DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury

The Role of Sleep, Activity, and Nutrition in the Treatment and Recovery of Traumatic Brain Injury (TBI)

Jan. 8, 2015, 1-2:30 p.m. (EST)

Presenter and Moderator: Heechin Chae, MD
Director, Intrepid Spirit Center, Fort Belvoir; Site Director, DVBIC, Fort Belvoir, Va

Presenters:

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Physiatrist, TBI, Contract Support, Intrepid Spirit Center, Fort Belvoir, Va

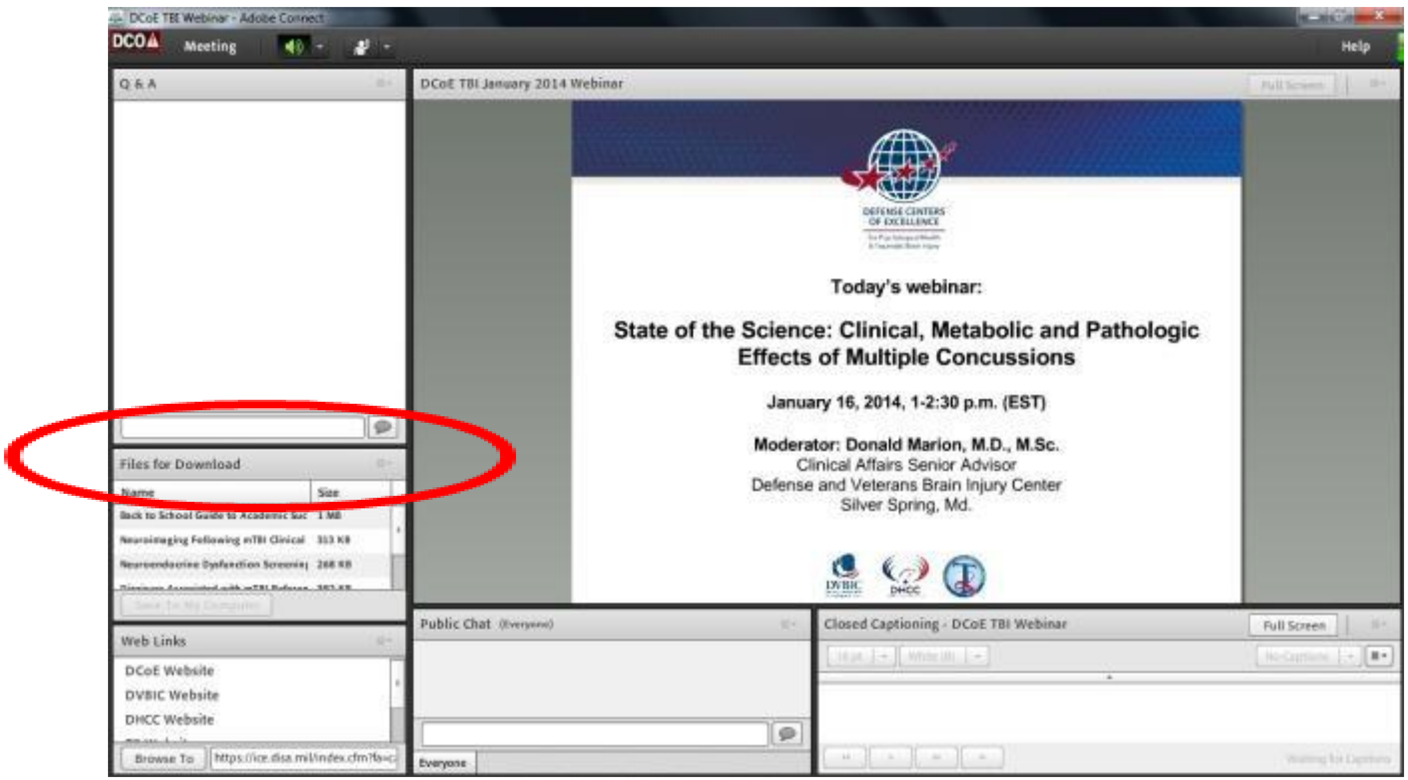
DVBIC DHCC

Webinar Details

- Live closed captioning is available through Federal Relay Conference Captioning (see the “Closed Captioning” box)
- Webinar audio is **not** provided through Adobe Connect or Defense Connect Online
  - Dial: CONUS **800-369-2075**; International **312-470-7430**
  - Use participant pass code: **9942561**
- Question-and-answer (Q&A) session
  - Submit questions via the Q&A box

Resources Available for Download

Today's presentation and resources are available for download in the "Files" box on the screen, or visit **dvbic.dcoe.mil/online-education**



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- The authority for training of contractors is at the discretion of the chief contracting official.
  - Currently, only those contractors with scope of work or with commensurate contract language are permitted in this training.

- All who registered **prior** to the deadline on **Thursday, Jan. 8, 2015,** at 3 p.m. (EST) and meet eligibility requirements stated above are eligible to receive CE credit or a certificate of attendance.

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- Credit Designation – The Duke University School of Medicine designates this live webinar for:
  - 1.5 AMA PRA Category 1 Credit(s)
- Additional Credit Designation includes:
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  - 0.15 IACET continuing education credit
  - 1.5 NBCC contact hours credit commensurate to the length of the program
  - 1.5 contact hours from the American Psychological Association (APA)
  - 1.5 NASW contact hours commensurate to the length of the program for those who attend 100% of the program

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NASW North Carolina Chapter
National Association of Social Workers
Approval Year
2014

Questions and Chat

- Throughout the webinar, you are welcome to submit technical or content-related questions via the Q&A pod located on the screen. **Please do not submit technical or content-related questions via the chat pod**.
- The Q&A pod is monitored during the webinar; questions will be forwarded to presenters for response during the Q&A session.
- Participants may chat with one another during the webinar using the chat pod.
- The chat function will remain open 10 minutes after the conclusion of the webinar.

Webinar Overview

- In 2013, Lt. Gen. Patricia D. Horoho, the U.S. Army surgeon general, launched an organizational initiative to improve the health, readiness, and resilience of the Army family. The performance triad is a comprehensive plan to promote the balance of sleep, activity, and nutrition among Army family members to improve health and wellness.

- The three components of the performance triad are instrumental in the recovery process for service members with a TBI, particularly those with persistent symptoms and chronic injury.

- At the conclusion of this webinar, participants will be able to:
  - Discuss the critical role of sleep, activity, and nutrition in brain health and recovery
  - Examine current evidence-based treatment practices associated with recovery care
  - Evaluate how sleep, activity, and nutrition impact recovery care practices

Lt. Gen. Patricia Horoho and the Performance Triad

- VIDEO/LINK

The Performance Triad is a tool for healthcare providers to use that will improve their health and the health of their patients. Now we will play a short video clip of Lt. Gen. Patricia Horoho talking about the three step pilot course designed to improve the activity, nutrition, and sleep.

