

Regaining homeostasis with diet (and exercise)

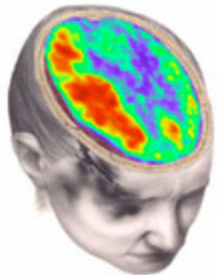
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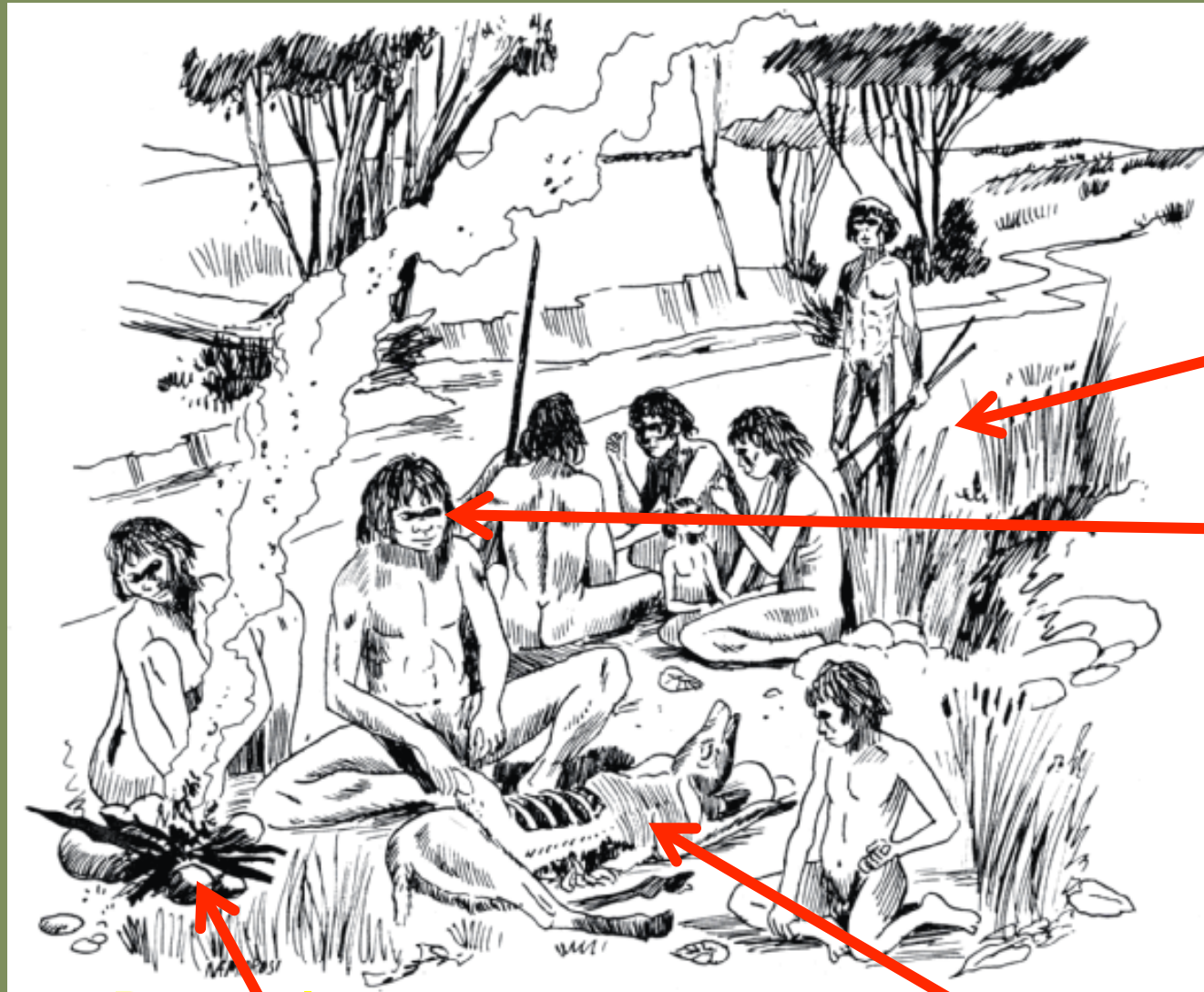


Brain Injury Research Center



**BRAIN
RESEARCH
INSTITUTE
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Feeding and exercise have been essential tools for survival and development of the modern brain



