Concussion, Traumatic Brain Injury, CTE: A Functional Medicine FSM Approach

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Goals

- Definitions of Concussion, CTE(Chronic Traumatic Encephalopathy) and Traumatic Brain Injury(TBI)
- Introduced to neuropathology and pathophysiology of TBI
- Learn about Blood Brain Barrier(BBB) dysfunction
- Become aware of symptoms in TBI and CTE
- Learn assessment methods for brain injury
- Learn about common hormonal dysfunction
- Introduced to brain region injury with subsequent alteration in brain region function
- FSM approaches to treating TBI

Goals

- ❖Compare Conventional vs Functional Medicine Approach to Treatment
- ❖Learn how to limit brain damage and increase brain repair and reserve
- ❖Learn a dietary approach for TBI and CTE
- ❖Learn which supplements are appropriate for treating TBI and CTE
- ❖Learn how to prescribe exercise for brain neuroplasticity
- ❖Learn how to prescribe brain training

Treatment Strategies

- Treat the pathophysiology to limit brain damage
- Decrease neural inflammation
- Decrease excitotoxicity but preserve normal function at the synaptic connection
- Limit and manage oxidative stress
- Repair the BBB
- Support brain mitochondrial health
- Decrease ischemia and cerebral blood flow dysregulation
- Encourage maximum repair of brain tissue in regard to neurogenesis, nerve stem cell stimulation and differentiation, synaptogenesis

TBI Studies

- Limitation of TBI studies:
- Most done on rats and mice
- Most studies evaluate acute and early stage subacute TBI but do not look at treatment for TBI that is more than 1.5 months(and most only look at 2-4 weeks after Concussion.
- Doses used for rats and mice have to be divided by from 6-12 to get the effective dose in humans

Concussion

- A head injury from direct or indirect forces with or without LOC that may lead to symptoms immediately after the injury or for weeks or months after an injury
- Concussion may or may not lead to Traumatic Brain Injury
- Symptoms may vary but have been called Post Concussion Syndrome

Post Concussion Symptoms

- Headache
- Fatigue
- Dizziness
- Nausea or vomiting
- Seizures
- Fatigue
- Depression
- Photophobia
- Sensitivity to sound
- Sleep dysfunction
- Visual symptoms
- Hearing problems
- Anxiety, Depression, Irritability
- Possibly PTSD

CDC Chart to give to patients

Thinking/ Remembering	Difficulty thinking clearly	Feeling slowed down	Difficulty concentrating	Difficulty remembering new information
Physical	Headache	Nausea or vomiting (early on)	Sensitivity to noise or light	Feeling tired, having no energy
	Fuzzy or blurry vision	Dizziness	Balance problems	
Emotional/ Mood	Irritability	Sadness	More emotional	Nervousness or anxiety
Sleep	Sleeping more than usual	Sleeping less than usual	Trouble falling asleep	

TBI

- TBI is a brain condition with a loss of cognitive functions with an onset either after a concussion or with trauma to the brain from a head injury with or without skull trauma.
- Compression and shearing forces result in brain injury and brain dysfunction
- Patients can have Post Concussion Syndrome and Traumatic Brain Injury
- Traumatic Brain Injury symptoms and signs will persist longer than post concussion syndrome

Traumatic Brain Injury

- Of importance is that a certain amount of the brain injury and dysfunction that many patients have is due to pathophysiology of events occurring after the injury that can be treated with Functional Medicine approaches
- Such as BBB permeability and autoimmunity, brain tissue autoimmunity, excitotoxicity, neural inflammation, ROS, excessive neurotoxin insult etc.
- Because this approach is not usually taken many people with head injuries lose much more brain reserve and function than they should have from the original head injury!

CTE: Chronic Traumatic Encephalopathy

- CTE is a condition that can occur in an individual that has had repeated concussions
- Boxers, Football, Ice Hockey, Motocross players are the most likely to develop CTE
- It is a condition that manifests with a multitude of moderate to severe brain symptoms/dysfunction and mood disorders

CTE

- Patients can present like Mild Cognitive Impairment or moderate to severe Dementia
- Problems with decision making and poor judgement
- Memory problems
- Organization difficulties
- Attention problems
- There can be Alzheimer like changes, ongoing oxidative stress and neural inflammation
- There can be significant areas of the brain with decreased activity(especially the PFC and the Temporal lobes and increased activity in the limbic system)

CTE

- Serious and possibly life or relationship threatening Mood disorders:
- Depression, Anxiety
- Addiction: alcohol, pain medications, Benzos etc
- Personality changes
- Explosive anger, aggressive behavior, dark thoughts and they may be suicidal

Team Approach

- Use a team approach to manage CTE and TBI patients because of the complex physical, brain and mood disorders
- FM Dr.(quarterback) , FSM clinician, Psychotherapist (trained in EMDR, EFT, stress management), possibly a Psychiatrist(if severe mood dysfunction), Speech Therapist trained in TBI Cognitive training. Every head inured patient needs a health representative that can make appointments and keep track of treatment plans

ATMs

- Likely you will see head injured patients with mild TBI especially if you know how to take a history to elicit it
- The head injury may not be someone's chief complaint but it can be an important triggering event or antecedent condition or be the cause of the MCI or contribute to their hormone or mood problems

Incidence, Prevalence, Cost of TBI

- Leading cause of death in individuals under age 45
- Every year 1.7-2.5 million people in the US will suffer a mild TBI
- 1 in every 200 people worldwide will suffer a mild TBI
- Annual cost of about 76 billion
- 5.3 million in the US may live with long term disability

TBI

- At least ½ million are children <14 years
- Children sustain Traumatic Brain Injury from bike, scooter, playground and other falls(Note Children must always wear helmets on scooters and bikes)
- Males age 14-24 have the highest incidence
- TBI from sports are mostly from bike, skateboard, ski, snowboard, wrestling, boxing, football, soccer, hockey, rugby
- 20 % of those returning from military deployment have TBI or multiple TBIs from a blast or a fall

Causes of TBI

- Very common in Football as well as Soccer
- In soccer heading long balls may cause subclinical injuries
- May occur after falling even if wearing a helmet(most helmets are not designed to absorb the impact and rotational forces)
- May occur from domestic violence: if there is any history of domestic violence must ask about head trauma
- May occur from a slip and fall on a hard surface
- MVAs can lead to a TBI

Traumatic Brain Injury MVA

- Common w/moderate to high velocity MVAs
- More common if the patient hits their head on something other than the head rest like the steering wheel, windshield or side window
- Can occur with impact against the headrest
- Must get the mechanical forces front impact vs side impact
- The areas of injury are usually anterior temporal lobe

MVA TBI: Forces and Brain Areas

- Front impact and rear impact MVA are more likely to cause anterior temporal lobe, frontal lobe and possibly occipital lobe injury
- Side impact injury like T bone MVA may cause more extensive Temporal lobe, Parietal lobe and mid brain injury
- If you know the brain areas damaged from imaging and cognitive testing you may be able to target your FSM treatments to the forebrain midbrain and hindbrain. The short concussion program does not get at the forebrain and hindbrain enough and does not get at the Blood Brain Barrier

Brain Injury Factors

- The prior TBIs, Concussions and the brain reserve that the person starts with can relate to an amplification effect from the shearing and compression forces and may lead to a more severe TBI
- The older a person is the more likely TBI will result from less shearing and compression
- Other factors: prior leaky BBB, leaky gut, very poor diet with many neurotoxins, sedentary, low B12 status increase brain injury
- Untreated Hormone and Stress issues
- Their APOE4 status and many other factors may affect their ability to repair after a head injury

APO E status

- "Apolipoprotein E plays a critical part in the maintenance, repair and growth of neurones, and seems to have an important part in the neural response to brain injury"
- "The E4 isoform results in reduced growth and branching of neurites in vitro and seems to have an important part to play in the neural response to injury."

APO E

- There appears to be increased ischemic damage and decreased protection from excitotoxicity with the APO E4 status
- Take home: Measure APO E status because it might help to motivate a patient to fully participate in a neuroprotective and brain repair program
- If they are APO E 4 you may consider being even more comprehensive with supplements, HBOT, FSM etc

APO E Reference

- Smith C, Graham DI, Murray LS, et al. Association of APOE e4 and cerebrovascular pathology in traumatic brain injury. J Neurol Neurosurg Psychiatry 2006;77:363–6.
- Ariza M, Pueyo R, del Mar Matarı́n M, et al. Influence of APOE polymorphism on cognitive and behavioral outcome in moderate and severe traumatic brain injury. J Neurol Neurosurg Psychiatry 2006;77:363–6.

