

NUTRITIONAL APPLICATIONS FOR TRAUMATIC BRAIN INJURIES: FROM RESEARCH TO CLINICAL PRACTICE

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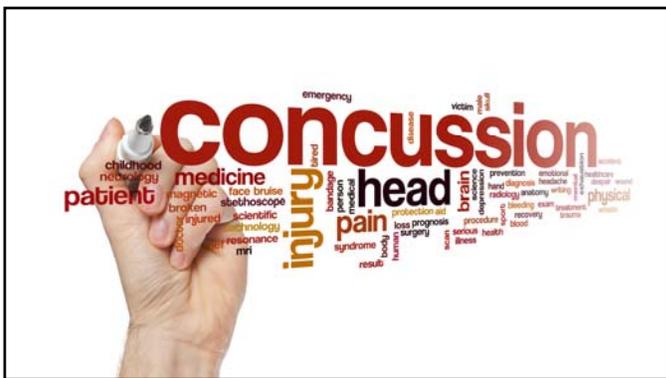
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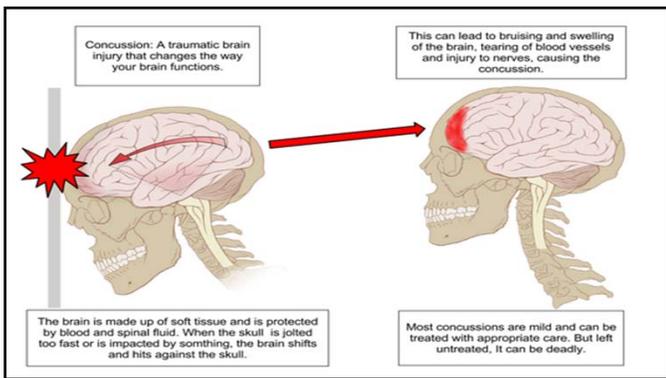
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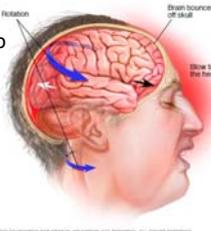
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WHAT IS A CONCUSSION?

- A type of traumatic brain injury (mTBI).
- Sudden bump, blow, jolt, hit causes brain to bounce or twist.
- Described as "mild" brain injury because seldom life-threatening. Can be serious.
- Creates chemical changes in brain & stretch/damage to brain cells. Called the "secondary injury".
- This is NOT "second impact syndrome."

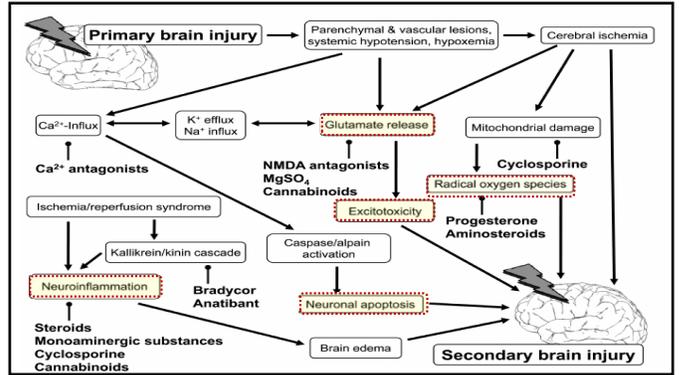


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**“SECONDARY INJURY”
THE BIOCHEMICAL CASCADE**

- Mechanical trauma initiates harmful biochemical cascades referred to as the “secondary injury”, i.e., indirectly caused by the original trauma.
- Secondary cascade: Synaptic, nerve signaling, and behavioral changes due to:
 - **Inflammation**
 - **Cell death** (apoptosis)
 - **Release of ROS** (free radicals)
 - **Excitotoxicity** (excess glutamate firing)

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INTERVENTION

- Currently NO effective treatment for concussions/mTBI
- Most clinical drug trials failed to report any benefits
- There are guidelines & interventions
- There is stabilization & prevention
- There is reasonable, research-guided balancing of brain biochemistry
- Most studies are animal models. Need human research for all “treatments”.

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GENERAL CDC BRAIN-RECOVERY GUIDELINES

- Rest considered best intervention ASAP after injury.
- Good night sleep & day time naps.
- Keep room dark. Maintain routine schedule.
- Limit physical & mental activities.
- No TV, phones, work or school, reading, and so on.
- No activities that may further injury.
- Meds (pain/nausea) & topical ice for symptom relief
- Gradually return to regular (non-strenuous) activities, work, school as symptoms improve.
- If symptoms worsen, stop activity until tolerated.

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REST your injury!

This means...