transport

**Larger brain than
preys to compete
for survival**

Power plant

food

Table 1 | **Select nutrients that affect cognitive function**

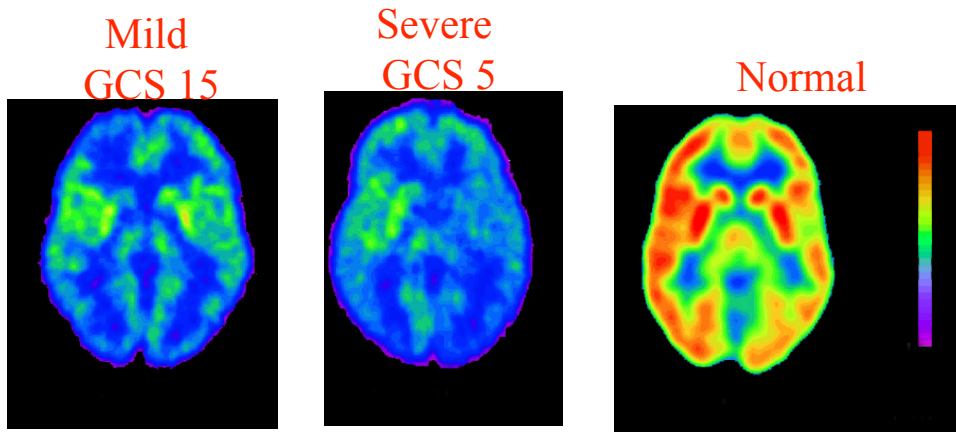
Nutrient	Effects on cognition and emotion	Food sources
Omega-3 fatty acids (for example, DHA)	Amelioration of cognitive decline in the elderly ¹⁴⁸ ; basis for treatment in patients with mood disorders ⁹⁰ ; improvement of cognition in traumatic brain injury in rodents ⁹¹ ; amelioration of cognitive decay in mouse model of Alzheimer's disease ^{149,150}	Fish (salmon), flax seeds, krill, chia, kiwifruit, butternuts, walnuts
Curcumin	Amelioration of cognitive decay in mouse model of Alzheimer's disease ¹²³ ; amelioration of cognitive decay in traumatic brain injury in rodents ⁸⁹	Turmeric (curry spice)
Flavonoids	Cognitive enhancement in combination with exercise in rodents ⁹² ; improvement of cognitive function in the elderly ¹⁵¹	Cocoa, green tea, Ginkgo tree, citrus, wine (higher in red wine), dark chocolate
Saturated fat	Promotion of cognitive decline in adult rodents ⁴ ; aggravation of cognitive impairment after brain trauma in rodents ⁸⁶ ; exacerbation of cognitive decline in aging humans ³	Butter, ghee, suet, lard, coconut oil, cottonseed oil, palm kernel oil, dairy products (cream, cheese), meat
B-vitamins	Supplementation with B6, B12 or folate has positive effects on memory performance in women of various ages ¹⁵² ; vitamin B12 improves cognitive impairment in rats fed a choline-deficient diet ¹⁵³	Various natural sources, B-12 not available from plant products
Vitamin D	Important for preserving cognition in the elderly ¹⁵⁴	Fish liver, fatty fish, mushrooms, fortified products, milk, soy milk, cereal grains
Vitamin E	Amelioration of cognitive impairment after brain trauma in rodents ¹⁰² ; reduces cognitive decay in the elderly ¹¹⁹	Asparagus, avocado, nuts, peanuts, olives, red palm oil, seeds, spinach, vegetable oils, wheat germ
Choline	Reduction of seizure-induced memory impairment in rodents ¹⁵⁵ ; a review of the literature reveals evidence for a causal relationship between dietary choline and cognition in humans and rats ¹⁵⁶	Egg yolks, soy beef, chicken, veal, turkey liver, lettuce
Combination of vitamins (C, E, carotene)	Antioxidant vitamin intake delays cognitive decline in the elderly ¹⁵⁷	C: citrus fruits, several plants and vegetables, calf and beef liver. E: see above
Calcium, zinc, selenium	High serum calcium is associated with faster cognitive decline in the elderly ¹⁵⁸ ; reduction of zinc in diet helps to reduce cognitive decay in the elderly ¹⁵⁹ ; lifelong low selenium level associated with lower cognitive function in humans ¹⁶⁰	Calcium: milk, coral. Zinc: oysters, a small amount in beans, nuts, almonds, whole grains, sunflower seeds. Selenium: nuts, cereals, meat, fish, eggs
Copper	Cognitive decline in patients with Alzheimer's disease correlates with low plasma concentrations of copper ¹⁶¹	Oysters, beef/lamb liver, Brazil nuts, blackstrap molasses, cocoa, black pepper
Iron	Iron treatment normalizes cognitive function in young women ¹⁶²	Red meat, fish, poultry, lentils, beans

Diet and exercise are important modulators of brain plasticity and disease

- Reduces cognitive decay in aging (Hillman, Nat Rev Neurosci 2008)
- Reduces risk of Alzheimer's disease
- Reduces anxiety and depression (Krogh, J Clin Psych 2010)
- Reduces incidence of addictive behaviors in humans (Roessler Scan J Public Health 2010, van Rensburg Addiction 2009), and animal models (Lynch, Biol Psych 2010)
-
- Promotes metabolic homeostasis: Better ability to control weight – obesity

Lack of exercise is somehow toxic for the CNS, particularly combined with unhealthy diets..... increasing risk of many diseases

Metabolic Depression after TBI

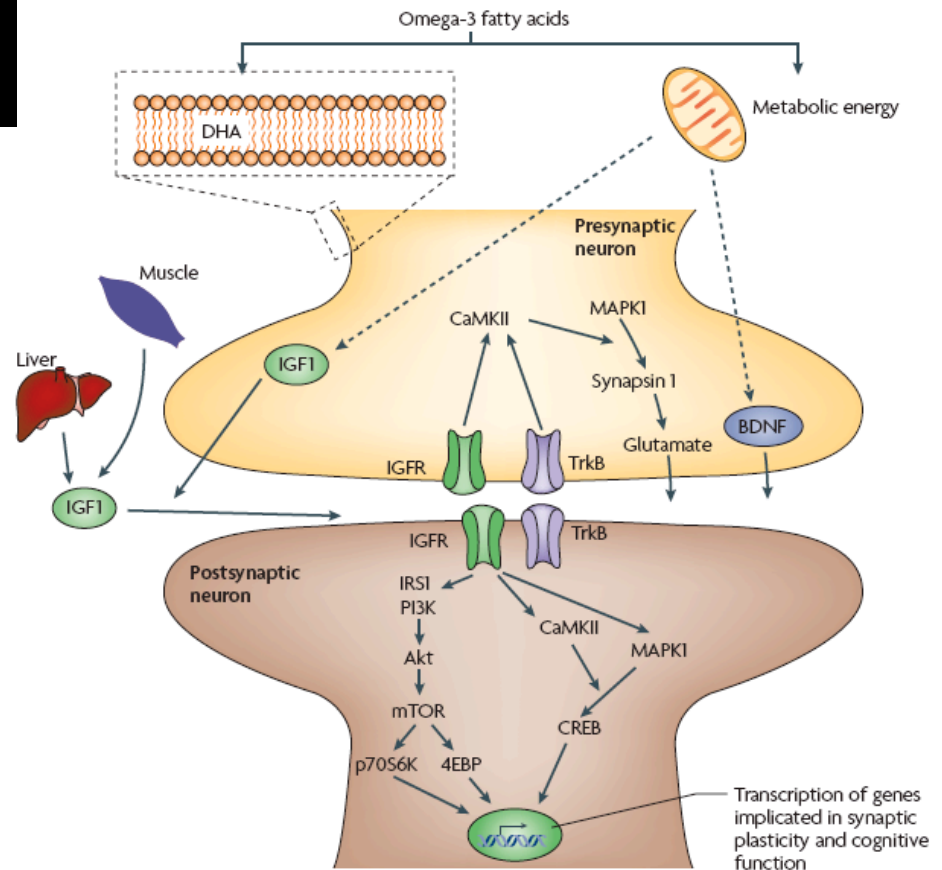


Giza and Hovda, 2001

Therapeutic targets to moderate cognitive and emotional distress after TBI:

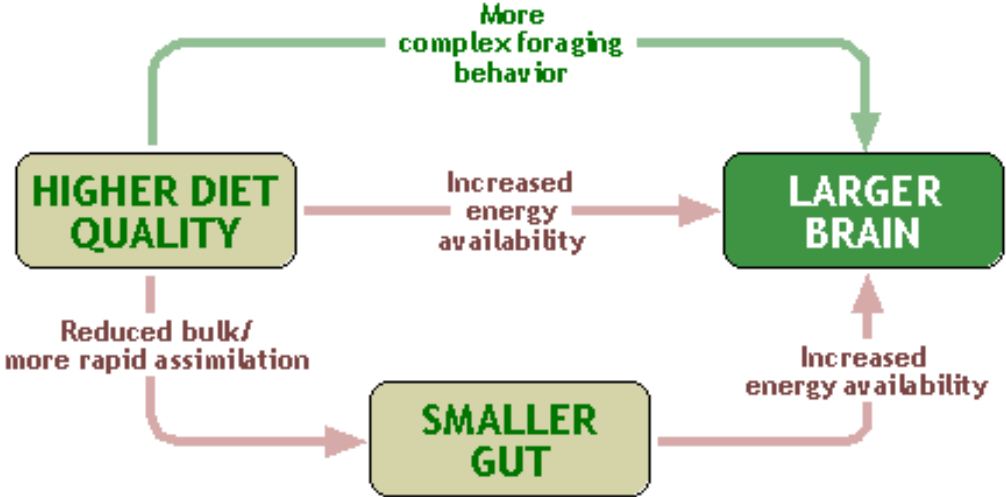
- To reduce energy crisis and promote membrane repair
- To elevate the potential for synaptic plasticity
- To support neuronal signaling
- To stimulate mechanisms that can provide broad protection

Can nutrients help accomplishing these goals?



Gomez-Pinilla, Nature Rev. Neurosci, July 2008

The modern brain was built on efficient use of energy and high quality structural components (origin of green technology)



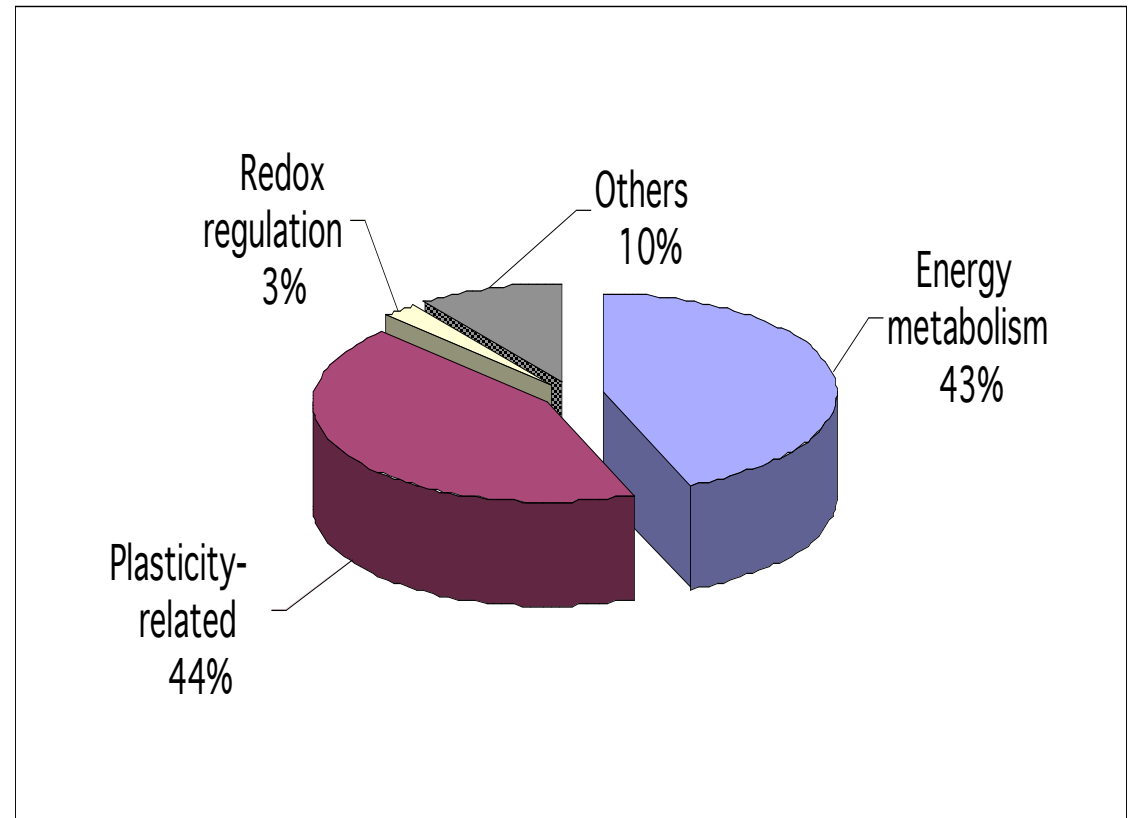
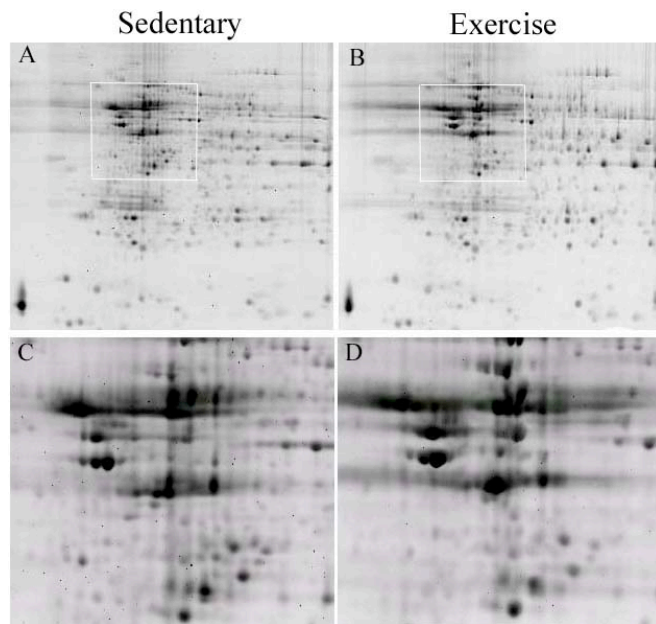
Exercise and foods important for development of cognitive skills, and maintaining metabolic homeostasis