Moderator and Presenter: Heechin Chae, MD

Heechin Chae, MD

- Board certified physiatrist, pain medicine, and brain injury medicine
- Director, Intrepid Spirit Center, Fort Belvoir
- Site director, Defense and Veterans Brain Injury Center (DVBIC), Fort Belvoir
- More than fifteen years experience in clinical practice and research in traumatic brain injuries (TBI)
- Assistant professor of psychiatry and physical medicine and rehabilitation (PM&R) at the Uniformed Services University of Health Sciences; previously assistant professor of PM&R at Spaulding Rehabilitation Hospital, Harvard Medical School System
- Education:
  - Medical degree – Medical College of Virginia
  - Residency in PM&R – Spaulding Rehabilitation Hospital, Harvard Medical School System

Presenter: Maulik Purohit, MD, MPH

Maulik Purohit, MD, MPH

- Board certified physiatrist and brain injury medicine
- Director of research, neurorehabilitation and TBI, Intrepid Spirit Center, Fort Belvoir
- Senior scientific director, DVBIC, Fort Belvoir
- Integrative medicine and stress management specialist
- Served as faculty in the Harvard Medical School Department of Physical Medicine
- Established one of the premier sports concussion programs through Massachusetts General Hospital
- Research interests include novel treatments for brain injury and neurological disorders with a particular focus on integrative medicine and lifestyle medicine practices
- Education:
  - Medical degree – University of Texas Southwestern
  - Residency in PM&R – Baylor College of Medicine, University of Texas Houston, Texas Institute of Rehabilitation and Research
  - Fellowship in brain injury and neurorehabilitation – Harvard Medical School
  - MPH – Harvard School of Public Health

Presenter: Emerald Lin, MD

Emerald Lin, MD

- Board certified physiatrist and brain injury medicine
- Coordinates the interdisciplinary care of primarily active duty service members with acute and chronic TBI at the Intrepid Spirit Center, Fort Belvoir
- Course director, continuing medical education lecture series for Intrepid Spirit Center staff
- Developed the botulinum toxin headache clinic at Intrepid Spirit Center
- Served in many leadership roles with regional and national physiatrist societies, including program director of the New York Society of PM&R; program director/secretary and fellowship representative of the Residents and Fellows Council of the Association of Academic Physiatrists
- Education:
  - Medical degree – Robert Wood Johnson Medical School
  - Residency in PM&R – Mount Sinai School of Medicine
  - Fellowship in Traumatic Brain Injury – University of Medicine and Dentistry of New Jersey/Kessler Institute for Rehabilitation

Disclosures

- The views expressed throughout this presentation are those of the presenters and do not reflect the official policy of the Defense Department (DoD) or the U.S. Government.

- The presenters do not intend to discuss the off-label/investigative (unapproved) use of commercial products or devices.

- The presenters have no relevant relationships to disclose.

Outline

- **TBI Introduction (Heechin Chae, MD)**

- Exercise (Maulik Purohit, MD, MPH)
  - Background
  - Traditional
  - Relaxation and mind-body medicine

- Sleep (Maulik Purohit, MD, MPH)
  - Background
  - TBI and sleep
  - Treatments

- Nutrition (Emerald Lin, MD)

TBI Introduction

Heechin Chae, MD
(Disclosure)

TBI Military

- TBI
  - 19.5% of servicemen from Operation Enduring Freedom/Operation Iraqi Freedom
  - Posttraumatic Stress Disorder (PTSD) – 18.3% of service members
  - 80% result of blast exposure (RAND Corporation, 2008)

- Garrison vs Deployed TBI
  - 76% of all TBIs that occurred in the Army from 2000-2012 occurred in garrison
  - TBI will remain a military concern long after 2014 Afghanistan troop withdrawal (Armed Forces Health Surveillance Center, 2014)

Photo courtesy of: Landscaping Gallery

State of the Brain

- Deployment setting and risk factors for TBI
  - Poor sleep quality
    - Inconsistent sleep cycle
    - Heavy use of sleep medications and energy/caffeine drinks
    - Nightmares
  - Poor nutrition
    - Meals Ready-to-Eat (MREs) have low content of omega 3 fatty acids
    - Processed/pre-packaged foods

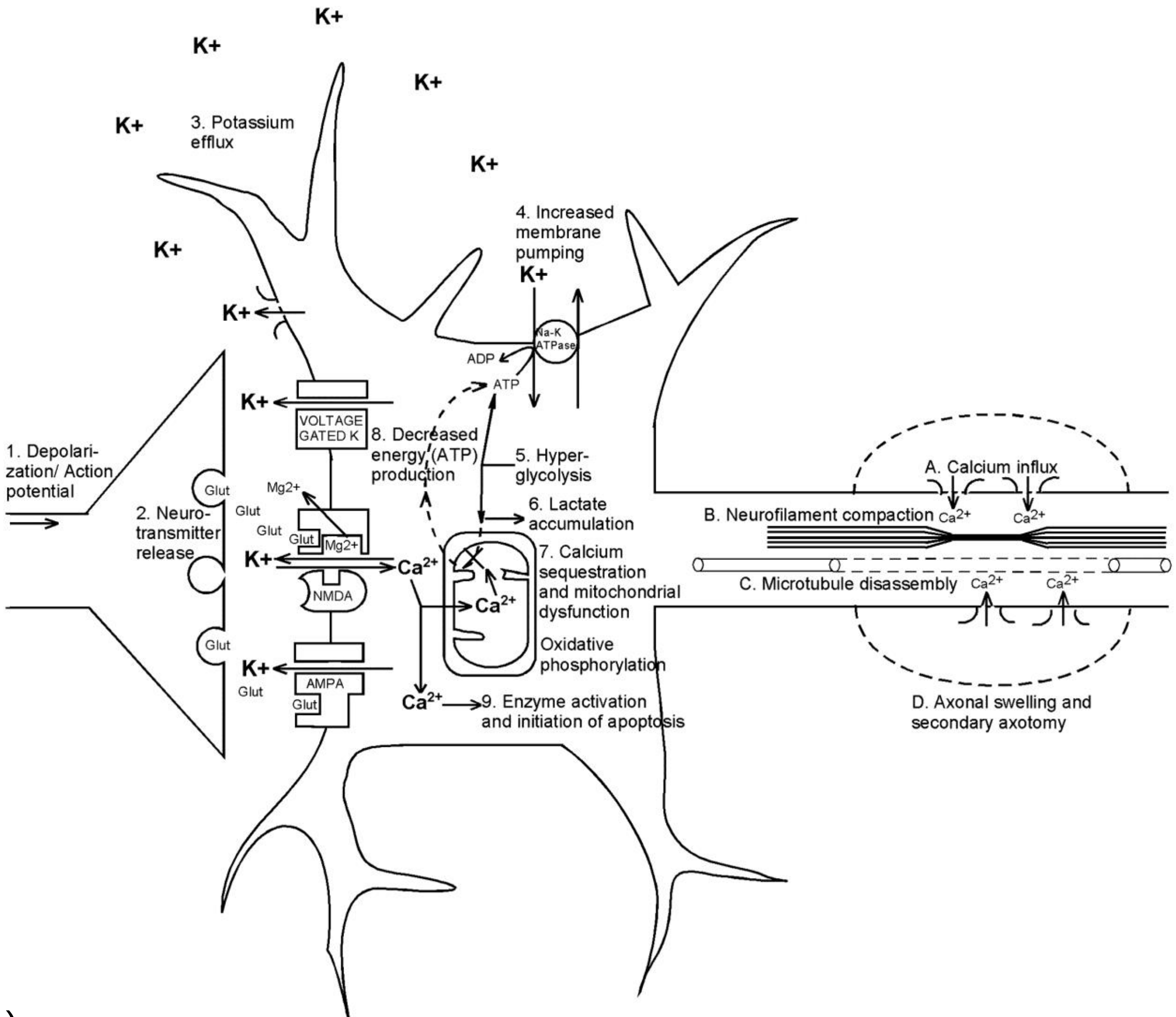
State of the Brain

- Deployment setting and risk factors for TBI
  - High stress environment
    - Combat
    - Daily mission
    - Long work hours
    - Improvised explosive device exposures
    - Surprise attacks
  - Extremes of temperature and weather
    - Temperature ranges from 15-100º F (sometimes in the same day)
    - Humidity ranges from 10-90%