NO sports NO school work NO screens
NO computers NO video games NO TV

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SLEEP-WAKE CYCLES

- Sleep-wake disturbances (SWD) are prevalent in TBI population
- 40-70% have SWD for years after TBI
- Worsens mTBI-related neurobehavioral impairments: agitation, depression, anxiety, slowed processing speed, attention, memory, cognition.

“Important to recognize and treat SWD early to allow for optimal cognitive recovery following a TBI.”

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“Greater attention should be given to the diagnosis and management of insomnia in persons with mTBI/concussion.”

Evaluated workers about 7 months after mTBI/concussion. Higher disability found with more severe insomnia, depression, anxiety and pain. Better sleep quality improved the other factors. Sleep speeds healing.

“The relationship between insomnia and disability in workers with mild traumatic brain injury/concussion: Insomnia and disability in chronic mild traumatic brain injury.” Sleep Med. 2016;20:157-66. Mollayeva T, Pratt B, et al.

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PINEAL HORMONE MELATONIN

- 42% lower production at night after TBI.
- Salivary level correlates with severity of trauma and with sleep difficulty in this group.
- Animals given melatonin or melatonin receptor agonist after mTBI.
- Daily dosage timed to animal sleep pattern.
- Reduced severity of early brain damage
- Reduced long-term neurobehavioral deficits.



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MELATONIN BENEFITS IN TBI

- Given within 1 day post-injury, brain & serum had:
- Increased anti-inflammatory & anti-oxidant proteins: IL-10, IL-4, SOD, GSH, glutathione peroxidase, & anti-inflammatory gene expression.
- Reduced inflammatory proteins: IL-1 β , TNF α , & malondialdehyde.
- Decreased Keap 1 expression & promoted Nrf2: (main protection against cell oxidative stress damage)



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MELATONIN DOSAGE IN TBI

- Randomized double-blind placebo-controlled two-period crossover study.
- Human subjects with mild to severe TBI & post-injury sleep disturbances.
- Took oral time-released 2-5 mg melatonin caps or placebo 2 hours before bed nightly for 4 weeks.
- Significantly improved sleep quality.
- Reported improved vitality & mental health.
- Decreased anxiety & fatigue
- No serious adverse events. Considered safe.



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REF: MELATONIN

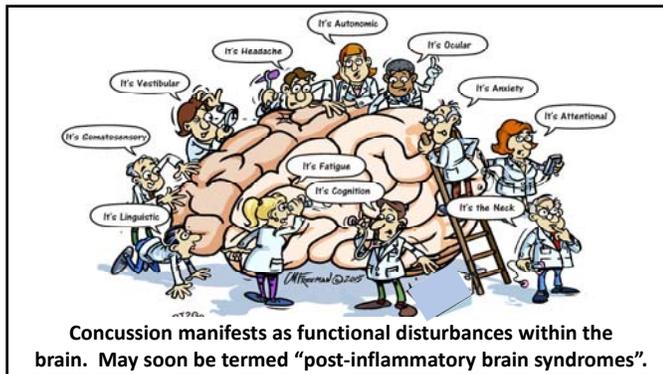
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DEVELOPING EFFECTIVE THERAPIES

- Must better understand & identify precise mechanisms underlying TBI-related pathology.
- **Primary injury:** at time of head impact. Causes direct damage to neural tissue: focal intracranial hemorrhage, epidural & subdural hematoma, brain contusion, & direct axonal damage. Currently no treatment. Only stabilization.
- **Secondary injury:** develops minutes to months following mechanical insult. Contributes to neurological impairment. Most amenable to treatments.

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S&S CONCUSSION

Physical, Cognitive, Emotional, Sleep

Signs	Symptoms
<ul style="list-style-type: none"> • Can't recall events before or after a hit or fall • Appears dazed or stunned • Forgets an instruction, is confused about an assignment or position, or is unsure of the game, score, or opponent • Moves clumsily • Answers questions slowly • Loses consciousness (even briefly) • Shows mood, behavior, or personality changes 	<ul style="list-style-type: none"> • Reports headache or "pressure" in the head • Nausea or vomiting • Balance problems, dizziness, double or blurred vision • Bothered by light or noise • Sluggish, hazy, foggy, or groggy • Confusion, concentration, or memory problems • Reports "not feeling right" or "feeling down"

Source: Centers for Disease Control and Prevention. 2015.

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SECONDARY INJURY: THE BIOCHEMICAL CHANGES

At the cellular level, mediated by several pathways:

- neuroinflammatory** response of local & systemic immune activation.
- free radical generation** causing damage to proteins & phospholipid membranes of neural cells
- excitotoxicity** caused by excess of neurotransmitter glutamate

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GOAL OF NUTRITIONAL INTERVENTION

- Reduce brain inflammation
- Reduce oxidative stress
- Support brain neuronal repair
- Reduce glutamate excitotoxicity

Failure to address secondary biochemical imbalances leads to future brain degenerative diseases.