TBI without Skull Impact

- Most common in a high to moderate MVA(if it occurs with a low velocity MVA the patient had much less brain reserve before the MVA)
- Can occur with little to no direct head impact if the head moves rapidly
- This is due to compressive and shearing forces especially to the PFC and the anterior temporal areas
- This is more common in patients older than 55 because they have less brain reserve or their has been brain shrinkage
- More common in women of Menopausal age
- More likely if prior Concussion with TBI
- It is much more likely if someone's brain function was marginal or slightly impaired before an accident

Traumatic Brain Injury

- Impairment of: short term memory
- Focus of attention and ability to concentrate is shortened
- Coordination and balance problems
- Problems with the PFC(prefrontal cortex) and lack of inhibition
- Poor organization abilities
- Problems with time management and organization(late or forget appts)
- Mood instability

TBI: Symptoms

- Problems with:

Understanding speech and word finding

Brain fog, brain fatigue

Lower effectiveness at work, home or school

Judgment problems like leaving the stove on or water in the tub etc are not usually associated with mild TBI but more severe TBI

History

- Many people will not bring up symptoms of brain dysfunction because:
- They take their physical symptoms more seriously
- They are embarrassed
- They think they will be labeled or discriminated against
- They are afraid they might lose their job
- No one has asked the right questions to make them feel that Traumatic Brain Injury symptoms are real and can happen

History: How to Ask

- People under report head injuries especially if they have had other bad injuries or if most of the head injury symptoms have gone away
- QUESTIONS address incidents, memory, organization, mood, balance, brain function
- Have you ever had a head injury or a concussion or TBI?
- Have you had any unusual symptoms since the accident?
- Have you had any problems finding words
- Have you found problems remembering things at work, school or at home?
- Have you had any problems with:
- Balance feeling like you might fall or you are walking slowly
- Being able to focus your attention
- Staying organized
- Problems with your judgement like leaving the stove on or the house or car unlocked

History: How to ask

- Are you forgetting things?
- Do you go into a room and forget why you went there?
- Do you feel like you are in a fog?
- Having any problems with your vision or hearing?
- Are you having any problem with energy?
- Are you functioning slower at work?
- Are you feeling really depressed, angry or irritable?
- Have you been saying angry words that hurt people's feelings since the accident?

TBI: Pathophysiology: Initial

- Primary injury of shearing and compression
- Initially hypoxia, ischemia, edema and possibly raised intracranial pressure
- Disruption of blood vessels and axons and cell membrane damage
- Decreased O2 delivery to neurons
- Increased need for glucose in the brain

Pathophysiology

- Secondary cascade after initial injury
- Significant increase in free radicals and oxidative stress leading to further damage of nerve cells
- Increase in neuronal inflammatory mediators acute and subacute(first 6 weeks) and can become chronic
- Increase in brain glutamate and increased intracellular calcium and neuronal death

Pathophysiology

- Neurotransmitter dysfunction both pre and post synaptic
- Decreased production of neurotransmitters including: Acetylcholine, Dopamine and Serotonin
- Excitotoxicity: leading to increased free radical formation, inflammation, brain edema
- Disrupted brain cell metabolism, mitochondrial damage and poor cellular function

Pathophysiology: Brain Inflammation

- TBI causes the release of endogenous danger signals (extracellular ATP and HMGB)
- These bind to pattern recognition receptors such as TLR4 on neurons and glia to activate the immune response.
- Activated microglia can shift from an anti inflammatory to a proinflammatory form. These proinflammatory microglia proliferate and can migrate to injured tissue.
- There is an increase in the brain of proinflammatory cytokines and ROS.
- Chronic microglial activation develops and may mediate (CTE)

Neuro inflammation

- Counter Neuroinflammation: High dose fish oil biased towards DHA 4 grams per day
- Longvida form of Curcumin 400 mg 3x a day (much more likely to go into the brain than other forms of curcumin) It is a bit more expensive and extremely important

FSM for Neuro Inflammation

- For at least the first 6-8 weeks after head injury assume there is neuroinflammation
- For on going symptoms after 8 weeks BBB antibodies need to be ordered
- For the first 6-8 weeks Run 40/1 for 10-15 minutes
- 40/84, 94, 89, 90, 92 for 5 minutes each
- Consider 40/245, 253, 255, 415 if motor dysfunction
- Consider: 40/984 if temporal lobe symptoms

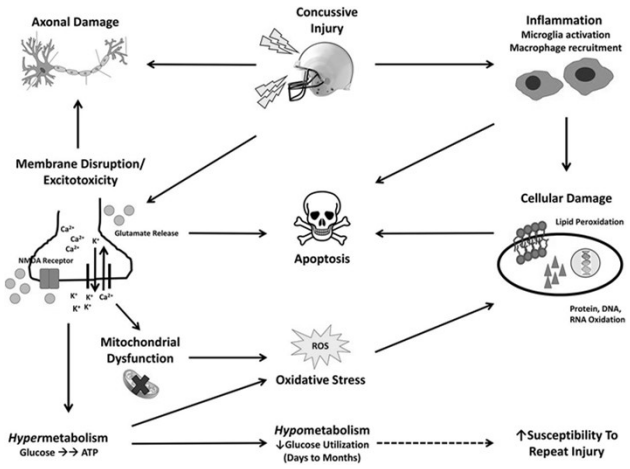
Neuroprotective: Excitotoxicity

- NMDA and AMPA receptors can be over stimulated leading to calcium influx which can lead to excessive intracellular calcium build up
- Excessive intracellular Ca can lead to enzyme activation which can damage neuronal cytoskeleton, membranes and DNA
- It can also lead to increased Mitochondrial permeability, Mitochondrial damage, release of ROS and loss of mitochondrial ATP production
- Very important to limit excitotoxicity after brain injury
- Stop Calcium supplements, stop all sources of Aspartame and MSG http://www.truthinlabeling.org/hiddensources.html print this list and give it to the patient and family

Structural Damage

- Dendritic and axonal damage
- Axonal damage: cytoskeletal damage, transport impairment, axon swelling, beading of axons may continue for years after TBI
- Damaged dendrites and axons disrupt neuronal connectivity, synaptic dysfunction leading to functional impairment
- For FSM use 50 on the A channel for all suspected brain injured areas for the first 6 weeks

Molecular cascade of events after a mild traumatic brain injury.



Erin Cernkovich Barrett et al. Adv Nutr 2014;5:268-277

Advances in Nutrition

CTE

- CTE patients may have significant brain damage
- They are likely to have loss of brain tissue volume on NeuroQuant MRI studies(loss of frontal and temporal cortex and if severe also loss of Hippocampus, amygdala and other brain areas)
- Autopsy has shown extensive neurofibrillary tangles in brain tissue
- There may be antibodies to brain tissue found in the serum and there is thought to be a defective blood brain barrier

Pathophysiology: BBB

- The brain has about 10 billion capillaries The capillaries in the brain have a highly specialized endothelial lining which has tight junctions, basement membranes, pericytes and astrocyte projections.
- The BBB may admit particles of 400 and less daltons BBB and brain tissue use transporters which control the efflux of waste products and the influx of small solutes needed by the brain (nutrients such as glucose and amino acids)
- Transporters exclude many toxic compounds, as well as food antigens and peptides present in the circulation.

BBB

- Astrocytes beneath the BBB produce a protein labeled as BBB and antibodies can be measured to it
- A healthy BBB prevents developing B cells from contact with antigens from brain tissue proteins and thus they do not develop brain tissue autoantibodies
- If the BBB is damaged there can also be damaging effects from TH1 and TH17 lymphocytes
- The BBB can be damaged by structural damage from the injury, by inflammatory mediators after brain injury or by autoimmune insult

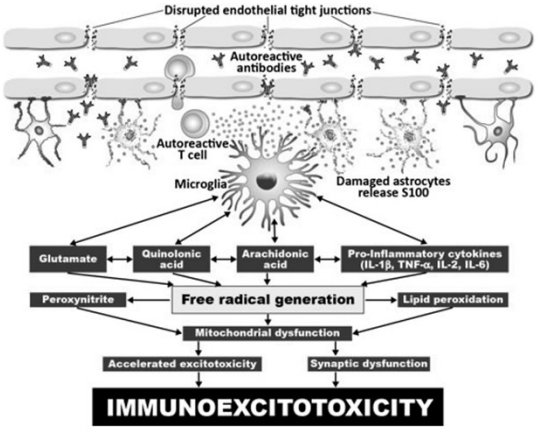
BBB

- A leaky BBB can result in: Autoimmune damage to brain proteins and structure
- Poor removal of wastes from the brain
- Poor clearance of excitotoxins after brain injury and excessive excitotoxic injury
- Leaky BBB leads to poor healing after TBI, more extensive brain injury, and lower brain reserve as well as possibly ongoing damage after 12 weeks

BBB Dysfunction

- Mediators for ongoing brain damage:
- Autoreactive antibodies and T Lymphocytes
- Damaged astrocytes
- Microglial activation generates free radicals, proinflammatory cytokines and glutamate
- Enables damage to brain cell mitochondria and to synaptic connections
- Autoimmunity to the BBB can lead to persistent and prolonged excitotoxicity

Excitotoxicity from Leaky BBB courtesy of Dr Aristo Vojdani



Chronic Brain Inflammation

- Brain cells including microglial cells can produce TNF alpha, IL1b and IL6
- Inflammation can continue to damage brain cells
- Brain injury and disruption of the BBB can lead to chronic ongoing brain inflammation and ongoing brain damage from a leaky BBB
- ***If you take care of patients with head injury you must assess and treat the BBB***

Triggers that Damage the BBB

- Molds and Mycotoxins
- Neurotoxic chemicals disrupt BBB tight junctions (They are found in food, by inhalation or through the skin: pesticides, herbicides, solvents, cosmetics or cigarette smoke)
- Intestinal permeability toxic exposures (endotoxins from bacteria, PCBs, toxins in food and water, heavy metals)
- Chronic sleep restriction can damage the BBB(you must address sleep in these patients)

BBB and Brain Protection

- Assess and treat mold if it is present
- Treat leaky gut, SIBO and heal the intestinal lining
- Follow the TBI diet(organic, gluten, dairy and GMO free)
- No spraying of pesticides or herbicides

BBB and Brain Protection:EMF

- EMF can injure the BBB as well as healthy brain tissue and can make it more difficult for injured brain tissue to heal
- Children are even more susceptible to EMF brain cell and BBB damage but
- Limiting EMF to the brain may significantly increase the number of healthy neurons and the synaptic density
- EMF has been shown in rats to lead to BBB damage and leakage of albumin
- In humans EMF exposure can lead to albumin leakage, headaches, memory issues, etc.