Blast Injury

- Layers of blast injury
  - Rapid transfer of potential energy to kinetic energy from blast
    - Shearing injury, white matter most affected
  - Impact from external objects
    - Similar to classic TBI with contusion-related injuries
  - Soldier displaced in the environment
    - Increases injury potential
  - Noxious fumes and heat
    - Enhances secondary injury

Neurometabolic Cascade After Traumatic Injury



(Giza & Hovda, 2001)

Figure 1. Neurometabolic cascade following traumatic injury

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References

Armed Forces Health Surveillance Center. (2014). External causes of traumatic brain injury, 2000-2011. *Medical Surveillance Monthly Report (MSMR), 20*(3), 8-14. Retrieved from http://www.afhsc.mil/documents/pubs/msmrs/2013/v20_n03.pdf

Giza, C. C. & Hovda, D. A. (2001). The neurometabolic cascade of concussion. *Journal of Athletic Training, 36*(3), 230.

RAND Corporation, Center for Military Health Policy Research. (2008). *Invisible wounds: Mental health and cognitive care needs of America's returning veterans.* Retrieved from http://www.rand.org/pubs/research_briefs/RB9336/index1.html

Sleep and Exercise

Maulik Purohit, MD, MPH (Disclosure)

Outline

- **TBI Background**
  - Role of stress
- Exercise
  - Background
  - Traditional
  - Relaxation and mind-body medicine
- Sleep
  - Background
  - TBI and sleep
  - Treatments

Metabolic Changes with Brain Injury

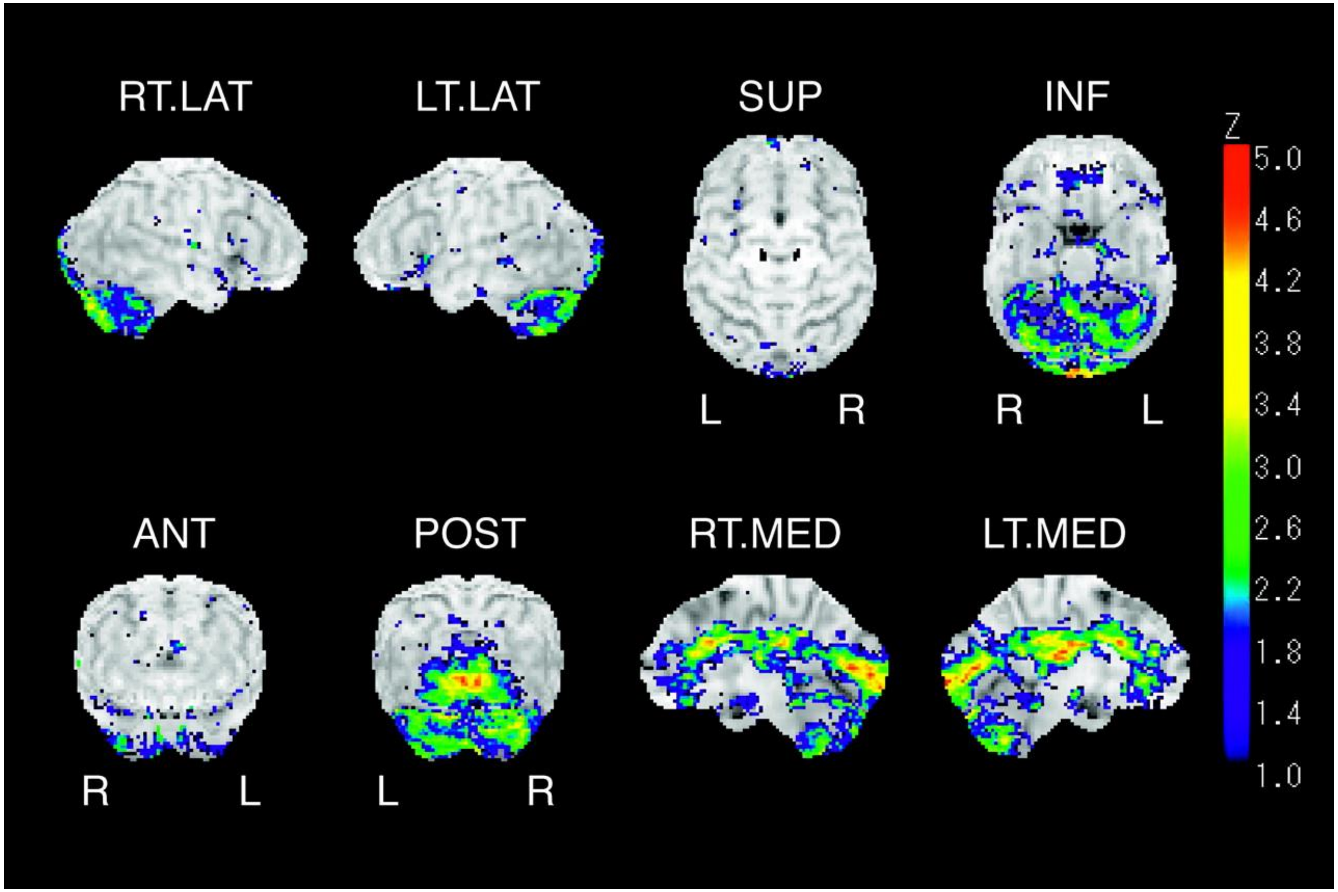


Figure 2. Z-score brain surface map represents areas of metabolic reduction in patients in comparison with healthy subjects. Areas affected include primarily medial aspects, particularly cingulate gyrus, lingual gyrus, and cuneus.