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NUTRITIONAL WINDOW OF OPPORTUNITY

- Not done immediately after acute, primary trauma.
- Post-concussive inflammatory response & cytokine release is neuroprotective to initiate repair processes.
- Prolonged activation of inflammatory state becomes neurotoxic.
- Person must first be stabilized & categorized as to injury status.
- Most research agrees nutritional interventions should start 24-48 hours post-injury.
- Must normalize cascade of **secondary biochemical injury**.

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NEUROINFLAMMATION

“A basic premise is that inflammation is associated with almost all brain injuries.”

TBI & concussion leads to chronic, systemic inflammation & dysfunctional BBB.

“Neuroimmunology of Traumatic Brain Injury: Time for a Paradigm Shift.”
Neuron. 2017;95(6):1246-1265. Jassam YN, Izzy S, et al.

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Identifying the factors that sustain pathogenic pro-inflammatory reactions is critical to the development of efficacious TBI therapies in humans.

Rather than completely block the immune response to TBI, future studies should **focus on therapeutically guiding TBI immunity toward a favorable wound-healing response** that rapidly stabilizes or restores CNS function.

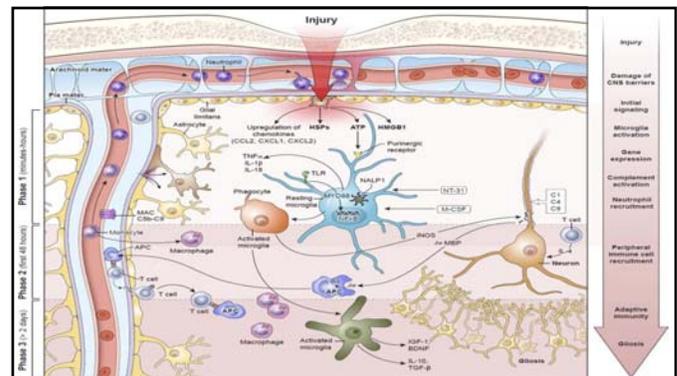


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TBI INFLAMMATORY PROCESS

- Damaged CNS releases protein signaling molecules
- Proteins sense danger & help initiate inflammatory cascade
- Neuronal cells triggered to release several kinases
- Microglia & astrocytes secrete local inflammatory cytokines
- Cytokines bind to TLR4 or RAGE to up-regulate inflammatory genes
- Inhibiting these pathways reduces BBB damage & inflammation
- Minimizing inflammatory & improving anti-inflammatory pathways is crux of current drug studies for TBIs.

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SYSTEMIC INFLAMMATORY MARKERS

- Athletes with prior concussion have more & higher amounts of inflammatory markers compared to those without prior concussion.
- Have significant up-regulation of genes which raise inflammatory markers weeks after injury compared to baseline and control group.
- Inflammatory liver markers elevate indicating a systemic organ response.
- Future musculoskeletal injuries respond with greater inflammatory response indicating muscle dysfunction.



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“Nutritional supplementation and nutraceuticals have shown neuroprotective promise when provided before and after mTBI and TBI.”

“While pharmaceutical therapies may target only one mechanism of injury and have not shown great promise, nutritional supplementation has emerged as a potential neuroprotective agent that targets multiple mechanisms within the complex sequelae.”

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FAT

"Accumulating evidence suggests that DHA may act as a promising recovery aid, or possibly as a prophylactic nutritional measure, for mTBI."

"With evidence of unsurpassed safety and tolerability, n-3FA should be considered mainstream, conventional medicine..."

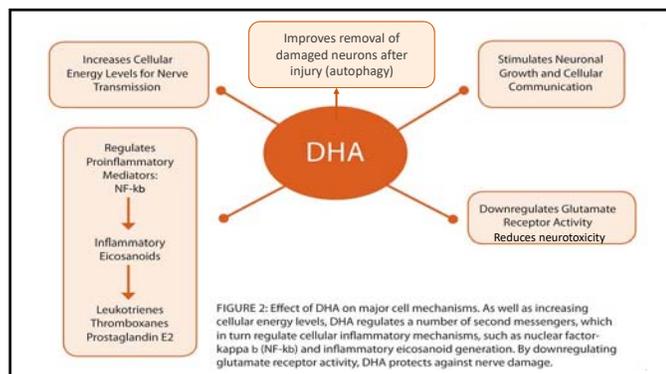
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NUTRITIONAL INTERVENTIONS: FATS

- Saturated fats increase inflammatory response
- Long chain omega 3 PUFA DHA is main brain fat
- DHA required for brain growth, repair, maintenance
- Stored in neuronal cell phospholipids



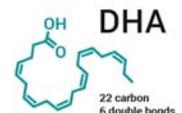
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DHA

- Decreased brain content after mTBI.
- Dietary DHA before or after mTBI improved functional outcomes (spatial learning, cognition, memory).
- Reduces excitotoxicity (counteracts excessive glutamate activity & normalized dopamine release)
- Reduces oxidative stress (improves glutathione enzyme markers).
- Regulates microglial phenotype towards anti-inflammatory M2 pathway.
- Limits structural damage to axon & neuronal apoptosis & improved cell membrane function.