EMF Guidelines

- No Bluetooth head pieces(use blue tube or the speaker phone) No cordless phone
- Keep the cell phone away from the head and turn it off at night
- Limit wireless and use a wired connection if possible
- Turn wireless off at night
- Keep clock radios 8 feet from the head
- Have the home, especially the patient's bedroom tested for EMF by a trained technician

Leaky BBB

- A leaky BBB will allow neurotoxins into the brain increasing the damage from a brain injury
- A leaky BBB will not transport nutrients efficiently for brain tissue repair
- The problem may be compounded if there is also a leaky or excessively permeable intestine
- Treatment must be directed at healing the BBB as well as limiting Neurotoxins and using Neuroprotective strategies

BBB and FSM

- Order array 20 from Cyrex labs in Arizona to determine if there are antibodies to the BBB
- If the test is positive run 40,50, 94,9, 321/62, 162
- Run 124/62,162 for 45 minutes each for at least 2 sessions of FSM

Leaky BBB and Leaky Gut

- If the brain injured patient already had or develops leaky gut, brain injury can be worsened, brain repair can be compromised
- Leaky gut can allow large and foreign molecules to pass into the blood stream of the small intestine which can travel into the brain
- Also the Microbiome changes after TBI
- It is a more dysbiotic, dysfunctional and inflammatory.
- Microbiome and bacterial endotoxins can damage the brain

Leaky Gut and Leaky BBB

- LPS from bacteria in the intestine can be transported in the blood from a patient with Leaky Gut and can enhance immune cell and viral transport across the BBB leading to more extensive damage
- Leaky gut can increase the likelihood of brain autoimmunity and leaky gut must be diagnosed and repaired

Leaky Gut and FSM

- Consider running over the abdomen:
- 40, 9, 321, 94/ 22
- 124/22 for 45 plus minutes

Barriers and Questions

- In CTE or after TBI ask yourself:
- "Are the intestinal barrier and the BBB intact?"
- Are there food allergy or cross reacting food triggers?(Minimize and eliminate them)
- Are there neurotoxic chemicals or heavy metal triggers that can damage the BBB and or the brain (Minimize them)

Lab Testing for Barrier Function

- Do a lab assessment for antibodies against the intestinal lining including Zonulin and Occludin(Cyrex array 2 or Dunwoody Labs)
- Test for antibodies to the blood brain barrier (Cyrex Array 20)

BBB Antibodies

- S100B may be used acutely or subacutely (within 6-12 weeks) or in the chronic stage(greater than 3 months) or in CTE
- BBB antibodies should be repeated after treatment strategies to heal the BBB have been used for at least 8 weeks
- We want to minimize the chance for a second brain injury before the BBB and the brain are as healed
- You also want to demonstrate healing of the BBB

BBB Disruption: CTE

- Even in the absence of concussion, football players may experience repeated BBBD and serum surges of the potential auto-antigen astrocytic protein S100B.
- Marchi N, Bazarian JJ, Puvenna V, Janigro M, Ghosh C, Zhong J, Zhu T, Blackman E, Stewart D, Ellis J, Butler R, Janigro D (2013). "Consequences of repeated blood-brain barrier disruption in football players". PLoS ONE. **8** (3): e56805

Assessment

Assess by

- History(ask about vision and eye symptoms as well as post concussive and brain symptoms)
- Ask a sig other or someone who lives with the patient to help answer the questions
- Physical Exam
- Lab studies to assess APO E status, folate, B12, Vitamin D, Hormone status, barrier status, Stool analysis for Microbiome
- ESR, CRP and Cardio CRP for inflammation
- Brain function testing with questionnaires and testing(online CNS Vital Signs or similar)
- Imaging Studies functional or structural are optional unless suspected bleed

TBI: Exam

- Do a complete Neuro exam including Upper Motor Neuron signs
- Do a mini mental status exam
- Assess gait, cerebellar function and coordination
- Eval the neck, thoracic, low back and any other injured areas
- Palpate the skull and cranial sutures
- Are the eyes and ears level?
- Check Visual acuity and eye movements
- Refer to a TBI vision specialist if vision problems

TBI: Assessment

- Consider giving a questionnaire on Brain Function such as the AMEN Brain System Checklist to try and localize brain areas involved and limbic system mood dysfunction
- Have the patient and a significant other, family member or close friend also fill one out
- Use the SCAT questionnaire for post concussion symptoms and for return to play considerations if an athlete

B Vitamin Status

- B Vitamins are essential for methylation, brain repair and brain cell energy production
- Check B12 levels, Homocysteine and Folate
- Elevated levels of homocysteine have been shown to induce apoptosis, DNA damage and PARP processes so it is important to bring Homocysteine down to less than 8 after a TBI
- Optimize B12 as it is involved with Methylation and nerve regeneration: Target a level at the upper range of normal
- Use methyl B12 if normal COMT gene status Use about 1 mg of B12 sublingually Use Adenosyl or hydroxocobalamin B12 if COMT gene positive

Genetic Testing after TBI

- APO E4
- Run "23 and me" to determine SNPs to COMT, folate ,B12 problems, Vitamin D receptor problems and detoxification dysfunction(SOD2 (compromised SOD2 enzyme compromises antioxidant), GPx1P1(reduced capacity to detox Hydrogen peroxide), GSTP1(Decreased capacity to conjugate certain toxins with glutathione)

Hormone Assessment

- Hormone dysfunction can impair brain healing after TBI
- Most common is dysregulation of Adrenal and sex hormones
- Pituitary damage can result in dysfunction of anterior pituitary hormones
- Goal: Assess all important hormones and treat to normalize hormones after TBI

Hormones: Testing in TBI

- Thyroid: Free T3 and T4, TSH(with pituitary may see low TSH and low free T3 and T4)
- Correct Thyroid status to mid range
- Adrenals: check serum DHEA-S, ACTH and AM Cortisol and 4 point salivary Cortisol and DHEA test
- (Pituitary may show as low ACTH and low Cortisol and low salivary cortisol)
- Correct Adrenal dysfunction in regard to DHEA, cortisol
- Blood Sugar: HgA1C, fasting glucose(important to treat glucose imbalance, use a low glycemic load diet and limit high glycemic snacks)

Hormones: Cortisol

- Cortisol is commonly elevated after the injury as a stress response but it may damage the Hippocampus and must be modulated
- If elevated use Ashwagandha(400-500 mg 2x a day) and Rhodiola 300 mg 2x a day) as adaptogens to bring Cortisol to a reasonable range
- May use FSM to Quiet the Adrenals if high at night

Hormones: IGF1 and Growth Hormone

- Assess Growth Hormone status via a serum test for IGF-1
- Growth Hormone is very important for MSK repair as well as brain neurogenesis, repair
- If low consider stimulating by:
- Adequate sleep and to bed by 10 pm
- Alpha GPC 120-180 mg 2x a day
- Weight lifting to fatigue 3 sets of 10 large muscle groups(Only if BP is normal and if no MSK injuries)
- Sermorelin may help

Growth Hormone

- Sermorelin may stimulate GH release, increases IGF-1 and may enhance sleep and improve lean body
- Analogue to Ghrelin and stimulates the Pituitary to produce GH
- Increases IGF-1
- Rapid dissolve minitab to take at night
- Prescribe as Sermorelin Acetate300 ug)/GHRP(2)(300ug)/GHRP(6)(300 ug) rapid dissolve mini tab 1 qhs

Hormones

- Assess and correct sex hormones in men and women
- In men and women check free and total Testosterone, SHBG, estradiol
- In women also check progesterone,
- Normalize sex hormone status as sex hormones are neuroprotective and may promote neurogenesis

TBI Progesterone

- "In traumatic brain injury (TBI), progesterone has the ability to reduce edema and inflammatory cytokines, prevent neuronal loss and improve functional outcomes. Clinical trials have shown that short-and long-term progesterone treatment induces a significant improvement in the level of disability among patients with brain injury."
- Progesterone improved mortality and functional recovery after contusions in the frontal cortex
- Front Neuroendocrinol. 2009 Jul;30(2):173-87. doi: 10.1016/j.yfrne.2009.03.001. Epub 2009 Mar 24.**Progesterone neuroprotection in traumatic CNS injury and motoneuron degeneration**