Foods and adaptive behaviors provided structural material supporting a brain capable for cognitive skills



Efficient use of energy

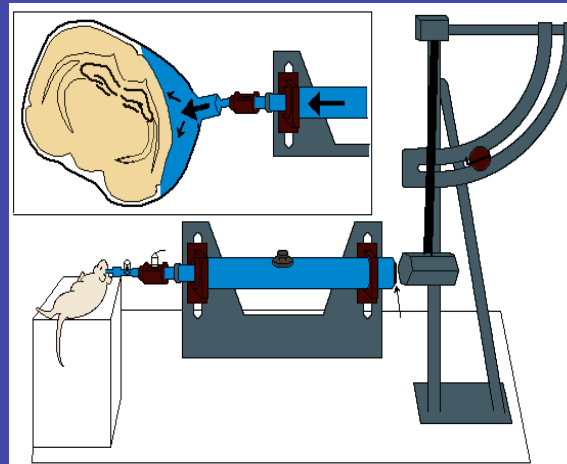
Preponderant action of exercise on proteins associated with energy metabolism and synaptic plasticity



Can dietary supplementation protect the brain against the effects of trauma?

TBI: Metabolic dysfunction, protracted synaptic plasticity and behavior

- We tested the effects of diet on a brain trauma model -- a type of concussive injury



Curcumin (turmeric)



Turmeric plant

Anti-inflammatory, Anti-oxidant, Anti-mutagenic

Curcumin is one of the most prevalent nutritional and medicinal compounds in India; main candidate responsible for reduced (4.4-fold) prevalence of Alzheimer's disease (AD) in India compared to USA (Ganguli et al., 2000 Arch Neurol 57:824)

Several studies have confirmed its neuroprotective role in various neurodegenerative conditions such as

Alzheimer's Disease (Lim et al., 2001 The Journal of Neuroscience, 21(21):8370-8377),

Cerebral ischemia (Zhao et al., 2008 Brain Research 1229:224-232) and also in

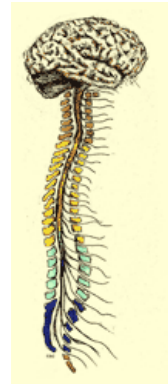
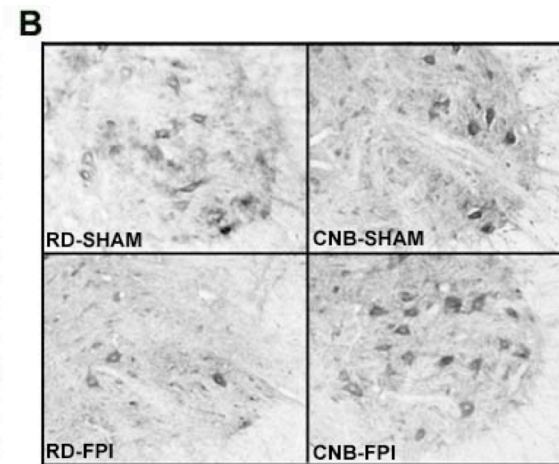
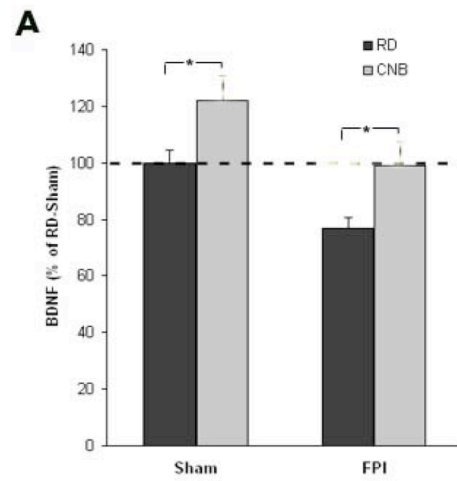
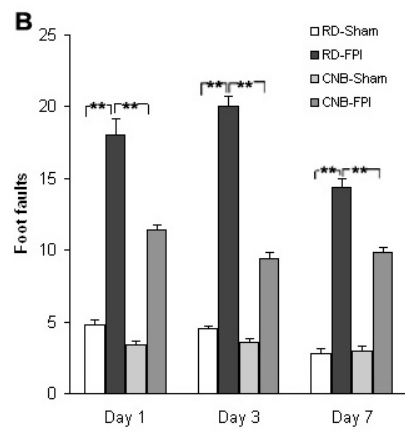
Traumatic Brain Injury (Wu et al., 2006 Experimental Neurology 197:309-317).