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ENDOCANNABINOID EPOXIDES

- Lipid-derived metabolites from EPA/DHA.
- Form EEQ-EA and EDP-EA.
- Both naturally made & present in brain & organs
- Activated brain microglial & liver cells.
- Reduced inflammatory IL-6 cytokines
- Increased anti-inflammatory IL-10 cytokines
- In mTBI animal model, blocking breakdown of EC metabolites attenuated neuroinflammation, glutamate dysregulation, and improved recovery of neurobehavioral function during first 1-10 days post-injury.

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DHA DOSAGE POST-CONCUSSION

- Considered safe.
- Use fish oil or cold-water algae with assayed DHA content.
- Use 2-6 grams QD depending on body size.
- Dose daily starting 1-2 days post-injury for 2 weeks.
- For those with residual symptoms, do for 2 weeks and reevaluate.
- Increases risk for bleeding if done too high or too early. May cause GI symptoms.

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GLUCOSE PROBLEMS POST-TBI

- Too high blood glucose & too low brain levels
- Most likely due to increase in stress hormones & inflammatory chemicals.
- Related to poor clinical outcome
- Brain needs glucose for energy, but cannot get it or use it
- BBB disrupted, cells become acidic
- Injured nerve cells cannot metabolize excess glucose
- Leads to ischemia, edema, necrosis of neural tissue

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HYPOTHETICAL MECHANISMS

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FYI FOR THE BIOCHEMISTS

- Postinjury period of poor glucose metabolism accompanied by:
 - Decreased ATP
 - Increased flux of glucose through pentose phosphate pathway
 - Increased free radical production
 - Increased activation of poly-ADP ribose polymerase via DNA damage
 - Inhibition of glyceraldehyde dehydrogenase via depletion of cytosolic NAD



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Intense regulation and maintenance of blood sugar within normal range reduces complications of TBI.

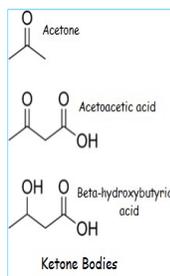
Promising intervention for better neurological outcome.

Can be done with diet &/or drugs.

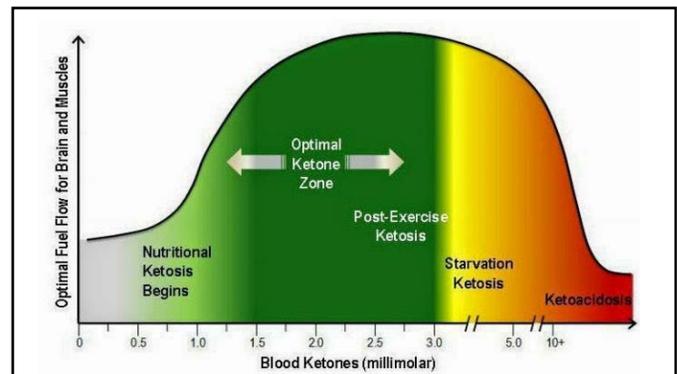
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KETONE BODY ALTERNATIVE

- Only known natural alternative for brain energy metabolism.
- Influenced by diet
- Cross BBB using protein transporters
- Optimal & safe glycemic/ketone body target range has not been determined
- Studies are mixed & mainly animal.
- More effective in young, not adult rats.
- Ketoacidosis damages the brain.
- Want mild ketosis not ketoacidosis.



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RATIONALE: HIGH FAT/LOW CHO DIETS

- Increases blood & brain ketone bodies levels
- Forces body to burn fats not carbohydrates
- Only researched use is childhood seizures
- Improved structural & functional outcome in mTBI/concussion animal models
- Exact neuroprotective mechanism unknown
- KB influence neuron metabolism, cell signaling, genetic regulation. Can reduce inflammation.
- Side effects: constipation, high cholesterol, slowed growth, acidosis, kidney stones, hypoglycemia.

