Food As Medicine: Managing TBI Through Nutrition

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6th Annual Northern Kentucky TBI Conference
March 23, 2012
www.bridgesnky.org

The Brain

- The brain contains 15 billion cells.
- Glial Cells - Glial cells function as support cells to help maintain the signaling abilities of neurons
- Neurons - involved in information transmission – receiving, processing and transmitting information.

Incident of TBI

- Civilian
  - Approximately 1.4 million individuals each year suffer from TBI
  - 91 per 100,000
- Military and Veterans
  - 7,000 peacetime admissions annually
  - Active Duty males: 225 per 100,000
  - Active Duty females: 150 per 100,000

Common Causes

- Motor vehicle accidents
- Falls, assaults, gun shots to the head
- Explosive Blasts
  - 64% of war TBI related to blast
  - Identified as the signature wound of the Iraq war

TBI Characteristic

- Primary Injury (initial injury)
  - Typically occurs due to a direct injury to the brain
  - In many cases permanent damage can occur due to direct tissue destruction
- Secondary Injury
  - Appears to be related to the inflammatory cascade
  - Typified by brain cell swelling and apoptosis

Consequences of TBI

- Cognitive
  - Attention
  - Information processing (speed & efficiency)
  - Memory and Learning
  - Abstract Reasoning
  - Executive Functions
    - Problem solving, planning, insight/awareness, set shifting, sequencing

Consequences of TBI

- Behavioral-emotional
  - –Irritability
  - –Impulsivity
  - –Affect Regulation: apathy, agitation, aggression
  - –Depression, Anxiety
  - –Social Pragmatics
- Cognitive and behavioral impairments are the most disabling long-term, more so than physical injuries

Interdisciplinary Team and Interdisciplinary Rehab Approach

- Rehab Medicine physician
- Rehab nurses (primary nurse model)
- Physical, Occupational, Recreational, and Vocational Therapists
- Speech Therapists
- Social Workers
- Case Managers (including long-term)
- Rehab or Counseling Psychologists
- Neuropsychologists

Missing Consequences

- Metabolic Alterations
  - – Hormonal changes
  - – Blood-Brain Barrier Disruption
    - Shift in amino acid balance
    - Shift in neurotransmitter levels
  - – Aberrant cellular metabolism
  - – Cerebral inflammatory response
  - – Systemic inflammatory response

Psychoneuroendocrinology

- The clinical study of the interaction of emotions/thoughts, neurotransmitters, and hormones and their relationship to physical and psychological health.
- Deals with the interrelated disciplines of psychology, neurobiology, endocrinology, immunology, neurology, and psychiatry, with an emphasis on multidisciplinary approaches to treat the whole organism.

Neuroendocrine Dysregulation

- The injured brain secretes hormones that impact the Hypothalamic-pituitary-adrenal axis (HPA)
- HPA axis dysfunction is closed linked to Hypothalamic-pituitary-gonadal and Hypothalamic-pituitary-thyroid dysfunction

Neuroendocrine Dysregulation

- The estimated incidence of acute hormone reduction is adrenal 15%, thyroid 5–15%, growth hormone 18%, vasopressin 3–37%, and gonadal (25–80%).
- Chronic hormone deficiency occurs in 30–40% of selected patients after TBI.

Inflammatory Cascade

- Alterations in plasma protein concentrations.
- During the systemic inflammatory process, pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-alpha), interleukin 1 (IL-1beta) and interleukin 6 (IL-6) are released.
- These cytokines have been linked to a number of chronic disease processes.

The Big Picture

- Stress impacts HPA, which impacts all other areas (HPG, HPT).
- Activation of HPA suppresses immune function.
- Low gonadal hormones increases pro-inflammatory cytokine production.
- Cytokines impact BBB and neurotransmitters.

The Big Picture

- The brain's function as the regulator for metabolic activity leads to a complex milieu of metabolic alterations.
- End result of alterations is catabolism, protein wasting, glucose intolerance, lipid dysregulation, and imbalance in neurotransmitters.

The Big Picture

- Pro-inflammatory cytokines act on the brain to promote cognitive alterations, listlessness, depressed activity, sleep disturbances, and loss of interest in social activity.