Curcumin derivative reduces cognitive and locomotor dysfunction

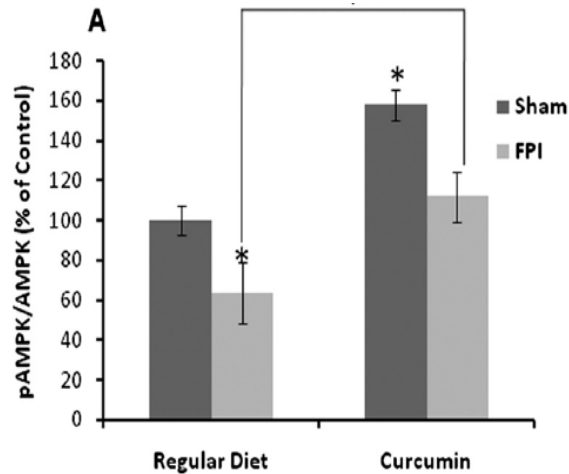
Sham

FPI

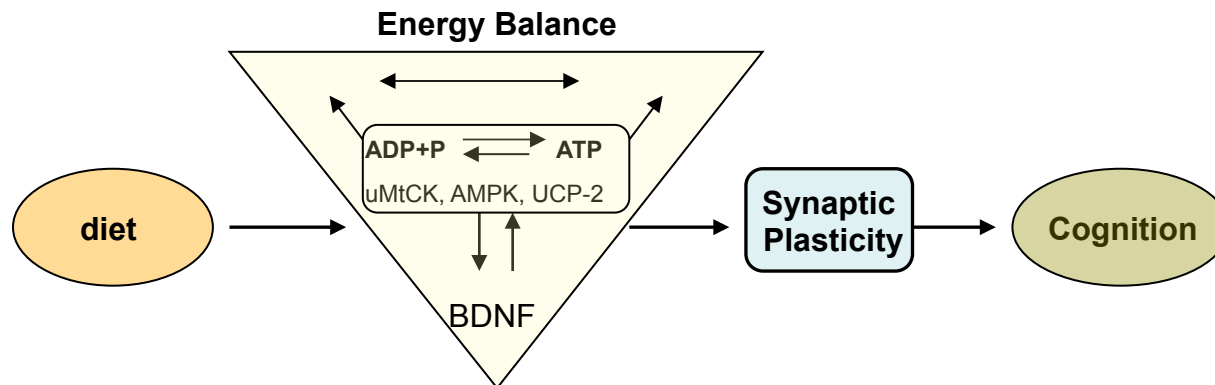
FPI + Cur



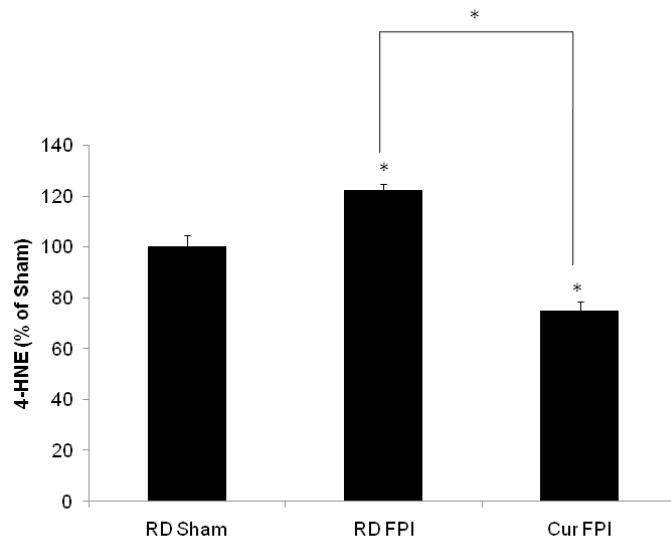
Curcumin helps stabilize energy homeostasis after TBI



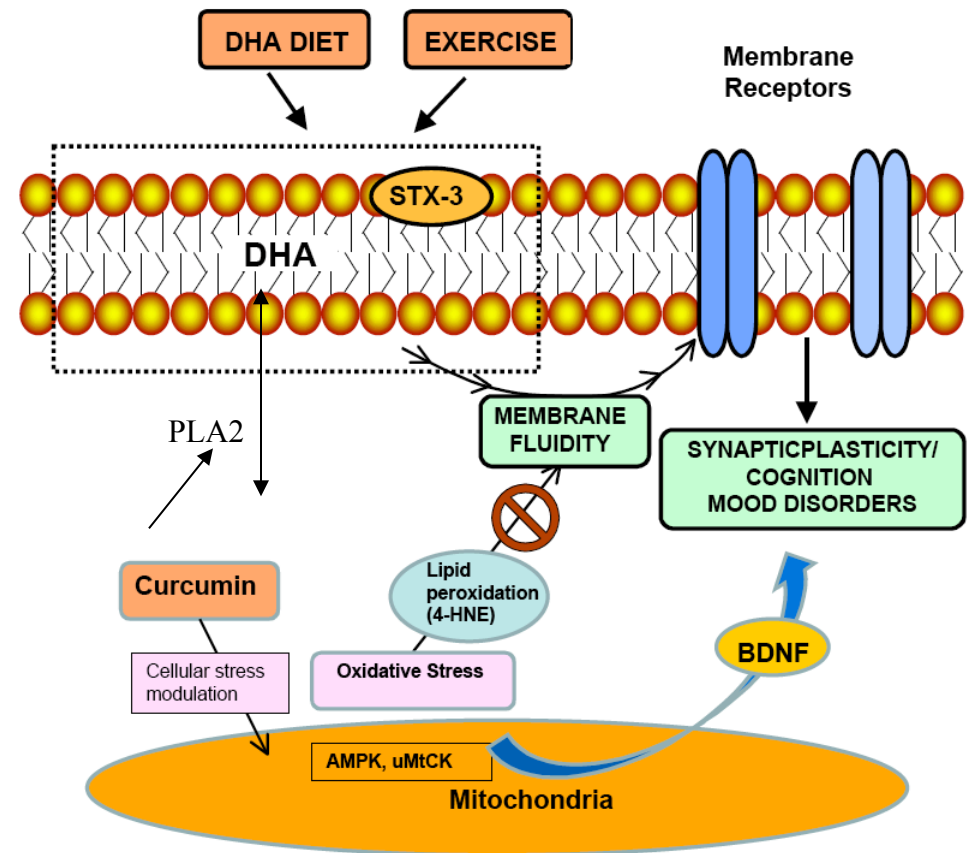
AMPK is a kinase that increases cell energy by turning on catabolic pathways that generate ATP while switching off pathways that consume ATP (Hardie, 1998,1999).