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EXAMPLE OF KETOTIC MEAL PLAN

- 80–90 % fat, adequate protein, limited carbohydrates.
- Traditional ketogenic diet: 4:1 FAT to PRO. Primarily LCFA.
- Modified ketogenic: 3:1 FAT to PRO. MCT & low-glycemic-index CHO.
- Requires V&M supplement
- No clinical trials for human TBI.
- Limited data on dosing & duration
- Compliance is difficult



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FOOD EXAMPLES		
fats	carbohydrates	protein
<ul style="list-style-type: none"> • Heavy cream • Butter • Oils -Vegetable - Olive - Coconut - MCT 	<ul style="list-style-type: none"> • Vegetables - Green beans - Salad - Carrots • Fruits - Berries - Applesauce - Peaches • Pasta substitutes 	<ul style="list-style-type: none"> • Beef • Chicken • Fish • Tofu • Cheese

Avoid: Candy, pastry, bread, pasta, cereals, rice, potatoes, crackers, yams, sugar, HFCS, soda, juices.

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SUPPLEMENTAL BETA-HYDROXYBUTYRATE KETONES
<ul style="list-style-type: none"> • Astrocytes produce βOHB from FA & amino acids • Astrocytes damaged with mTBI. βOHB levels drop. • Diet alone may not elevate levels adequately. • Potential therapeutic benefits of βOHB supplements: <ul style="list-style-type: none"> • reduce mitochondrial ROS • open K^+ & regulate Ca^{2+} channels • upregulate genes to protect against oxidative stress • regulate brain metabolism • reduce inflammatory cytokines • enhance GABA & reduce glutamate

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SUPPLEMENT CAUTION	
<ul style="list-style-type: none"> • βOHB must elevate in blood to encourage entry into brain. • Supplemental βOHB elevates KB in rats after injury. • Mixed results in animal studies. • Did not protect BBB after injury • Led to BBB disruption in healthy animals • Does not control hyperglycemia. • 2 small human trials used IV not oral. • Some side effects. No clinical outcomes noted. • Not recommended at this time for concussions • Use high fat ketogenic diet instead 	

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REF: KETOSIS Pg 1
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MICRONUTRIENT COFACTORS
<p>Vitamins Minerals Phytochemicals</p> 

54

ANTIOXIDANT THERAPY

“development of antioxidant strategies is of primary interest in ongoing efforts to optimize brain injury treatment.”

“overall trend of using antioxidant therapies to improve the clinical outcomes of TBI was positive.”

Both pharmaceutical and nutraceutical anti-oxidants are being used and developed for TBI.

55

RATIONALE: VITAMINS & MINERALS

- Cofactors for all bodily functions and biochemical pathways.
- Deficiencies common.
- Levels rapidly depleted after injury.
- Beneficial effects:
 - Reduce inflammation
 - Protect mitochondria from ROS
 - Improve glucose utilization
 - Normalize glutamate (reduce neurotoxicity)
 - Enhances neuronal repair & function

For excellent details of individual V&M in relationship to neurological diseases & trauma:
See references: Vonder Harr (2016) and Lucke-Wold BP (2018)

56

OXIDATIVE STRESS

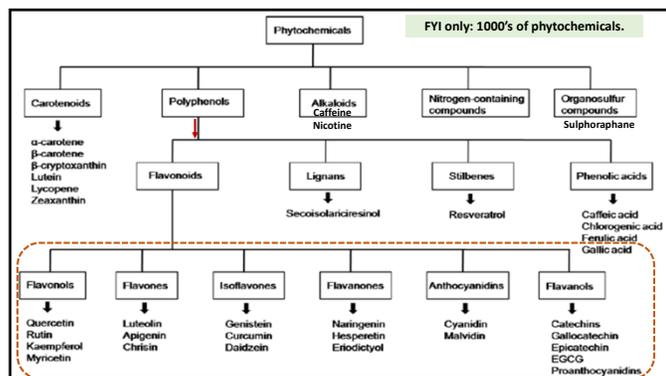
- TBI generates oxidative stress:
- Increased oxidants & ROS
- Decreased antioxidant defense enzymes (GSH, GPx, SOD, CAT)
- leads to neural dysfunction, cell death, lipid peroxidation
- animal models of TBI show great promise
- most human treatment of TBI have failed
- Difficult to deliver to correct area of brain at critical time

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ANTIOXIDANTS

- Dietary sources:
 - Vitamins A, C, E, some B's,
 - Minerals: selenium, zinc, copper, manganese
 - polyphenol flavonoid family
- Endogenous:
 - glutathione, SOD, catalase, peroxidase, CoQ10, lipoic acid, n-acetylcysteine
- Can cross BBB in varying degrees
- Exact mechanism of action unknown
- Considered safe orally
- Animal research testing transcranial injections

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PLANT FLAVONOID: CURCUMIN

- Difficult to absorb: oil-based phytosome formulas & C+E enhance gut absorption
- normalized BDNF
- improved neuronal survival
- improved motor & learning performance
- Activated Nrf2 pathway (major protection pathway) (inflammatory cascade)
- Reduced expression of TLR4 & NF-κB in microglia (inflammatory cascade)
- Up-regulated anti-inflammatory genes
- Enhanced expression of anti-inflammatory enzymes (SOD, CAT)
- DHA + curcumin reduced oxidative damage to phospholipids in brain