(Nakashima, Nakayama, Miwa, Okumura, Soeda, & Iwama, 2007)

Brain Injury and White Matter Damage

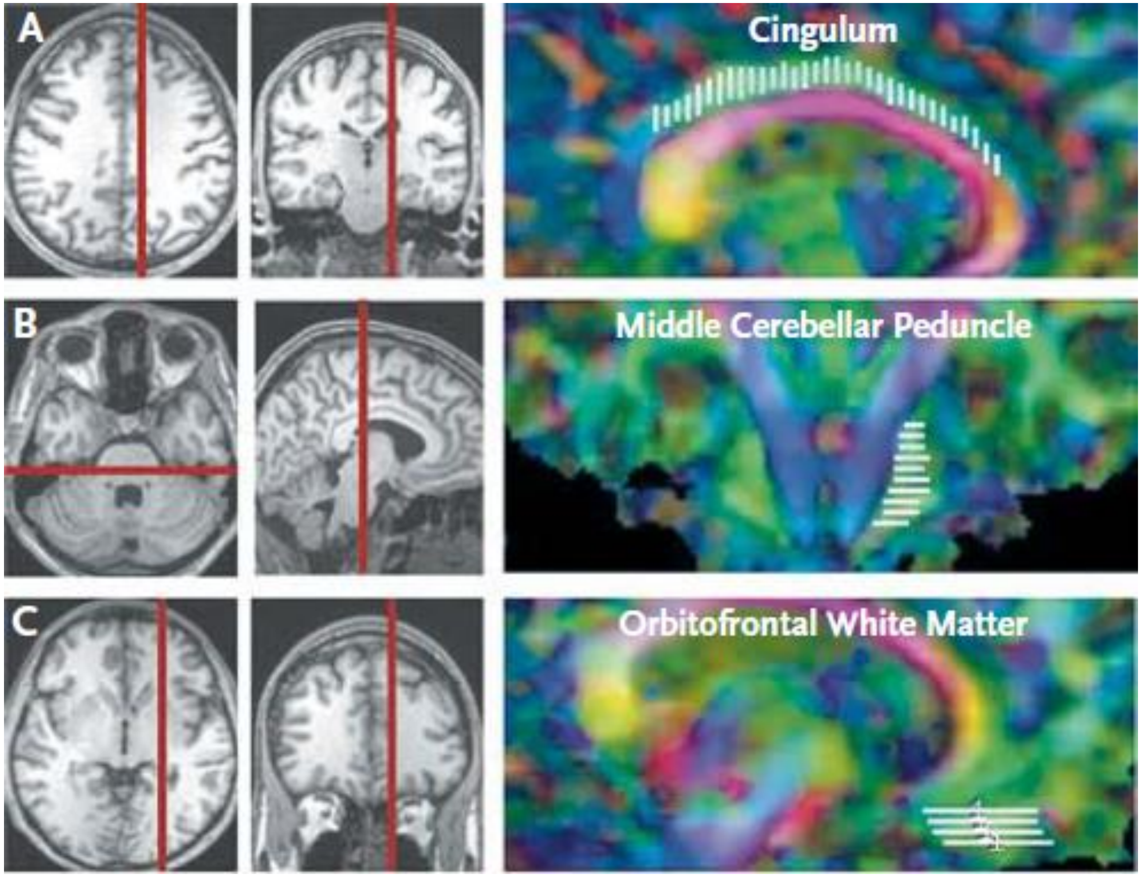


Figure 3. White Matter Damage

(Mac Donald et al., 2011)