Curcumin appears to restore metabolic homeostasis and to reduce oxidative stress

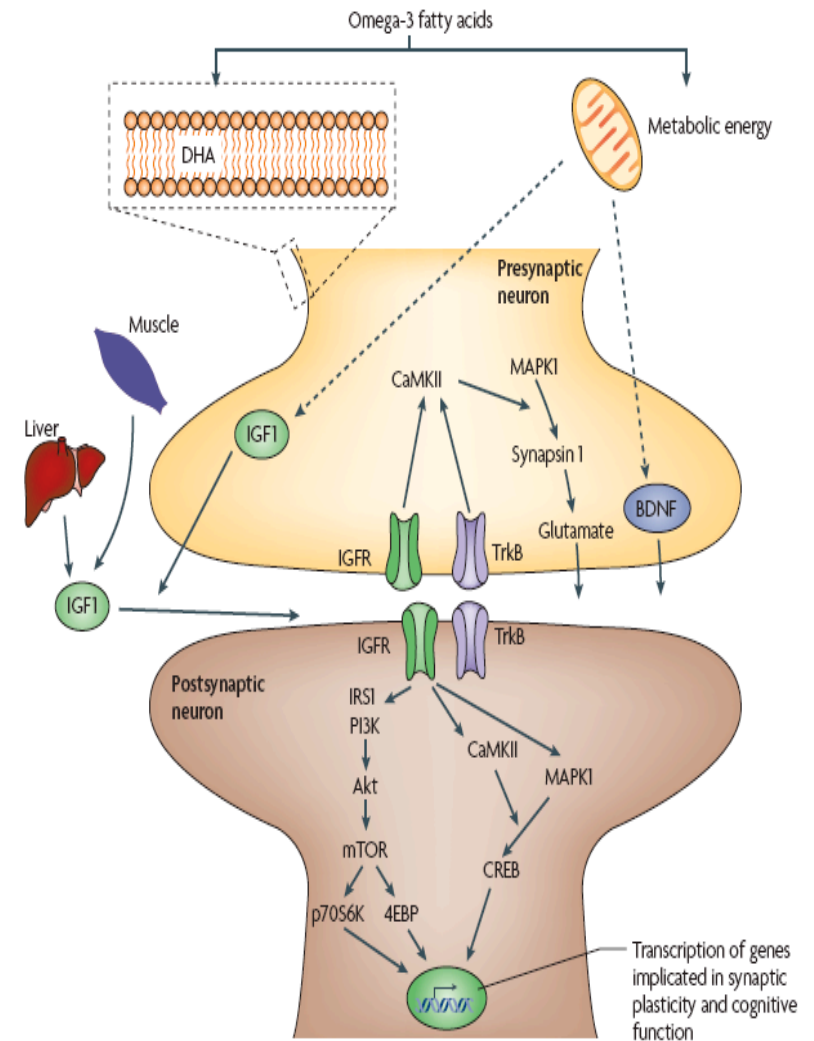


4-hydroxynonenal: membrane peroxidation indicator



Energy homeostasis is essential for signaling through the plasma membrane

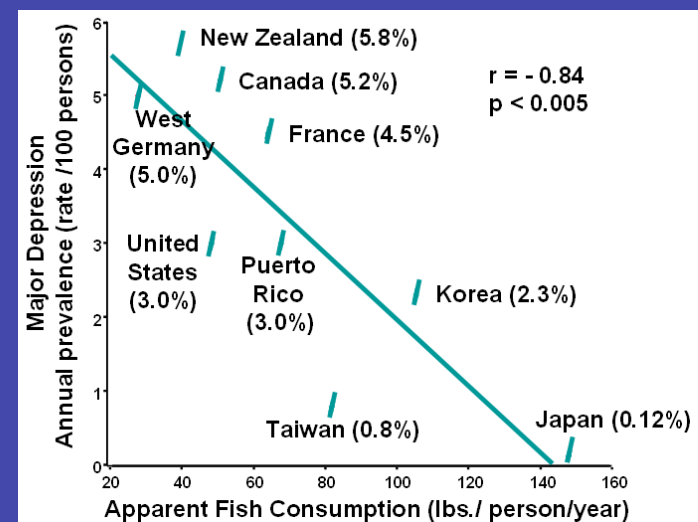
- Cell energy supply: failure in the mechanisms that procure energy and maintain membrane can lead to poor neuronal signaling, lack of repair capacity, and a dysfunctional brain
- Brain structure: DHA structural component of membranes: brain food