Progesterone

- Allopregnanolone may promote hippocampal neurogenesis
- Goes to GABA receptors, is anxiolytic and acts as a sleep promoter
- Attenuates excitotoxicity
- Decreases inflammatory cytokines
- Use only natural Micronized Progesterone 20 mg for men and 100-200 mg for women qhs
- Intranasal Progesterone may be helpful in certain patients

Assessment: Cognitive

- Assess cognitive status and Post Concussion symptoms with written questionnaires(SCAT) and cognitive testing
- Initially use low cost cognitive testing that can be repeated to track response to treatment
- May use CNS Vital Signs, Web Neuro etc.
- May refer for Neurocognitive testing if Med legal case or significant deficits

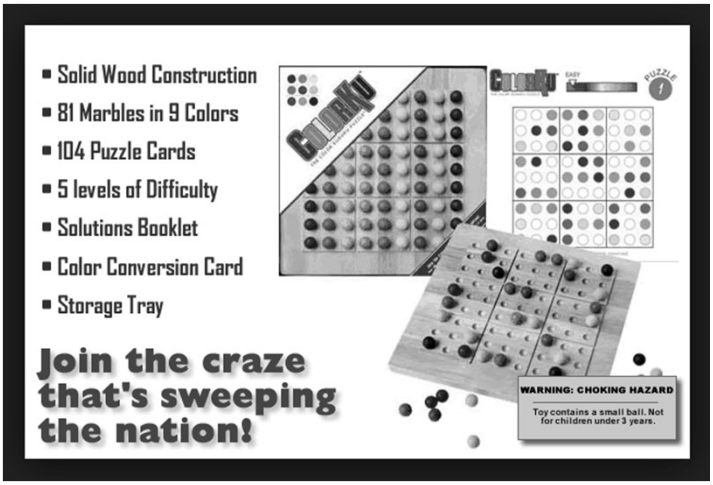
Treatment: Cognitive

- Treatment outlined to stimulate nerve stem cells, BDNGF and to increase synaptogenesis is going to improve cognitive function on a structural level
- Brain Cross training is what is required to increase synaptic connections and long term potentiation
- Use of multiple methods of active learning that are multisensory and require active problem solving and learning

Daily Brain Training

- Brainhq and have them and you open up a paid account $96 per year (have them do personalized brain training as well as do certain courses depending on their needs)
- Crossword puzzles, Scrabble, Brain Game Books 1,2 and 3
- SIMON color flashing memory game
- Balance exercises if balance tests poor (clock balance, alternating lunge, single leg balance)
- Ping pong, dance lessons
- Color Sudoko(Colorku) uses visual and shape stimuli with more complex problem solving

ColorKu



Treatment Strategies

- Treat the pathophysiology to limit brain damage
- Decrease neural inflammation
- Decrease excitotoxicity but preserve normal function at the synaptic connection
- Limit and manage oxidative stress
- Repair the BBB
- Support brain mitochondrial health
- Decrease ischemia and cerebral blood flow dysregulation
- Encourage maximum repair of brain tissue in regard to neurogenesis, nerve stem cell stimulation and differentiation, synaptogenesis

Treatment Strategies

- Use ongoing Neuroprotection strategies to limit excessive damage
- Treat to the Stage: Acute, Subacute, Chronic or CTE
- Treat toxic brain if it exists(SPECT or by history)
- Treat other systems in the body i.e. the GI tract to decrease brain injury and brain autoimmunity or brain cross reactivity
- Treat and improve Stress, Sleep and pain to enhance repair
- Treat hormone dysfunction to enhance repair
- Activate NRF-2 gene response to decrease oxidative stress and neural inflammation

Treatment

- Treat PTSD and Mood disturbance(Anxiety, Depression, Anger)
- Treat cognitive dysfunction deficits
- Treat injured brain areas if you have a SPECT, QEEG or can figure them out on questionnaires
- Note for any treatment have a handout with the reason/goals so that the patient can remember and does not discontinue the treatment because they forgot the rational or they are overwhelmed

Motivation

- Need to educate the patient and motivate the patient to do comprehensive treatment
- "This is your brain that has been injured"
- "You may not heal well or you may end up with lower brain function if you do not participate as fully as possible"
- You may be at higher risk of Dementia if you do not participate and take this program seriously
- Have a partner with normal brain function and a lot of patience to help you
- You may need to seek financial assistance as this program is comprehensive and a lot of it may not be covered by insurance

FSM Frequency Specific Microcurrent

- Treat with Frequency Specific Microcurrent to treat both the pathophysiology, the stage of injury and the brain area
- A channel 18 Hemorrhage(only use for the first 2-4 days), 40 inflammation, 50 congestion(use for days 3 to 4 weeks out), 94 concussion and nerve trauma, 81 (use for chronic stage to increase activity especially in the hindbrain Cerebellum) Use 9 longer for BBB antibodies, use 124 in the post 6 week stage to repair the part of the brain and use it for 45 plus minutes
- B Channel tissues(1 brain as a whole, 90 Forebrain, 84 Midbrain, 94 Medulla, 310 anterior Pituitary, 62 arteries, 162 capillaries)

Treatment: Heal the BBB

- If you have measured antibodies to the BBB and they are positive you must direct treatment to heal the BBB
- Decrease neurotoxins, ETOH, EMF
- Use Curcumin(inhibits microglial activation, and MMP-9, prevents damage to tight junction BBB proteins)
- R Lipoic Acid(200 mg BID) decreases oxidative stress at the BBB
- Sulforaphane(inhibits MMP-9 and activates NRF2) use a product with Myrosinase 30-50 mg
- Resveratrol regulates MMP-9 and TIMP-1 and protects against ox LDL damage of the BBB

Neuroprotective Strategies

- Decrease damage from excitotoxicity and decrease calcium influx
- Decrease oxidative stress
- Decrease ischemia and improve blood flow
- Decrease neural inflammation
- Decrease Neurotoxins
- Decrease EMF exposure to the brain

Rx: Neuroprotection: Avoid/Minimize Neurotoxins

- Avoid alcohol
- Avoid Marijuana
- Minimize cosmetics with neurotoxic chemicals
- Avoid antiperspirant
- Avoid pesticides, herbicides
- Avoid large ocean fish (Hg)
- Minimize and avoid all foods and drinks(coffee) that contain Acrylamide
- Follow the TBI Diet
- Minimize tap water
- Avoid flame retardant pajamas in head injured kids

RX: Limit Excitotoxicity and Neuronal Death

- Consider blocking NMDAR early after TBI with:
- Magnesium Threonate may be able to pass into the brain better than other forms of magnesium use 144 mg 2x a day
- Use Riboflavin 75-200 mg/day
- Note additive effects have been shown in studies when B2 and Magnesium were used together
- Limit all free Calcium in supplements
- Heal the blood brain barrier

Neuroprotection: Vit. D

- Vitamin D3 appears to have neuroprotective effects but these are are inferred from data on vitamin D deficiency which suggest that it modulates apoptosis and reduces oxidative stress, inflammation and excitotoxicity
- It is reasonable to check Vit. D status after TBI(as well as in any athlete) and supplement to get to the med range
- It has shown synergistic effects when combined with Progesterone in TBI studies

Neuroprotection:Vit E

- Reduces amyloidosis and improves cognitive function after repetitive TBI in a model of Alzheimer's disease
- Decreases PUFA oxidative Chain reactions
- Alters protein kinase C signaling
- Reduces macrophage activation
- Increases brain derived growth factor
- Use in Chronic TBI and in CTE and in
- Consider 400IUs of mixed tocopherols

Neuroprotection: Flavonoids

- Ginkgo may improve motor and cognitive function and reduce neuronal cell loss. Doses in studies vary Consider 240 mg/day
- Quercetin improved cognitive performance and normalized firing rates of neurons in injured brains and may reduce markers of oxidative stress, inflammation and apoptosis
- Quercetin also can block mast cell activation
- Doses are not well defined, use 500mg 2-3 x/d before meals
- Pycnogenol reduced oxidative stress, inflammatory cytokines and improve markers of synaptic function after injury

Neuroprotection:B Vitamins: Riboflavin

- Riboflavin has been studied in TBI rat models and has been found to limit damage after TBI
- It acts as an antioxidant and decreases neuronal cell death under excitotoxic conditions
- It led to improvement in sensorimotor function as well as working spatial memory
- Converted dose from animal studies would be 75-200 mg per day

NRF2

- Nuclear factor-erythroid 2-related factor (Nrf2), a pleiotropic transcription factor, coordinates expression of genes required for free radical scavenging, detoxification of xenobiotics, and maintenance of redox potential.
- In TBI there is increased Oxidative stress, increased xenobiotics entering the brain because of damage to the BBB and increased neural inflammation. NRF2 when stimulated(DHA, exercise, curcumin, green tea) can activate NRF2
- There are no drugs that up regulate NRF2 but there are a number of natural products which can do this including Curcumin, DHA and green tea