Brain Injury and White Matter Damage

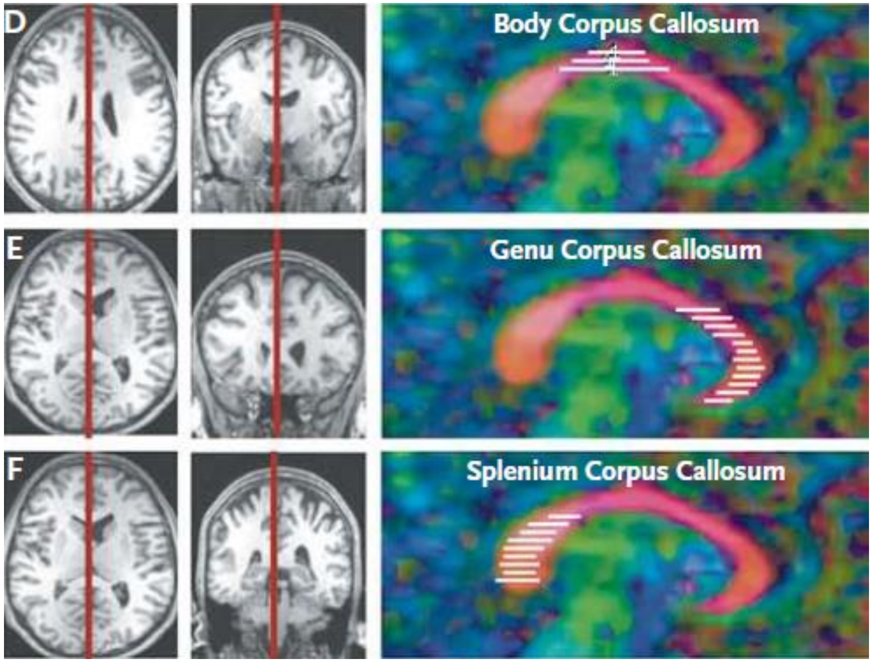


Figure 4. White Matter Damage

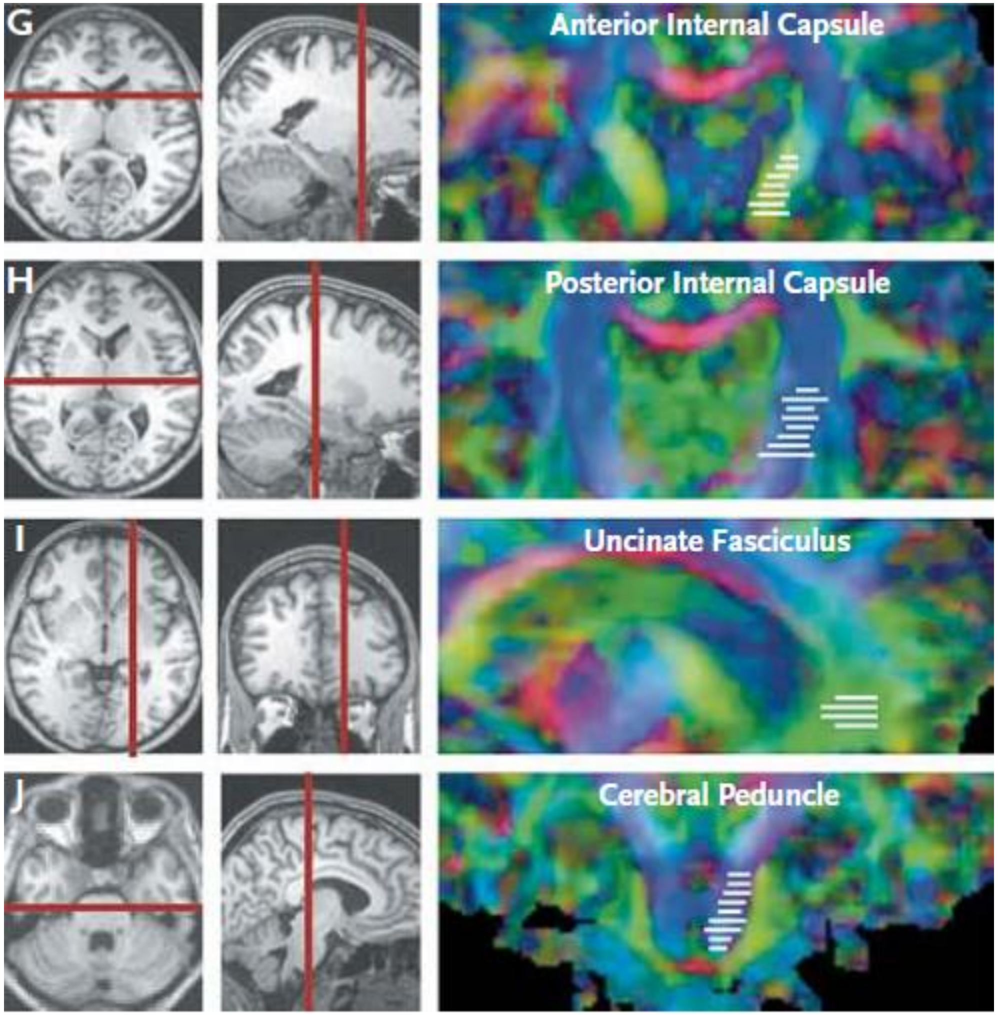
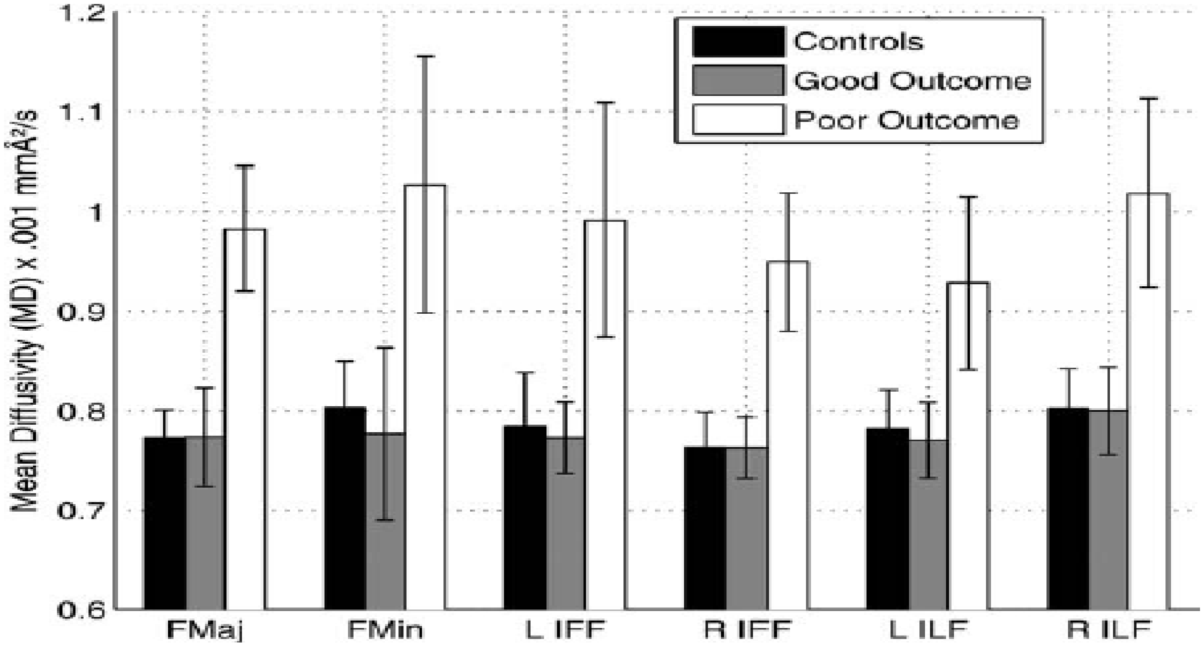


Figure 5. White Matter Damage

(Mac Donald et al., 2011)

White Matter



Mean and standard deviation of MD values in the six tracts of the TBSS results across the three groups.

Figure 6. Total of 46 patients in three groups based on PCS survey (23 control, 11 Good Outcome, 12 Poor Outcome)

(Messè et al., 2011)