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OTHER FLAVONOIDS USED FOR mTBI

- **Sulforaphane:** reduce cerebral edema, improve BBB integrity & cognition. Highest in broccoli.
- **Resveratrol:** protect astrocytes, decrease lesion size, reduce ROS, suppress excitotoxicity, reduce inflammation & lipid peroxidation. Highest red grapes, cocoa, peanuts, blueberries.
- **Luteolin:** up-regulated several genes to inhibit NFkB signaling & inflammatory cytokines. Highest broccoli, black pepper, thyme, celery.
- **Epicatechin:** crosses BBB. Activate Nrf2 pathway, reduce inflammatory markers, reduce iron deposition, lesion size, edema, and cell death. Improved SOD expression, neurologic function, cognitive performance. Decreased depression-like behaviors. Highest green tea, cocoa powder.

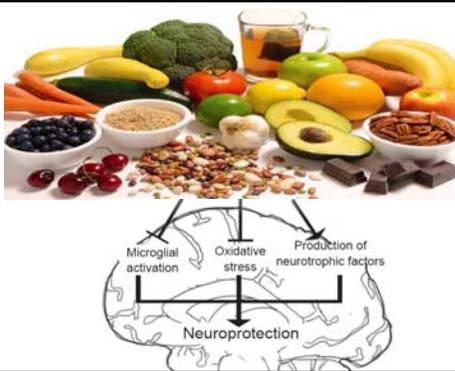
61

EAT FRUITS & VEGIES

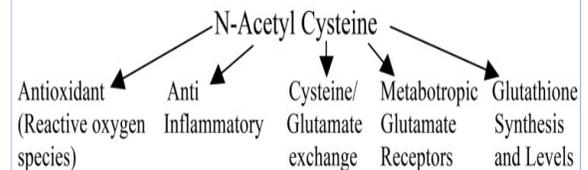
- TBI animals fed liquid formula of fruits and vegetables, high in natural plant chemicals, vitamins, & minerals, had smaller brain lesions, faster repair, and improved post-injury performance compared to typical animal chow diet.
- Diet following TBI should be high in variety of fresh, organic, fruits & vegies (especially cruciferous) spices (especially curcumin), cocoa (90-100%) & green tea to supply all flavonoids.



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- Most studied mTBI anti-oxidant
- A glutathione anti-oxidant precursor
- Difficult to cross BBB. Trauma allows easier entry
- Amide form being studied as more bioavailable.

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ANTI-OXIDANT: N-ACETYLCYSTEINE

- Human trials done after injury during active military duty
- Decreased brain inflammation & oxidative stress markers
- Increased brain glutathione
- May reduce glutamate neurotoxicity
- Reduced brain edema, BBB permeability, cell apoptosis.
- Supports neuron regeneration
- Substantial improvement of cognition & psychomotor performance
- No safety concerns noted. Can cause nausea.



65

ANTI-OXIDANT: ZINC EFFECTS

- Cofactor for anti-oxidants glutathione & SOD
- Reduces inflammation
- Serum levels decreased after mTBI
- Supplementation after mTBI:
 - reduced oxidative stress & inflammation
 - reduced neuronal cell death
 - decreased depression & anxiety
- May help preserve brain tissue & reduce neuropsychiatric symptoms.
- RDA 8-15 mg QD. Therapeutically has been used up to 100 mg QD.
- More is not better. Can cause nausea at high doses.

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SUPPLEMENT EXAMPLE

- No dosing guidelines for mTBI.
- Take small amounts of antioxidants: glutathione or NAC.
- Studies used 100-300 mg NAC QD.
- Get adequate glutathione cofactors (amino acids, E, C, CoQ10, zinc, selenium)
- Eat foods high in sulfur compounds (allium family), antioxidants, & protective plant chemicals.

Supplement Facts		
serving size: 1 capsule		
servings per container: 120		
	amount per serving	% daily value
Vitamin A (as beta carotene)	10,000 IU	200%
Vitamin E (as d-alpha tocopherol succinate)	100 IU	333%
Riboflavin (vitamin B ₂)	25 mg	1,471%
Zinc (as zinc picolinate)	5 mg	33%
Selenium (as selenomethionine)	100 mcg	143%
N-acetyl-cysteine (NAC) (free-form)	100 mg	*
Milk thistle (silybum marianum) extract (seed)	100 mg	*
*standardized to contain 80% silymarin		
Mixed carotenoids (from lutein, lycopene and zeaxanthin)	500 mcg	*