Neuroprotection:Decrease ROS

- ROS may build up in brain tissue because of ischemia, mitochondrial dysfunction, neurotoxins
- Goals: decrease free radicals passing thru the BBB from outside the brain
- Protect and repair mitochondria in the brain to decrease release of ROS
- Activate the NRF2 gene response in the brain to mobilize the brains production of endogenous antioxidants and endogenous anti-inflammatories
- Activate NRF2 by Green tea, exercise, Curcumin and DHA

RX: Decrease Oxidative Damage

- Diet rich in Polyphenols (wild blueberries, bilberries) Use in smoothies, eat berries and take capsules or powders of concentrates
- B2, Vit. C, Vit. E
- Use R Alpha Lipoic Acid to decrease ROS and can also inhibit Nf kappa B R alpha Lipoic acid 100 mg(2) 2x a day
- Melatonin 1.5 mg has antioxidant effects

ROS: Curcumin: Neuronal Effects

- Curcumin is probably the best studied supplement in regard to its use in brain injury in rat models
- Curcumin upregulates transcription factor Nrf2, HO-1 expression and protects rat brains against focal ischemia
- In rat studies of brain injury curcumin appears to be able to decrease inflammation, ROS and induce neuroplasticity
- In Alzheimer studies Curcumin appears to decrease microglial activation

ROS: Curcumin

- Curcumin appears to be quite safe without toxicity at normally used doses
- Curcumin is not well absorbed orally
- There are 4 forms of Curcumin that are more highly absorbed: Meriva Liposomal, BCM 95, Longvida and Curcumin with piperine
- Longvida uses an SLCP and appears to enable free Curcumin to absorbed thru the BBB and is therefore the preferred form in brain injury although might also consider a liposomal form
- Use Curcumin 400 mg 1-2 3x a day(Higher doses are preferable)

BDR1

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BDR1 band names ok since there is more than one? or omit?
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Decrease Neural Inflammation

- Eval and treat Gut Dysbiosis
- Eliminate cross reacting and sensitive foods
- Curcumin (Highly absorbable) 400 mg 1-2 3x/day
- DHA TG form 2-4 grams/day
- Diet rich in Blueberries and flavonoids
- Omega 3 FA bias towards DHA 2-4 grams
- Consider Minocycline(100 mg 2x a day)with a proposed mechanism of action including inhibition of microglial activation reduces IL-1β production, lesion volume, and functional deficits in TBI models.

Support Brain Mitochondria: Nicotinamide(NAM)

- Precursor for NAD+ for energy
- Free radical scavenger
- Supports numerous brain neuroprotective pathways
- Improved sensory, motor and cognitive function following frontal injury
- NAM has additive and synergistic effects when combined with Progesterone
- Translation from rodent studies 400-800 mg per day

Rx: Improve Mitochondrial Health and Brain ATP production

- TBI results in production of dysfunctional mitochondria and damaged mitochondria
- B complex with high dose Riboflavin, Nicotinamide
- Acetyl L Carnitine may increase mitochondrial energy and was used as part of a combination therapy which improved performance and brain perfusion in players who received multiple TBIs CTE (Amen et al., 2011).
- COQ10 in a highly absorbable form 200mg 2x a day(also consider MitoQ)
- Blueberries and blueberry concentrates
- Omega 3s with DHA for mitochondrial membrane repair

Omega 3: CNS

- CNS roles of Omega 3 FA
- Provides a substrate for neuronal membrane phospholipids
- Modulates neurotransmission
- Decreases inflammation(reduces TNF alpha and IL6)
- Decrease axonal loss after injury.
- Increase BDNF levels, reduces oxidative stress, and preventing synapse degradation
- May reduce excitotoxic damage
- Bias your Omega 3 towards DHA and the TG form
- Use GLA 250-400 mg when using high dose Omega 3s.

Neuroprotection, Repair: Multitaskers

- Melatonin 1.5 mg before bed
- Low dose Lithium about 20 mg one time per day
- Curcumin (Longvida)400 mg 3x a day may repair the BBB, antiinflammatory and [illegible] better absorbed from the BBB
- Taurine 1000 mg 3x a day(regulates water balance, decreases edema,repairs the BBB, supports learning and memory)
- Omega 3s DHA/EPA 3-4 grams/day Triglyceride form : cell membrane fluidity, receptor affinity and modulation of signal transduction. DHA accumulates in the Hippocampus and frontal cortex as a key structural component.

BDR [2]1

Neuroprotection Multitaskers

- Good multivitamin with activated B vitamins, Vit. A, D , Zinc and Magnesium
- TBI diet
- Aerobic Heart Zone exercise

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BDR [2]1 remove?
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Improve Blood Flow and Oxygen Delivery

- Vinpocetine 30 mg to increase brain blood flow, reduces brain excitotoxicity, (may also decrease infarct volume) dose 30 mg per day
- Ginkgo Biloba 120 mg 2x a day
- These supplements are appropriate in the acute and subacute phases of TBI as well as for CTE
- HBOT treatment at 1.3-1.5 Atm
- Theory of mechanism is that it drives O2 to areas of ischemia and poor blood flow
- Usually 20 treatments are done (4 days a week) Very good for CTE and can be used for Traumatic Brain Injury

What HBOT is

- 100% oxygen under pressure
- 1.5 ATA for brain injury
- 20-40 1 hr treatments
- Start with 10 treatments

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Is Hyperbaric Medicine Safe?

Source: "HBOT for TBI" Consensus Conference, December 2008

- **Treatment involves simply breathing pure oxygen under pressure** (often while sleeping or watching TV).
- **Ten thousand plus similar treatments are given every day at 1,200+ locations nationwide for other indications.**
- The DoD White Paper stated: **"side effects are uncommon and severe or permanent complications are rare…"** *(White Paper for the HBOT in TBI Consensus Paper, 12/08)*
- The DoD After Action Report stated: **"safety of the treatment is not an issue."** *(After Action Report HBOT in TBI Consensus Conference, Defense Centers of Excellence, 16 Dec 2008)*

Rx: Support Membranes and Synapses

- Use supplements and food to support brain cell membranes
- Omega 3 DHA 3-4 grams in 2 divided doses
- Pantothenate helps convert Choline to Acetylcholine and it also supports Adrenal health(500 mg 3x a day)
- Phosphatidyl Serine(PS) works with DHA to support the neural cell membranes and is concentrated at Synapses
- Use 300-600 mg 2x a day
- PS is derived from soy but there are no soy allergens in it

Rx: Support Neurotransmitters at Synapses

- Supply precursors with adequate and clean protein
- Support Methylation to make Neurotransmitters with B vitamins
- Huperzine A(100 micrograms) to support Acetyl Choline
- Augment and supply Choline in food and as Phosphatidyl Choline(1000 mg per day) and Citicoline (250 mg 2x a day)

Increase Synaptic Density: Synaptogenesis

- Aerobic exercise via BDNF
- Magnesium(Magnesium Threonate)
- Taurine 1000 mg 2x a day
- Brain training

Repair

- The brain has the capacity to promote cell repair through compensatory mechanisms known as neuroplasticity.
- After 4-6 weeks in the subacute phase if conditions are right the brain through trophic factors (BDNGF etc.) may stimulate axonal and dendritic sprouting, nerve stem cell differentiation, and enhance functional synaptogenesis
- Important in the late subacute phase and chronic phase to enhance this process with physical and mental exercise and supplements

Trophic Factors

- Certain brain growth factors may increase to respond to brain injury:
- Neurotrophin
- Nerve growth factor
- Basic fibroblast growth factor,
- Brain-derived neurotrophic factor (BDNF)(this is the easiest to modulate)
- IGF-1

Repair: Growth Factors

- Nerve growth factors are not increased enough in most patients to promote enough blood vessel, neuron and synaptic development
- IGF-1 represents one of the important regulators of adult brain angiogenesis and may enhance new blood vessel formation after brain injury.(measure IGF-1 and consider using Sermorelin)

Neural Brain Repair

- These strategies promote neuroplasticity and neuronal structure repair
- Protect or improve mitochondria
- Increase trophic factors like BDNF
- Increase synaptogenesis

Neurogenesis

- Ability to stimulate neural stem cells and synaptogenesis especially in the hippocampus
- Low dose Lithium 20 mg
- Melatonin 1.5 mg
- Vitamin D 5000 IU or amount to get to 50-70
- EGCG Green tea extract

Rx: Increase BDNF

- Decrease stress, decrease sugar
- Correct Thyroid deficiency
- Use Progesterone
- Resveratrol
- Huperzine A: acetyl choline esterase inhibitor
- 8 or more hours of sleep
- Polyphenols: Blueberries, Cacao, Zinc 30 mg
- Direct sunlight for 10-20 minutes a day
- Aerobic exercise is the most reliable