Nutrition Implications

- Hormonal and Inflammotary dysregulation impact physical health.
- Predisposing TBI sufferer's to the following;
  - Obesity
  - Insulin Resistance
  - Cardiovascular Disease
    - Increase triglycerides, diminished HDL-C
  - Dementia
  - Depression
  - Cognitive Delays

A New Team Approach

- So often nutrition is an afterthought in treatment and long-term management of TBI.
- A more comprehensive approach is needed that includes nutritional status.
- The body as an open chemical system receives chemical inputs from many sources, one being food.
- The chemical molecules of what you eat has an impact on all body systems.

Nutrition Assessment

- Hormones
- Oxidation/redox
- Mitochrondrial
- Immune Function
- Nutrients
- Inflammation
- Digestion/Detoxification
- Sleep/Stress

Nutrition Assessment

- Obtaining a good diet history is critical!
- Making sense out of multiple disease manifestations.
- Remember HOMINIDS!!

Stress and Amino Acids

- Prolonged stress exposure affects the pathways of amino acid utilization.
- Adaptive needs for specific amino acids increase.
- Amino acids may be able to delay or even block stress pathologies.

Stress and Amino Acids

- Tryptophan (Trp) and tyrosine (Tyr) neurotransmitter precursors.
- Trp influences the rate at which neuronal endings form serotonin.
- Trp deficiency results in decline in brain serotonin activity.
- Trp utilization impacted by large neutral amino acids.

Tryptophan

- Trp precursor 5-hydroxytryptophan (5-HTP) the direct precursor to serotonin.
- Serotonin function:
  - Arousal
  - Sleepiness
  - Mood

Tryptophan

- Trp use shows promise as adjunct therapy.
- Trp alleviated symptoms of mild stress induced mood disturbances and cognitive deterioration.
- In major mental dysfunction Trp not as effective.

Tyrosine

- Tyr precursor to dopamine, epinephrine, and norepinephrine.
- Tyr plays a role in cognitive performance.
- Tyr depletion impaired spatial working memory and recognition.
- Research on Tyr supplementation inconclusive.

Lysine

- Lysine (Lys) does not appear to be depleted by chronic stress.
- Lys deficiency increases impact of stress exposure.
- Lys blocks serotonin 4 receptors, which diminishes stress.
- Serotonin 4 receptors play a "pro-stress" role in the gut.

Neurotransmitters and Food

- Trp: Chicken, turkey, tuna, lean beef, nuts, seeds, bananas, shellfish, fish, soy + carbs
- Try:Milk, fish, meats, chicken, turkey, peanuts, sesame, cocoa powder, wheat, beets, Sugary and fatty foods –followed by a crash!
- Lys:Red meat, pork, poultry, cheese (particularly parmesan), certain fish (such as cod and sardines), nuts, eggs, soybeans (particularly tofu, isolated soy protein, and defatted soybean flour), spirulina, and fenugreek seed.

Stress and Fatty Acids

- Evidence suggest that n-3/n-6 ratio of 1:4 effect prostaglandin system.
- Prostaglandin (PG)has profound effects on sleep.
- PG enhance TRH and stimulate dopaminergic and noradrenergic receptor activity.

Stress and Fatty Acids

- Critically ill and trauma patients have lower levels of n-3 PUFAs.
- Level of n-3 is significantly and negatively correlated with level of depression.
- Omega 3s maintain neuron membrane fluidity and structure.
  - DHA comprises 10-20% total fatty acid composition in brain.

n-3 Deficiency

- Dysfunctions of neuronal membrane stability.
- Dysfunction of transmission of serotonin, dopamine and norepinephrine.
- Decreases in membrane fluidity.
- Decreases in ion channel activity and receptor functions.

DHA and The Brain

- DHA deficiency – Reduction in logical thinking, poor memory, and hormonal changes.
- Provides structure to neurons and facilitates neurotransmitter receptivity.
  - DHA increases neurotransmitter receptor density.
  - allows the brain to make use of serotonin and dopamine signals.
  - neuroprotective .

Stress and Carbohydrates

- Carbohydrate primary fuel source for the brain, boost concentration.
- High glycemic load diets increase insulin resistance, but they also shift the HPA axis toward sympathetic overactivity, with increases in cortisol, ACTH, and norepinephrine.