Omega-3 fatty acids provide building material and neuronal signaling support

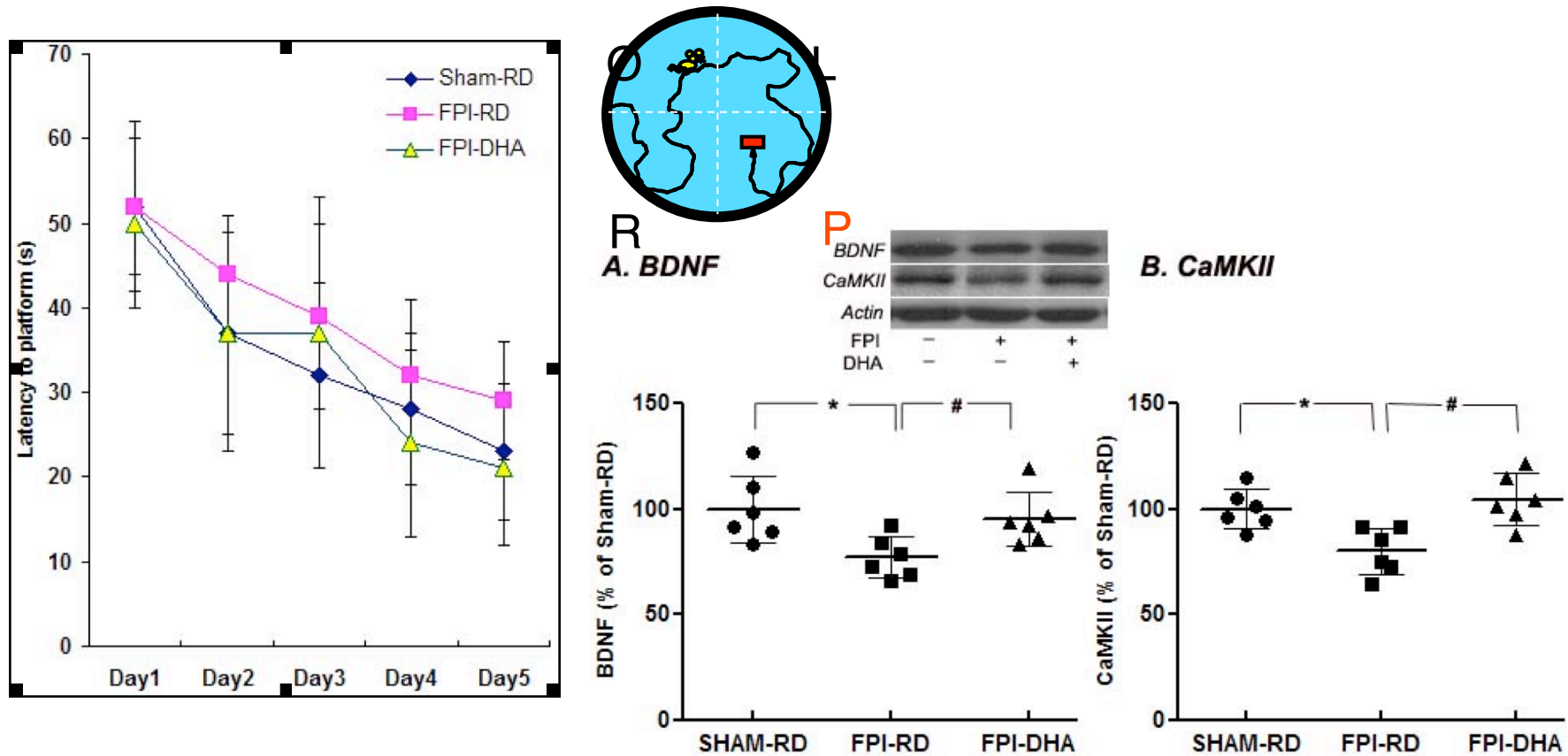
- Essential fatty acids- The body cannot synthesize Omega-3 fatty acids
 - **Linolenic acid (18:3 n-3) >>>docosahexanoic acid (DHA, n-3)**
- DHA (fish, algae) is crucial in brain/retina development and CNS maintenance
- DHA is high in brain (~31% of FA in PE in cortex) -- major component of gray matter nerve membranes, particularly at synaptic terminals
- DHA insufficiency affect membrane fluidity, serotonin transport, gene transcription, inflammation, and energy metabolism in the brain

Contemporary fish consumption Vs prevalence of major depression around the world



Hibbeln, The Lancet, 1998

DHA supplementation counteracts effects of TBI



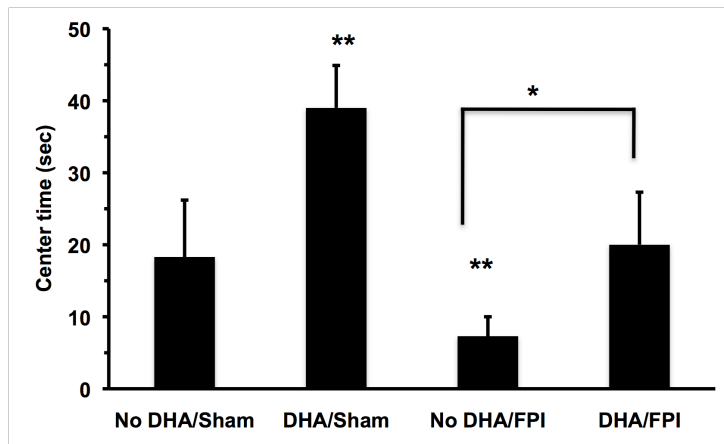
DHA supplemented 1.2% DHA in the diet after mild TBI for 12 days

Prevention effects: DHA deficiency during brain development can compromise adult plasticity

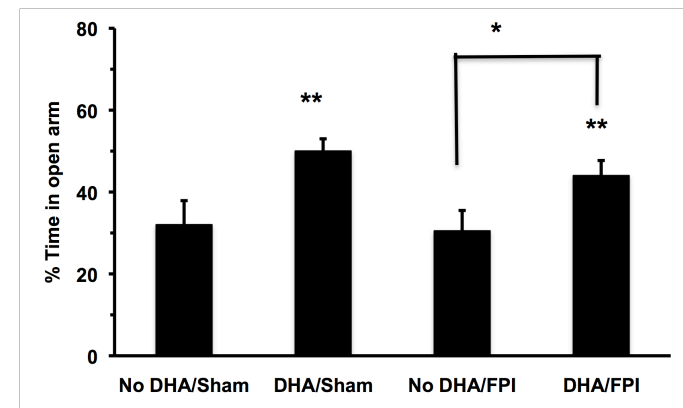
Diet protocol: rats were maintained in DHA deficient diet or DHA supplemented diets since gestation until young-adulthood