Exercise

- Brain Derived Nerve Neurotropic (growth)factor increases synaptic plasticity and increases synaptic connections
- Exercise increases the expression of brain-derived neurotrophic factor (BDNF) in rodents and in healthy humans
- Am J Physiol Regul Integr Comp Physiol. 2010 Feb;298(2):R372-7. doi: 10.1152/ajpregu.00525.2009. Epub 2009 Nov 18.
- **Endurance training enhances BDNF release from the human brain**

Increase BDNF: Exercise

- Aerobic heart zone(70-80% max HR) training for 30-40 minutes is the best stimulus
- Resistance training is important for building muscle but not for BDNF
- HIIT is not as effective as heart zone training in the 70-80% max heart rate zone
- Have patients monitor their heart rate
- Have them do walking when they are able and start with 15 minutes
- Progress to 10 minutes of heart zone training

Increase BDNF

- Gradually increase the duration of exercise
- Advise them there should be no pain(especially headaches) and no SOB with exercise
- Progress them to heart zone exercise(70-80% max heart rate) 5-7 days per week for 30-40 minutes

Reference

- Nokia, M. S., Lensu, S., Ahtiainen, J. P., Johansson, P. P., Koch, L. G., Britton, S. L. and Kainulainen, H. (2016), Physical exercise increases adult hippocampal neurogenesis in male rats provided it is aerobic and sustained. J Physiol, 594: 1855–1873. doi:10.1113/JP271552

Exercise: Benefits for TBI

- Activation of NRF2 for antioxidant and antiinflammatory benefit
- Increase in BDNF to increase neuroplasticity and synaptic connections
- Improves sleep
- Decreases stress and anxiety

Neurogenesis

- Adult CNS can generate new neurons in certain brain regions called neurogenic niches.
- The hippocampal subgranular zone and the forebrain sub ventricular zone (SVZ) are the major neurogenic niches
- Brain injury is known to stimulate neurogenesis in both these regions, purportedly to replace lost neurons

Nerve Stem Cells

- Goal to stimulate neural stem cells and synaptogenesis especially in the hippocampus
- Low dose Lithium 20 mg
- Melatonin 1.5 mg
- Vitamin D 5000 IU or amount to get to 50-70
- EGCG Green tea extract
- Exercise

Lithium

- Low dose Lithium causes the release of neurotrophic factors such as BDNF that induce neurons to repair themselves
- Lithium may lower toxicity of amyloid protein
- Lithium may induce neurogenesis of Hippocampal neurons

Taurine

- Taurine can be made in the brain from Cysteine but may be in short supply if there is inadequate cysteine or after a TBI
- In the brain Taurine has many functions: protection of cells against osmolar changes
- Neurotrophic effect
- Improvement of microvascular cerebral blood flow
- Activate neuronal stem cells
- Trigger new brain cells to grow in the Hippocampus
- Taurine may enhance neurite(axon or dendrite) growth which can enhance neuron communication
- Taurine can protect against excitotoxicity

Neural Repair: Taurine

- Use Taurine at any stage after a brain injury
- Use Taurine in doses of 1000 mg 2x a day
- Taurine can also be used alone to combat Anxiety or in combination with GABA 100 to 500 mg 2-3x a day

Food and the Brain: Pathophysiology

- There may be cross reactivity between an environmental trigger and a neurological tissue which can damage brain tissues that are trying to repair or that have not even been damaged
- These triggers can be bacterial LPS, Metals, chemicals or cross reacting foods
- This can set off an autoimmune reaction of a TH1 or TH17 immune cell
- Microglial cells are 15% of brain glial cells and are normally resting. They can also secrete trophic growth factors to help repair injured tissue but can become activated and start inflammatory reactions

TBI Diet: Cross Reactivity

- Gliadin from gluten can cross react with Asialoganglioside, Myelin basic protein, Synapsin and Cerebellar tissue
- Milk Butyrophilin with cerebellar tissue
- Dairy casein with synuclein and oligodendrocyte
- If there is a leaky BBB and the patient eats gluten containing grains or milk products there can be neurological damage and patients should be on a gluten and dairy free diet

Food Molecular Mimicry

- **Antibodies to aquaporin 4 (AQP4) have been associated with Neuromyelitis optica (NMO) . Antibodies to AQP4 can be triggered by exposure to environmental proteins.**
- **Corn, soy, spinach and tomato(beans, lentils, peanuts) share high similarity in peptide sequences and should be eliminated from a diet if the patient is not improving on the standard TBI diet.**

Diet

- Organic fruits, veggies
- Gluten and dairy free
- Free range grass fed meat, poultry
- Pasture raised eggs
- Provide Choline for Acetylcholine as well as for Phosphatidyl Choline in cell membranes
- Choline containing foods to supply a minimum of 500 mg a day and more like 3000 mg/day(eggs, Chicken, turkey, collard greens, Brussels sprouts, broccoli, Swiss chard, cauliflower, and asparagus)
- http://www.whfoods.com/genpage.php?tname=nutrient&dbid=50#function)

Concussion/TBI Food Plan

- Minimize and eliminate GM foods because of potential neurotoxicity
- Avoid all hidden sources of MSG and all aspartame(excitotoxins)
- Avoid all food allergens
- Support normal glucose levels and avoid hypoglycemia or hyperglycemia(low glycemic index and low glycemic load)

TBI Food Plan

- Protein at every meal or snack
- Avoid browned proteins, eggs and meats to limit AGES and oxidative stress. AGES may breakdown the BBB
- Avoid fried foods
- Avoid/minimize foods with Acrylamide(heat generated neurotoxin) as it is a neurotoxin (potato chips, coffee, browned starches)
- Use foods high in flavonoids(blueberries, onions, apples, strawberries etc)

More TBI Food Goals

- Include foods and supplements with Sulforaphane cruciferous veggies to repair the BBB, aid in detoxification
- Decrease aflatoxin by avoiding peanuts
- Have 1 – 1.2 grams of protein per kg of lean weight to supply neurotransmitter precursors
- Avoid hypoglycemia as that can aggravate build up of glutamate
- Stop all hidden sources of MSG and provide your patient with a list of these ingredients
- Have them stop all diet soft drinks as they may contain aspartame

Blueberry Polyphenols

- Blueberries contain certain polyphenols (anthocyanins) that have been shown to have neuroprotective properties
- Anthocyanins appear to protect the plant from stressors like UV light, cold temperatures, and drought
- Blueberry anthocyanins have been shown to cross the BBB and to accumulate in brain tissue
- They have been shown to improve cognitive function, have antioxidant properties, decrease neural inflammation, decrease excitotoxicity

Blueberries

- Blueberries in the CNS may be able to decrease proinflammatory cytokines and thus limit neural inflammation(brought on by Microglial cells and induced by bacterial LPS)
- Antioxidants may be higher in organic and in wild blueberries
- Ideally use wild blueberries especially in smoothies if they can be obtained as frozen and have the patient eat blueberries 1-3x a day
- Have them drink 100% organic blueberry juice not from concentrate and mix organic blueberry powder in water and tea and smoothies

Green Tea and Cocoa

- Green Tea contains polyphenols that can potentiate Nerve Growth Factor and BDNF induced neuritogenesis (Have then drink organic green tea)
- Cocoa polyphenols can pass the BBB and induce BDNF
- Encourage high % Cocoa >70%
- Limit or reduce alcohol as it reduces neurotrophic factors and can be neurotoxic to the Cerebellum

Treatment Goals: Acute TBI

- Goals: Acute first 1-7 days:
- Assess for intracranial bleed if indicated
- Decrease hemorrhage
- Decrease brain inflammation
- Decrease brain excitotoxicity
- Decrease brain edema
- Limit brain damage
- Reduce brain reactive oxygen species(ROS), reduce brain oxidative damage.
- Reduce excessive cortisol to decrease damage to the hippocampus

Treatment Goals: Subacute 5-60 days

- Assess for and treat for leaky gut and leaky BBB
- Assess cross reacting food allergens and foods and restrict/eliminate them
- Treat and limit brain excitotoxicity
- Reduce oxidative stress
- Reduce brain inflammation
- Assess for and treat brain/BBB autoimmunity
- Use Neuroprotective strategies to protect the BBB and the Brain

Goals: Subacute

- Start Nervous system repair and building strategies
- Use Stress Management
- Assess and treat MSK injuries especially of the neck
- Assess and treat all Pituitary and Hormone dysfunction
- Treat Mood disorders including PTSD, Depression, anxiety, anger, etc.
- Prescribe aerobic heart zone exercise
- Prescribe brain exercise and cognitive training
- Use Frequency Specific Microcurrent for inflammation and congestion and to heal the BBB
- Consider referral for HBOT

Goals: Chronic Stage TBI

- All of the goals for subacute stage
- More aggressive with repair and Neuroplasticity strategies
- Consider SPECT or QEEG if ongoing declines or decreased ability to improve cognitive functioning
- Physical and brain exercise
- Supplements to increase BDNF, Neural stem cells
- Supplements to improve Neurotransmitter levels
- Restriction of Neurotoxins and EMF
- Use FSM to heal the BBB and for 124 for 45 plus minutes to improve injured brain areas
- Use 81 to stimulate under active brain areas