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ANTI-OXIDANT FORMULA EXAMPLE

this vegetarian capsule contains		
vitamin A (as beta carotene)	75,000 IU	
vitamin D (as cholecalciferol(D3))	400 IU	
vitamin E (as d-alpha tocopherol succinate)	400 IU	
thiamin (as thiamin HCl (B1))	100 mg	
riboflavin (vitamin B ₂)	50 mg	
niacin (as niacinamide)	100 mg	
vitamin B ₆ (as pyridoxine HCl)	25 mg	
folate (as Methylfolate, L-5-MTHF)	800 mcg	
vitamin B ₁₂ (as methylcobalamin)	1,000 mcg	
biotin	400 mcg	
pantothenic acid (calcium pantothenate (B5))	400 mcg	
calcium (as calcium citrate/malate)	300 mg	
and (as zinc gluconate)	25 mg	
selenium (as selenomethionine)	200 mcg	
copper (as copper glycinate)	2 mg	
manganese (as manganese aspartate)	5 mg	
antioxidant enzymes		
superoxide dismutase (SOD)	100 mg	
glutathione peroxidase	100 mg	
polydatin (as polydatin aspartate)	50 mg	
boron (as boron glycinate)	2 mg	
vanadium (as vanadium aspartate)	200 mg	
inositol hexanicinate (no B6, niacin)	90 mg	
ascorbyl palmitate (fat soluble vitamin C)	100 mg	
riboflavin 5 phosphate (activated B ₂)	25 mg	
pyridoxal 5 phosphate (activated B ₆)	25 mg	
mixed carotenoids (as lutein, lycopene, zeaxanthin)	1,445 mcg	
antioxidant nutrients		
alpha lipoic acid (thioctic acid)	100 mg	
Coenzyme Q10	90 mg	
resveratrol (trans-resveratrol) (extract root and stem)	100 mg	
standardized to contain 2% resveratrol		
ginger (ginger officinalis) extract (root)	2 mg	
standardized to contain 5% gingerols		
Antioxidant Herbs		
licorice (licorice root) extract (root)	5 mg	
standardized to contain 80% silymarin		
licorice (licorice root) extract (root)	190 mg	
standardized to contain 80% silymarin		
licorice (licorice root) extract (root)	80 mg	
standardized to contain 80% silymarin		
licorice (licorice root) extract (root)	100 mg	
standardized to contain 80% silymarin		



68

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70

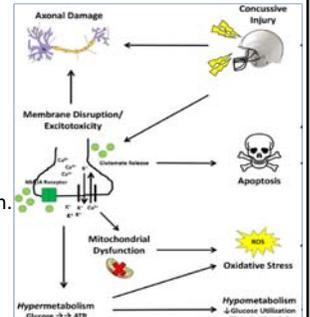
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NEUROTOXICITY

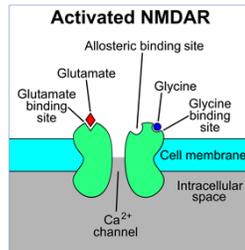
- Traumatic brain injury causes
- excess release of excitatory neurotransmitter glutamate
- activation of NMDA ion channels
- massive influx of cellular Ca²⁺ and efflux of K⁺
- Ca²⁺ influx damages axons & causes mitochondrial dysfunction.
- Must reduce calcium influx & glutamate release



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NMDA RECEPTOR MAIN ROLES N-methyl-D-aspartate

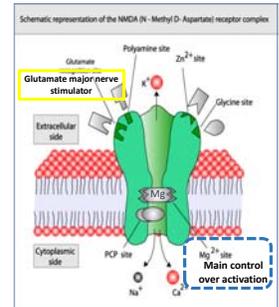
- controls critical events in formation & development of nerve synapse.
- important role in brain excitatory neurotransmission (glutamate)
- helps with learning & forming memories. Plays a role in emotions.
- over-activation promotes neurotoxicity diseases. Occurs with concussion/TBI.



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NMDA OVER-ACTIVATION

- Glutamate release up-regulated
- Promotes too much calcium delivery
- Excess intracellular calcium tells cell that something is wrong.
- Cells genetically up-regulate to make ROS & inflammatory chemicals
- Inflammatory products released into extracellular area
- Promotes mitochondrial oxidation, cell dysfunction & death (apoptosis).



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MAGNESIUM FOR mTBI

- Major cofactor for most biochemical pathways.
- Blocks NMDA (calcium-glutamate) neuroexcitation.
- Depleted after mTBI. Deficiencies common.
- Prevents excitotoxic (glutamate) damage.
- Deficiency leads to poorer functional outcome & increased cell death.
- Supplementation improved recovery & function after brain injury.
- Reduced brain edema, cell death, BBB damage.
- Improved symptom scores (pain, fatigue, headache, dizziness, sleep, etc.) when supplemented after mTBI.
- Used for mood disorders (anxiety/depression) and epilepsy.