Sources of Stress

Pre-injury Health

Family Obligations/ Commitment

Co-morbid Medical Conditions

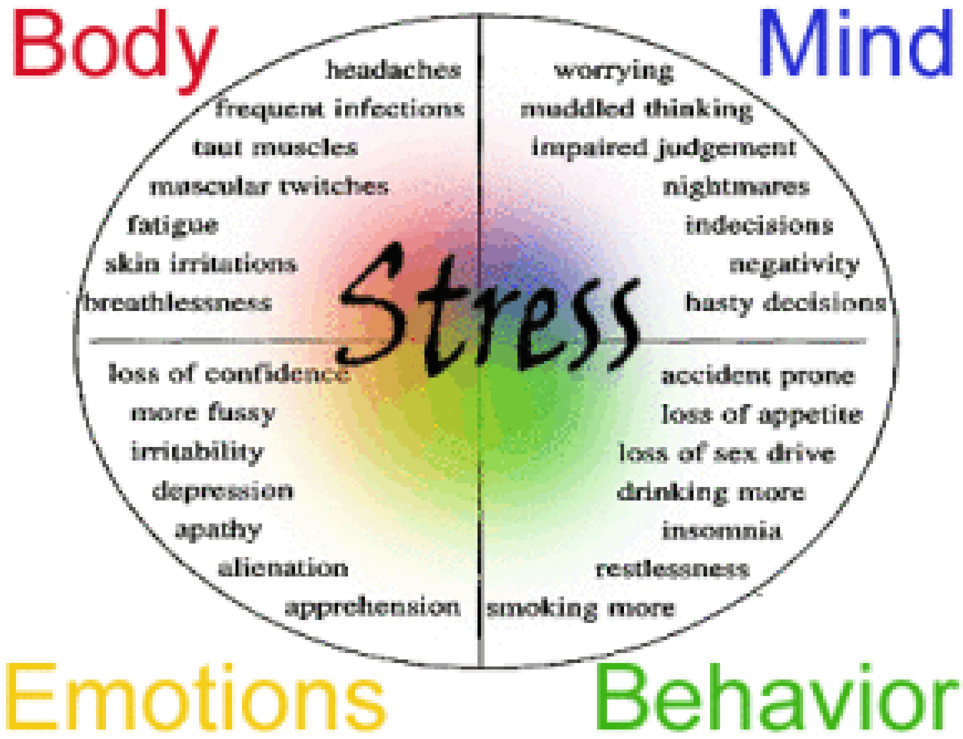
Support System

Career Impact

Financial Status

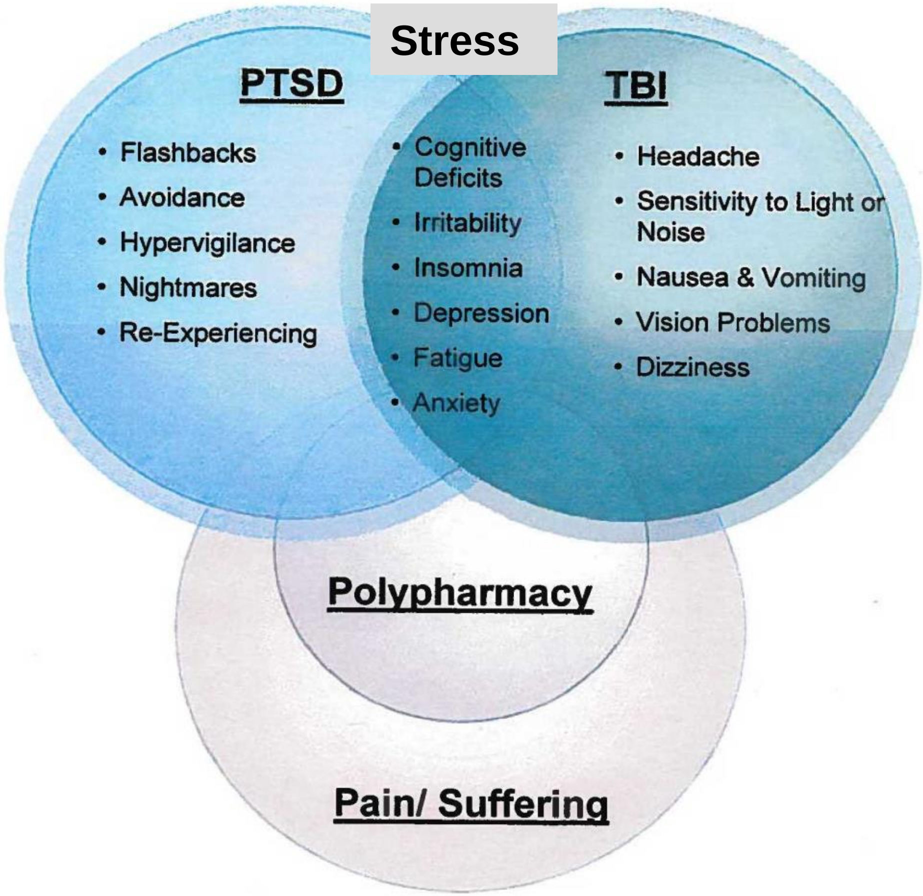
(Hanna-Pladdy, Berry, Bennett, Phillips, & Gouvier, 2001)

Effects of Stress



(Doman, n.d.)

But It's Complicated….



(Stein & McCallister, 2009)

Hypothalamic-Pituitary-Adrenal Axis

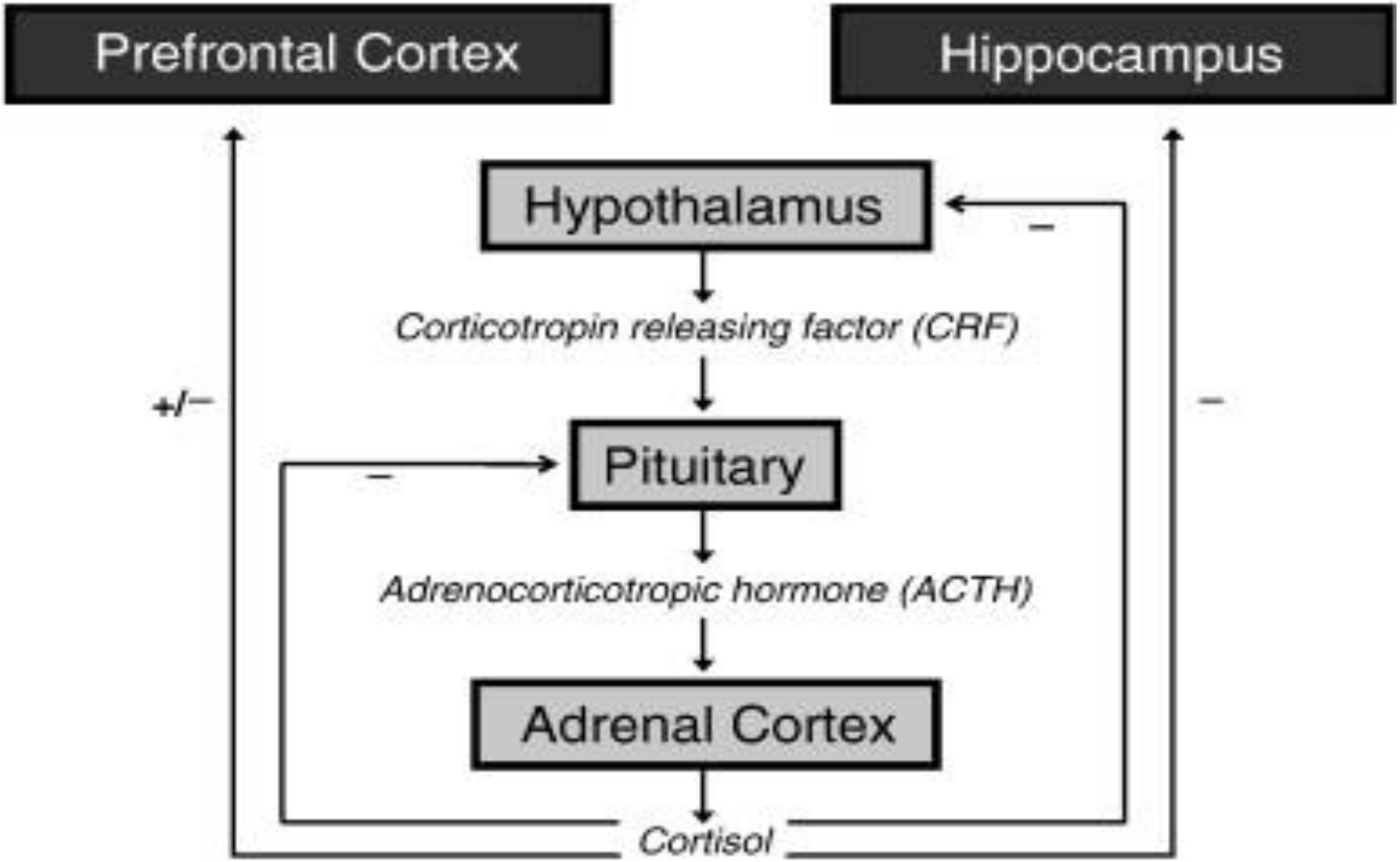


Figure 7. Neuroimage

(Kremen et al., 2010)