Chronic Stage Goals/Strategies

- Use of HBOT to improve repair and neuroplasticity
- Consider brain stimulation (transcranial) of hypofunctioning areas
- More fine tuned brain exercise for hypofunctioning areas
- Supplements, medications or other methods to decrease hyperfunctioning areas
- Frequency Specific Microcurrent
- Consider referral for Neurofeedback if a QEEG was done

CTE goals/strategy

- All of the Chronic goals and strategies as well as:
- Counseling and methods to avoid suicide
- Work on explosive anger by calming the cingulate, limbic system and the amygdala
- Establish a team of support(counselor, dietician, Functional Medicine practitioner, Psychiatrist)
- Treat PTSD if it is there with EMDR and Frequency Specific Microcurrent
- HBOT treatments
- Transcranial stimulation of hypoactive areas
- Definate imaging with either SPECT or QEEG
- Treat the Prefrontal cortex

CTE Goals/Strategy

- Teach stress management
- Assess and treat fatigue
- Assess the BBB and brain antibodies
- Assess and treat the gut
- Improve and balance neurotransmitters
- Augment GABA
- Re evaluate every 6-8 weeks
- Office visit every 2 weeks
- Home evaluation to remove guns, alcohol and drugs of abuse

Brain Injury Prevention

- Proper conditioning, technique and training for a sport
- Not doing the sport if conditions are too risky for head injury (icy ski slopes etc)
- Proper protective head gear
- Prophylactic Supplements if someone is likely to get a head injury

Prophylactic Supplements for Athletes in High Risk Sports

- NAC 500 BID
- Curcumin 400 mg 2x a day
- Omega 3 FA DHA 2-3 grams per day
- Vitamin E d alpha and mixed tocopherols 400 IU

- These may decrease the progression of pathophysiology if there is a head injury

Can I go Back to my Sport?

- Avoid second impact syndrome(rapid brain swelling and herniation after second injury). Usually leads to death
- Never let an athlete with persistent CNS symptoms at rest or with activity return to a contact sport
- Follow any of the following guidelines(Cantu, American Academy of Neurology or Colorado Medical Association see handout) or refer to a Neurologist for decision

Resources

- https://www.cdc.gov/traumaticbraininjury/mtbi_guideline.html
- Guidelines on assessment and return to sports decisions

Addendum

- Treatment of Mood Disorders w/TBI
- Brain region function and injured area dysfunction
- Specific brain region treatment
- Neuro imaging pros and cons
- Helmets and protection technology
- Additional details on certain supplements and HBOT
- Questions???????

TBI Emotional Issues

- Depression
- Irritability
- Anxiety
- Less tolerance to stress
- For Depression treat the Adrenals, Use Omega 3s, prescribe exercise, 5HTP 100 mg 2 in the am and pm
- Light therapy(30 minutes) in the morning

TBI Emotional Issues

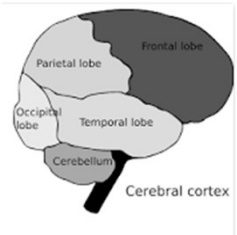
- If excessive stress and anxiety consider using the FSM ERB
- For Excessive stress use FSM to calm the Adrenals
- Also consider the Heart Math approach with the emWave2
- For excessive stress consider a supplement with Glycine, Taurine, L Theanine and relaxing herbs

PTSD

- PTSD can occur with TBI and CTE
- It can lead to elevated cortisol production and Hippocampus injury
- It can be a very disturbing symptom and needs to be treated
- Treatment methods are:
- EMDR therapy
- Frequency Specific Microcurrent
- Tapping methods(EFT etc)

Brain Regions

- It is important to understand the function and resulting dysfunction of the various brain regions that can get injured
- There are certain approaches to treatment that are brain region specific



Brain Areas: Frontal and PFC

- Problems with: Short term memory
- Impulse control
- Little forethought
- disorganization
- Empathy: injury leads to poor empathy for the needs of others
- Short attention
- Lack of tact and say whatever comes to their mind without concern for how it will affect others
- May seek conflict

Treatment for Brain Areas: PFC

- PFC: goal setting, EPA 3-4(give a product with more DEPA than DHA)
- Stimulating supplements(Green tea, Rhodiola, L Tyrosine, Ginseng)
- Stimulating medications(Wellbutrin, ADD meds)
- Neurofeedback

Brain Areas: Temporal

- Left temporal lesions can result in impaired verbal memory
- Right temporal lesions result in problems with recall of non-verbal material: as music and drawings.
- Difficulty in recognizing faces
- Difficulty in understanding spoken words
- Difficulty with identification of objects
- Right lobe damage can cause persistent talking
- Increased aggressive behavior and emotional instability especially anger
- Feelings of panic

Brain Area Treatment: Temporal

- Supplements for stabilizing mood: GABA, B6
- Supplements for memory(support neuronal membranes with Choline and Omega 3s, use Huperzine A to increase acetylcholine
- Medication for stabilizing mood(Lamictal, etc)
- Ketogenic diet
- Neurofeedback

Brain Areas: Parietal

- Left parietal lobe damage: "Gerstmann's Syndrome."
- Right-left confusion,
- Difficulty with writing
- Problems with mathematics
- Disorders of language
- Problems with object perception
- Right parietal lobe damage: Neglecting part of the body
- Problems with self-care skills such as dressing and washing
- Problems with drawing ability

Brain Areas: Occipital

- Problems with vision and cuts in visual fields
- Difficulty with locating objects
- Color vision problems
- Visual hallucinations and illusions - inaccurately seeing objects
- Problems with word recognition
- Difficulty in recognizing drawn objects
- Problems recognizing the movement of an object
- Difficulties with reading and writing
- Need to refer for a trauma vision specialist for testing and rx

TBI: Brain Areas: Cerebellum

- Cerebellar injury is less common than frontal and temporal injury but does occur
- Very important to ask questions about balance, gait and coordination as well as about weakness
- Important to do basic cerebellar neuro exam to pick up even subtle findings on gait and coordination
- Even small findings on exam can indicate cerebellar injury
- Cerebellar injury requires specific rehab strategies working on balance coordination. Also FSM can target the Cerebellum to aid in repair

Cerebellum

- Poor coordination of motor movement
- Decreased ability to judge distance and when to stop
- Poor ability to perform rapid alternating movements
- Movement tremors (intention tremor)
- Gait dysfunction: slowed walking and swaying to one side, wide based walking
- Poor balance and falling risk
- Weak muscles
- Speech slurred
- abnormal eye movements (nystagmus).

Cerebellum: Treatment

- Use Neuroprotection guidelines
- Use Guidelines for increasing BDNF, stimulating stem cells
- Practice coordination of motor movement, language
- Ping pong
- Dance lessons and dancing
- Balance training in Physical Therapy and at home
- Treat with FSM with 40,124/84
- Use 81/84 while doing exercises

Prevention: Bicycle Helmets

- Most bike helmets protect against skull injury but do not have enough protection against brain injury in case of an impact
- There are helmets with MIPS and ODS and these technologies make a helmet safer
- These technologies allow for the helmet to move in some rotational pattern to absorb some of the shearing forces
- MIPS is a plastic piece that can rotate slightly
- The 6D design has a dual shell, the inner shell is connected to the outer shell with hourglass shape dampers that compression and rotation

ODS Technology

- "6D's revolutionary patented Omni-Directional Suspension (ODS) embodies a fully active, in-helmet suspension and kinetic energy management system. The goal was simple; design a helmet that reduced energy transfer to the brain over a much broader range of energy demands, including LOW, MID, and HIGH-VELOCITY impacts for both LINEAR and ANGULAR ACCELERATIONS"

Functional Neuroimaging

- qEEG: electrical activity, non invasive(can not image Cerebellum)
- SPECT: blood flow, hypo, hyper perfusion areas of the brain(Amen Clinics) can image limbic structures better than qEEG, gives a 3D image but uses a radioactive nucleotide
- PET Scan: metabolic, hypo or hyper metabolism Very expensive
- AMIVID PET can detect amyloid plaques in early onset Alzheimer's(could be used in CTE)
- fMRI: Oxy and deoxy Hg (Measures hypo oxygenation) very loud and very expensive

Structural Imaging

- CT Scan: radiation, good only during acute phase to rule out a bleed
- MRI: 3T MRI with NeuroQuant can pick up brain atrophy Appropriate for an MVA so you can prove progressive atrophy following TBI
- Order an initial study within a few weeks of the TBI and order a follow up within 6-12 months if the patient does not resolve TBI symptoms

NeuroQuant MRI

BDR [4]1

- NeuroQuant MRI: can show progressive Hippocampal atrophy

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BDR [4]1 commercial?
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qEEG