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MAGNESIUM DOSAGE

- Safe to try along with other cofactors & meds.
- Adult doses:
 - 125-500 mg QD. Mainly glycinate or taurinate used.
 - 125-300 mg QID (with meals and at bedtime)
 - Or higher doses 400-500 QD.
 - Certain forms (citrate & hydrochloride) and higher amounts can cause diarrhea.
 - L-threonate form increased CSF levels.



76

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77

2014: FDA WARNING DIETARY SUPPLEMENTS CANNOT TREAT CONCUSSIONS

- Concussions & TBI cannot be prevented, treated or cured with dietary supplements (or medications).
- Issued consumer warning after false claims promising faster healing times.
- No scientific evidence exists to support this claim.
- Supplements may pose no harm, but are dangerous if person believes they are recovered enough to return to play or engage in activities that may put them at risk for re-injury.

www.fda.gov/ForConsumers/ConsumerUpdates/ucm519116.htm
www.fda.gov/ForConsumers/ProtectYourself/HealthFraud/ucm539205.htm

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DIETARY RECOMMENDATIONS FOR mTBI
THESE ARE NOT TREATMENTS, CURES, PREVENTIONS

- Increase dietary omega 3 DHA in diet & supplements
- Avoid sugar, alcohol, caffeine, stimulants, saturated/trans fats, highly salted foods (edema).
- Include many fresh, whole, organic fruits, vegies, spices.
- Can supplement additional anti-oxidants & phytochemicals
- Correct any underlying nutrient deficiency
- No recommendations for amount of FAT, CHO, PRO, BCAA as all have pros & cons. Eating healthy foods most important.
- If sleep disruption, use melatonin or sleep formula.
- If headache or pain with chewing, can puree or smoothie.

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THE END



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"Neuroimmunology of Traumatic Brain Injury: Time for a Paradigm Shift." Neuron. 2017;95(6):1246-1265. Jassam YN, et al.

- Phase 1 begins within minutes of brain injury due to the release of alarmins from the damaged meninges, glial limitans, and parenchyma, such as ATP, HSPs, HMGB1, etc. These signals bind to PAMP and DAMP sensors like TLRs and purinergic receptors that induce immediate activation of resident myeloid cells (e.g. microglia) and inflammasome assembly [NALP1] that promotes the generation of mature IL-1 β and IL-18. In addition, NF κ B translocates to the nuclei of these cells and induces an immunological program involving cellular proliferation and the release inflammatory amplifiers such as chemokines, cytokines, ROS, and NO, among others. Phase 1 also includes complement activation and the recruitment of neutrophils to the meninges and perivascular spaces. Neutrophil recruitment depends in part on purinergic receptor signaling. Secondary damage to CNS tissue occurs in Phase 1 and can continue into Phase 2. This can be mediated by inflammatory cytokines, complement, and ROS. T cells and monocytes are recruited to the damage site in Phase 2, where monocytes convert into macrophages and T cells have the ability to produce neuroprotective cytokines in response to alarmins. Macrophages participate in the cleanup of debris and damaged cells. Based on their state of functional activation, they can either promote further damage or initiate the process of inflammatory resolution and tissue repair. Inflammation can continue for an extended period of time into Phase 3. Self-antigens released from damaged neural cells can be presented by local APCs to T cells. The ideal outcome during Phase 3 is resolution of the inflammatory response, release of trophic factors, and isolation damaged areas via astrocytes. However, this is does not always occur following TBI and chronic inflammation can persist.
- Abbreviations: APC, antigen-presenting cell; ATP, adenosine triphosphate; BDNF, brain-derived neurotrophic factor; CCL2, chemokine (C-C motif) ligand 2; CXCL1, chemokine (C-X-C motif) ligand 1; CXCL2, chemokine (C-X-C motif) ligand 2; DAMP, damage associated molecular pattern molecules; HSPs, heat shock proteins; HMGB1, high mobility group box 1 protein; IGF-1, insulin-like growth factor-1; IL-1, interleukin-1; IL-4, interleukin-4; IL-10, interleukin-10; iNOS, inducible nitric oxide synthase; MyD88, myeloid differentiation primary response gene 88; NALP1, NAcHt leucine-rich repeat protein 1; NT-3, neurotrophin-3; NF κ B, nuclear factor kappa-light-chain-enhancer of activated B cells; MBP, myelin basic protein; M-CSF, macrophage colony stimulating factor; NO, nitric oxide; PAMP, pathogen-associated molecular pattern; ROS, reactive oxygen species; TGF- β , transforming growth factor beta; TLR, toll-like receptors; TNF- α , tumor necrosis factor-alpha

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