Cortisol: Long-term Effects

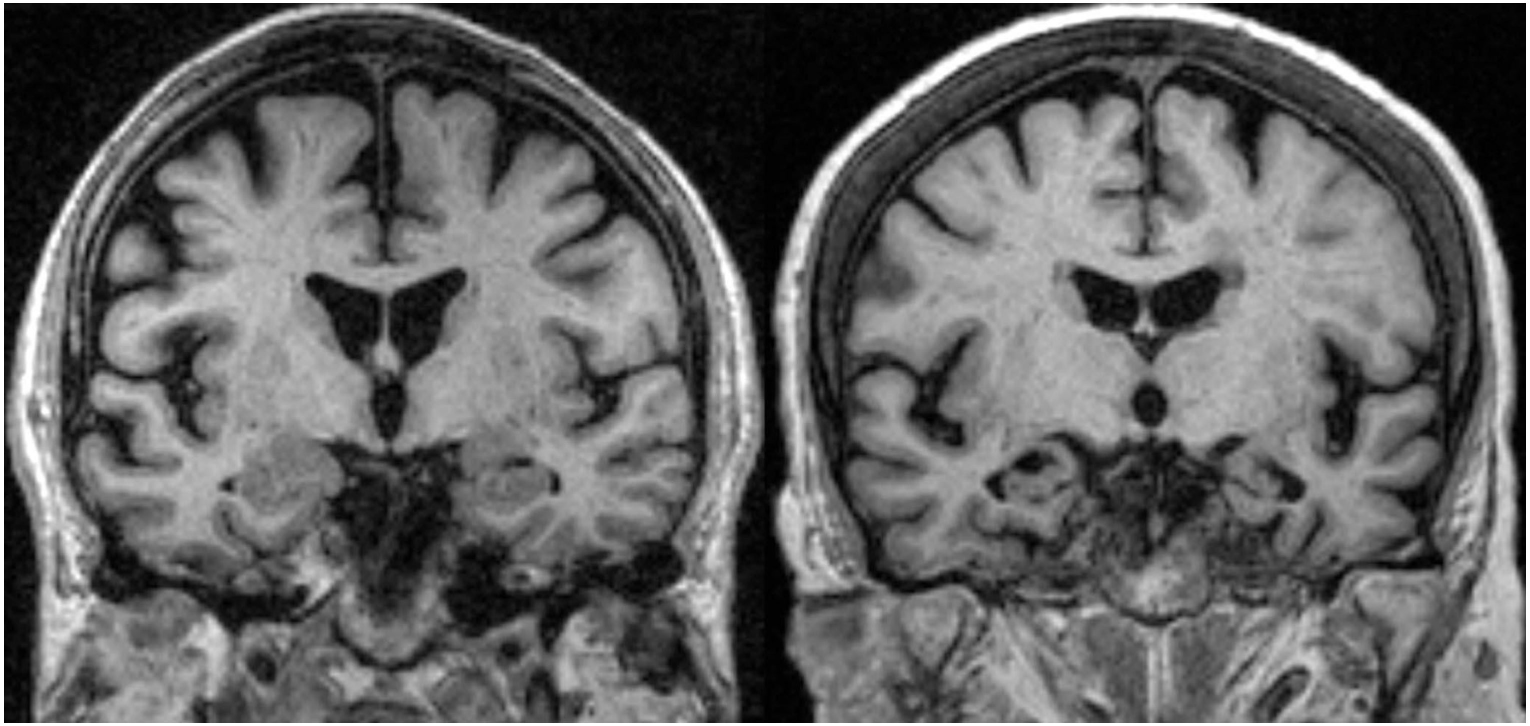


Figure 8. Imaging in Alzheimer's disease

(Scheltens, 2009)

Outline

- TBI Background
  - Role of stress
- **Exercise**
  - Background
  - Traditional
  - Relaxation and mind-body medicine
- Sleep
  - Background
  - TBI and sleep
  - Treatments

Exercise

- Traditional
  - Aerobic
  - Weight lifting

- Relaxation exercises
  - Mind-body medicine
    - Examples: Meditation, yoga, tai chi

Role of Exercise

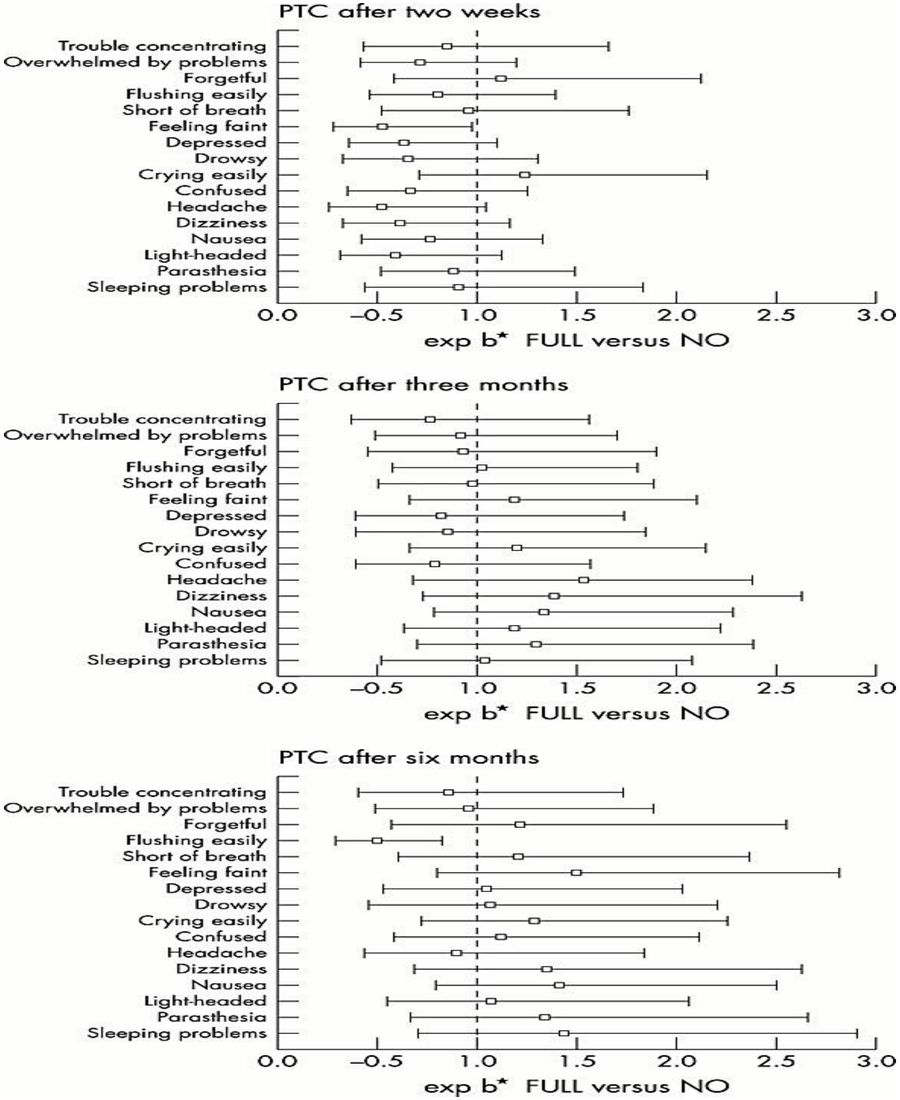
- Exercise has tremendous health benefits
  - Weight management
  - Blood pressure management
  - Depression management
  - Pain management
- Effects of exercise on acute low back pain
  - Improved recovery
- Challenges concept of rest for mild TBI

Bed Rest Versus No Bed Rest

- Effectiveness of bed rest after mild traumatic brain injury: A randomized trial of no versus six days of bed rest
  - 107 total patients enrolled
  - 1:1 randomization between full bed rest X six days and no bed rest
  - Outcome measures: Symptom inventory and short form health survey (SF-36)

(de Kruijk, Leffers, Meerhoff, Rutten, & Twijnstra, 2002)

Post-traumatic Complaints



(de Kruijk et al., 2002)

Figure 9. Post-traumatic Complaints

Exercise and Brain-Derived Neurotrophic Factor (BDNF)

- BDNF
  - Group of proteins associated with synaptic transmission
  - Potentially involved with neural development and neuro-plasticity
- Animal study
  - Male Sprague-Dawley rats randomized to TBI group or sham injury group
  - Tested both acute and delayed intervention of exercise

(Molteni, Ying, & Gomez-Pinilla, 2002)