Balancing Hormones

- Lose weight if you are overweight
  - *fewer calories more important than percentage of macronutrients:NEJM 2009:360:859-873)*
- Limit /avoid high glycemic foods (refined grains and sugar)
  - *(JAMA May 2007;297(19):2092-2102)*
- High fiber: at least 20 grams/ 1000 kcal
- Include protein/ "healthy fat" with meals and snacks

Balancing Hormones

- Eliminate hydrogenated oils
- Most fats should come from fish, nuts, seeds, avocado, extra-virgin olive oil
- Limit fats from dairy and meat to <7% of calories
- Exercise: goal to get to target heart rate for >30-40 minutes most days

Addressing Oxidative Stress

- CALERIE trial: 6 months calorie restriction lowered oxidative stress, body temperature, insulin, triglycerides, diastolic blood pressure, factor VIIc and liver lipid; increased HDL cholesterol
  - JAMA 2006 Apr 5;295(13):1539-48
  - OBESITY 2008 Jun;16(6):1355-62
  - Atherosclerosis 2009 Mar;203(1):206-13
- 3 months of calorie restriction improved verbal memory by 20%
  - Sensitivity to insulin and levels of CRP also improved
  - (PNAS Jan 2009 106(4):1255-80)

Addressing Oxidative Stress

- Eat fewer calories
- Minimize intake of red meat
- Include foods with a high nutrient:calorie ratio
  - High ORAC
  - "Color wheel" or "rainbow" approach
  - Cooking methods: lower heat/ longer cooking times

Inflammation and The Brain

- Individuals with the highest CRP's took longer to complete tasks related to executive functioning.
- On MRI scanning, those with the highest CRP's had brain changes equivalent to 12 years of aging compared to those with the lowest levels.
  - *Neurology 2010;74(13):1022-1029*

Reducing Inflammation

- Attica epidemiologic study: adoption of Mediterranean diet and moderate exercise reduced likelihood of elevated CRP by 72%
  - *(Angiology April 2007;58(2):225-33)*
- Also associated with reduction in BP, chol:HDL ratio, glucose
  - *(Arch Intern Med July 2006;145(1):1-11)*
- Med diet associated with 30% lower risk depression
  - *(Arch Gen Psychiatry 2009;66:1090-1098)*

Foods to Reduce Inflammation

- Intake of n-3 fatty acids (wild salmon, sardines, flax, walnuts)
- Add spices (turmeric, ginger, basil, rosemary, garlic)
- Add lots of color (berries, dark green leafy, purple grapes, cherries)

Strategies to Improve Nutrient Intake

- Make your calories count- the less processed the food, the better.
- 5-9 servings of fruit and veggies/day.
- Eat fish twice weekly (or supplement fish oil); include daily other omega-3 rich foods (nuts, seeds, soy foods).
- Supplements:
  - Consider adding 1000-2000IU vitamin D3; check 25-OH vitamin D levels
  - Consider B12 supplementation for vegans, those on PPI's, metformin, and hx of Etoh abuse; check B12/ methylmalonic acid levels

Enhancing Digestion

- Probiotics
- Prebiotics
- Reduce gastric irritants
- Bitter greens or herbal bitters (artichoke, fennel, dandelion greens, ginger)
- Consider digestive enzymes.

Improving Detoxification

- High fiber diet/regular bowel movements
- Adequate hydration
- Include foods that support liver detoxification
  - parsley, cilantro
  - brassica vegetables (broccoli, cauliflower, watercress); garlic and onions
  - pomegranate juice; green tea

Improving Detoxification

- Balance Phase I and II activity
  - Foods that can induce phase II
    - Ellagic acid (found in red grapes, raspberries and strawberries), cruciferous veggies (cabbage, bok choy, broccoli, brussels sprouts), garlic, rosemary, and soy.
  - Foods that are beneficial in balancing Phase I and II
    - Cruciferous veggies, veggies in the alluim family (garlic, onion, shallot), berries, red grapes, soy, basil, rosemary, cumin, turmeric, soy, black and green tea.

Conclusion

- These "imbalances" can be influenced by diet and lifestyle.
- But by using a integrated approach we can truly improve symptoms and reduce risk of disease!

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