- qEEG is a type of functional Neuro imaging which assesses electrical activity of the brain
- It is non invasive
- There are more than 2000 peer reviewed articles in which it is used to evaluate TBI
- qEEG can give you hypo and hyper function based on decreased and increased electrical activity
- qEEG can also give functional connectivity of brain areas
- qEEG looks at increased and decreased amplitudes of certain frequency bandwidths

qEEG: TBI

- Reduced power in higher freq bands 8-40hz linearly related to extent of cortical grey matter injury
- Increased slow waves in the delta freq band 1-4 Hz which is related to cerebral white matter injury
- Changes in EEG coherence and phase delays which is related to the magnitude of injury in both grey and white matter especially in the frontal and temporal lobes

qEEG

- Can use this to follow therapeutic interventions
- Can use it to determine Neurofeedback program to change electrical activity towards a more normal brain pattern

qEEG: Loreta

- To refer for qEEG:
- Clinical grade qEEG assessment
- At least 21 channels
- Manually as well as computer artifact the data
- Interpretation should be by minimum of QEEG-D, preferably a Neurologist or Neuropsychologist
- ALSO THE OPTION OF USING LORETA IMAGING(3D Tomographic image)

Imaging: SPECT SCAN

- SPECT scan is an image that can give very useful brain imaging information in regard to relative blood flow to areas of the brain including the limbic system and cerebellum
- It can show hypo, hyper and normally functioning brain areas
- 2 Scans are done 1. resting and 2. with concentration
- SPECT scan would be very useful in CTE as well as TBI to show areas receiving less blood flow thus hypofunctioning areas
- It would be very useful in a Medical Legal cases to show areas the head injury
- It can be used in cases of mood instability to direct treatment

SPECT Systematic Review on TBI

- *Raji, Tarzwell, et al. Plos One 2014*
- 99% of the Reviewed Articles showed that SPECT picked up abnormalities in TBI missed by structural CT or MRI.
- Almost 90% of the articles reviewed showed a significant correlation between SPECT and neuropsychological or neurological findings.
- 95% of the articles assessed judged SPECT to change clinical management.

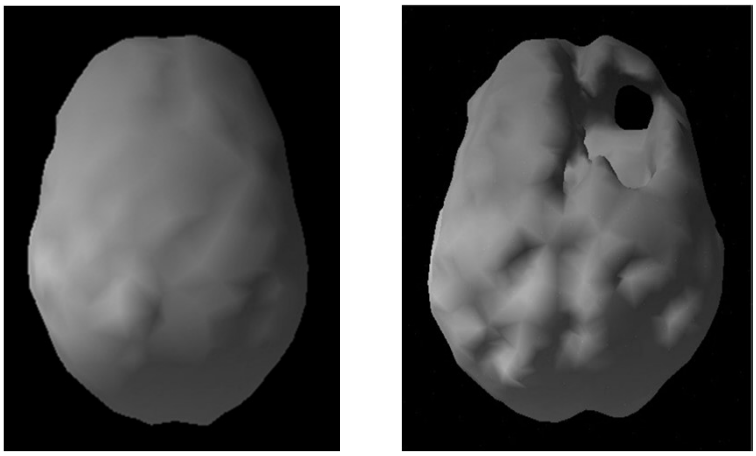
Imaging: SPECT Scans

- Common patterns are:
- Decreased function of a part of the pre frontal cortex and the anterior part of the Temporal lobes as in a head on or rear end collision or when an athlete is hit in the front of the head
- The tectoral membrane makes the anterior part of the temporal lobes more susceptible to shearing forces

Imaging: SPECT

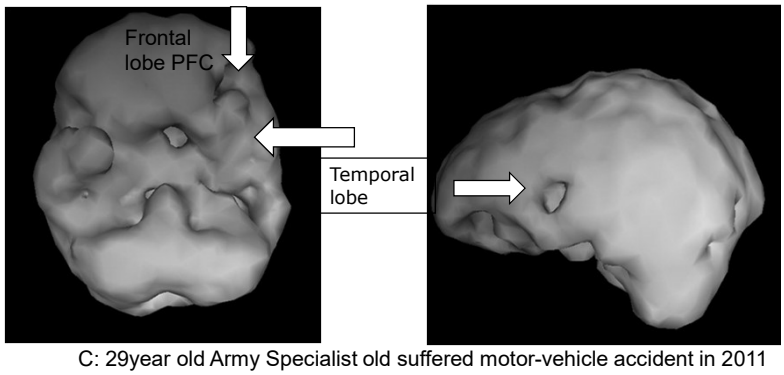
- Other patterns maybe more significant damage to one or both Temporal areas or global decrease in blood flow in multiple areas as in CTE
- There are also patterns specific for PTSD
- Note: A SPECT scan can not show the Pituitary
- Pituitary lesions may be visualized with MRI but it is better to do blood testing for Hormones

Healthy vs Traumatic Brain Injury



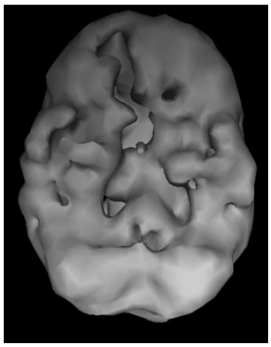
Healthy TBI

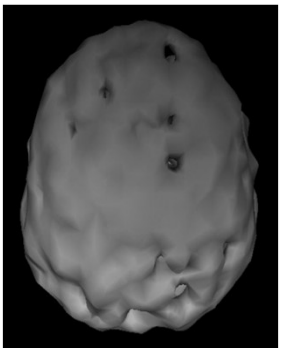
Left Frontal and Temporal Injuries from MVA



C: 29year old Army Specialist old suffered motor-vehicle accident in 2011 left her with a left frontal temporal skull fracture and moderate traumatic brain injury (TBI). After spending several months in rehabilitation she reports residual effects including worsening depression and anxiety and intermittent symptoms of irritability, anger, reliving or re-experiencing the trauma, hypervigilance (looking around in anticipation of further injury) and avoidance of settings that remind her of the trauma. In addition, she reports persistent anxiety dreams and nightmares

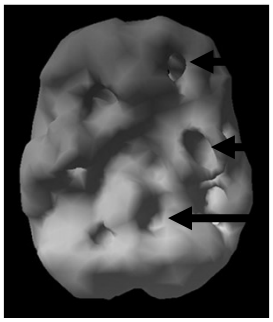
SPECT Image of 51 yr old prior NFL player with CTE



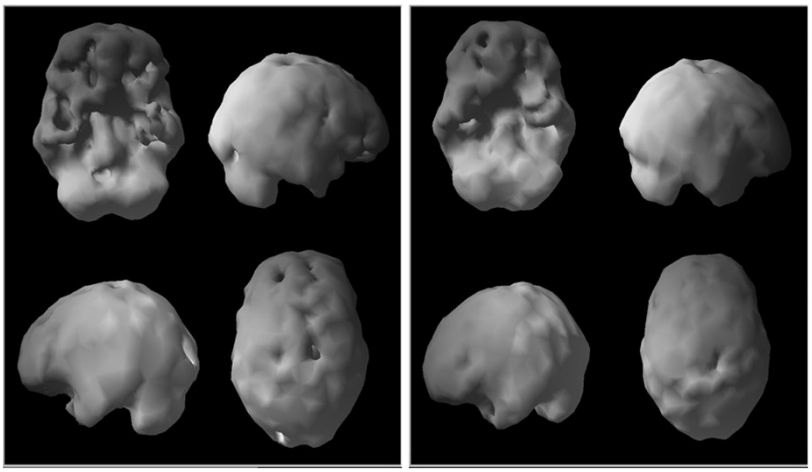


Results: Global Lack of Blood flow

- Frontal Lobes
- Temporal Lobes
- Parietal Lobes
- Cerebellum



Forgotten Brain Trauma



Before After

HBOT

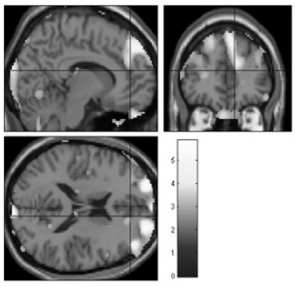
Significant Rehabilitation Possible

Journal of Psychoactive Drugs, 43 (3), (insert page range of article here), 2011
Copyright © Taylor & Francis Group, LLC
ISSN: 0279-1072 / 2159-9777 online
DOI: 10.1080/02791072.2011.566489

Routledge
Taylor & Francis Group

Reversing Brain Damage in Former NFL Players: Implications for Traumatic Brain Injury and Substance Abuse Rehabilitation†

Daniel G. Amen, M.D.*; Joseph C. Wu, M.D.**; Derek Taylor*** & Kristen Willeumier, Ph.D.****



- **80% improvement!**
- **Especially in:**
  - **Memory**
  - **Attention**
  - **Mood**
  - **Sleep**

Functional Med/TBI Resveratrol

- Resveratrol has been shown in studies to reduce cerebral ischemia in rats
- Resveratrol may stimulate the expression of heme oxygenase. Increased heme oxygenase activity has led to significant protection against models of in vitro and in vivo oxidative stress injury.
- Consider using 250 mg of trans resveratrol per day as that also appears to be a good dose for cardiac protection

References

- Numerous references were used for this lecture. The following is a good summary reference
- Brain research 1640 (2016) 114–129
- Vitamins and nutrients as primary treatments in experimental brain injury: Clinical implications for nutraceutical therapies
- Cole Vonder Haar, Todd C. Peterson, Kris M. Martens, Michael R. Hoane