

I thought 'clean eating' meant devouring cupcakes while mopping the floor.
Questions??