Low DHA influences BDNF function and anxiety-like behavior

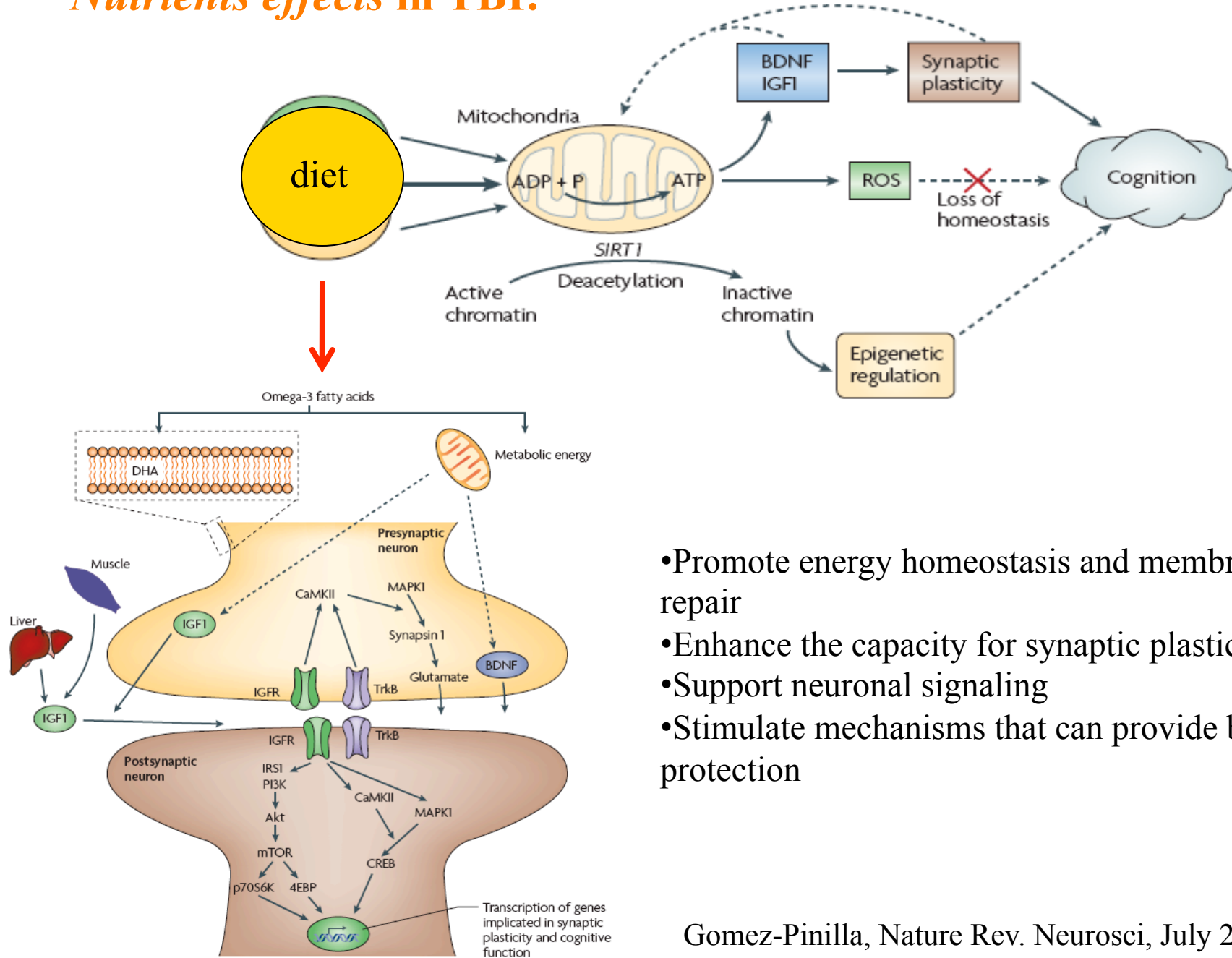
Open Field



EPM



Nutrients effects in TBI:



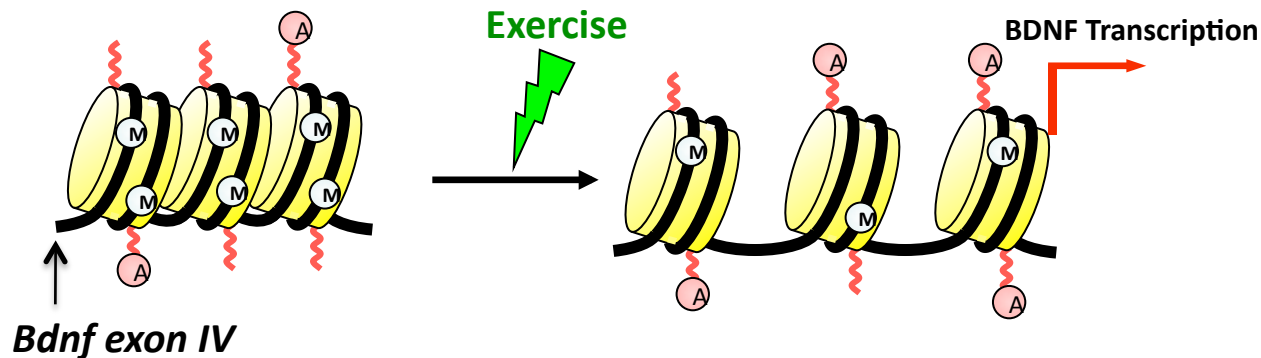
- Promote energy homeostasis and membrane repair
- Enhance the capacity for synaptic plasticity
- Support neuronal signaling
- Stimulate mechanisms that can provide broad protection

Can diet and exercise promote stable changes in the genome?..

Epigenetic Code: *DNA modification that can alter the function of the DNA without changing DNA sequence -- regulation of psychiatric disorders and potential to be inherited*

DNA methylation and post translational modification (**acetylation**) of histones are important mechanisms for controlling gene function

BDNF gene highly susceptible to epigenetic regulation



Gomez-Pinilla, Eur J Neurosci, Jan 2011

Adult Sprague-Dawley rats exposed to seven days of voluntary running wheel exercise

Diet and exercise and translational epigenomics

- Prevention and alteration of course of disease: Exercise (and select diets) non-invasive means to promote mental health and alleviate the effects of depression, anxiety, cognitive impairment, etc
- Combined exercise, dietary factors and pharmacological approaches can promote synergism, or open targets
- lack of exercise and healthy eating, obesity, diabetes, depression, etc.*
Tremendous implications for the mental health of society.

Conclusion: What to do?

- Increase awareness in hospital environments
- Applications in the military
- Combination with rehabilitative practices
- Public health awareness
-

Participants

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