Exercise and BDNF

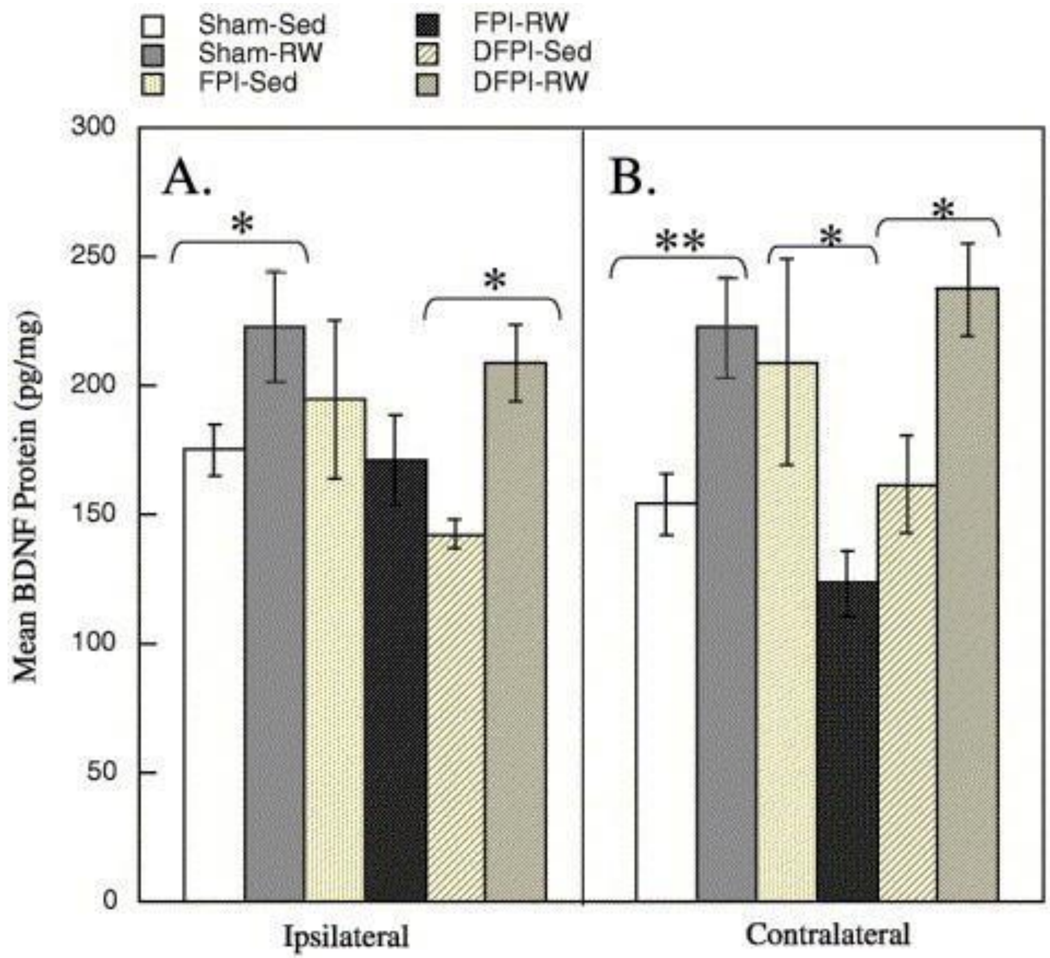


Figure 10. Effects of exercise following fluid percussion injury (FPI) on BDNF protein.

(Griesbach, Hovda, Molteni, Wu, & Gomez-Pinilla, 2004)

Exercise and BDNF

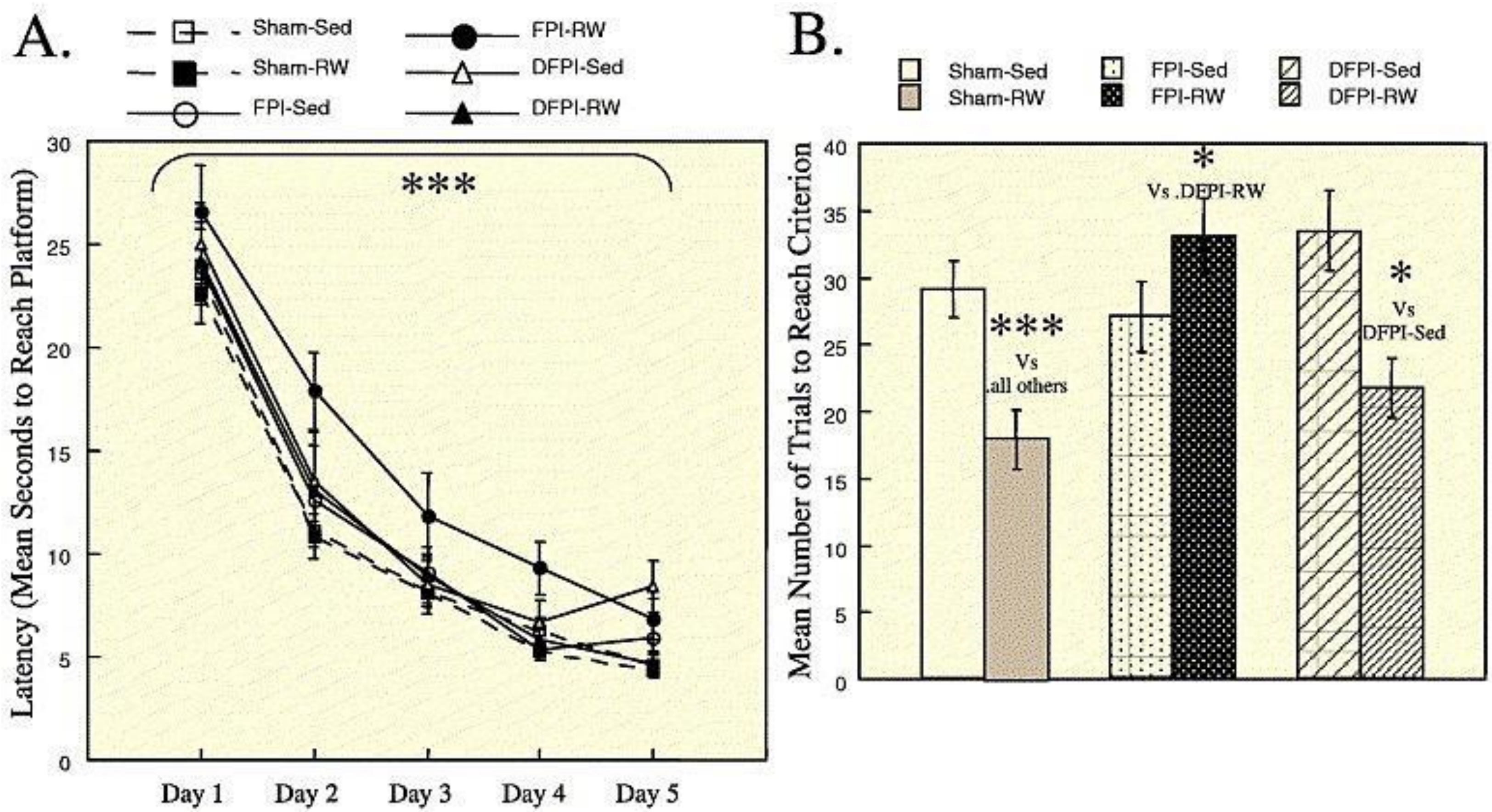


Figure 11. Effects of exercise immediately following FPI on Morris water maze.

(Griesbach et al., 2004)

Exercise Versus Medications

- Michael W. Marlatt, Paul J. Lucassen and Henriette van Praag studied brain research in 2010 to compare neurogenesis in the hippocampus after treatment with fluoxetine (Prozac), duloxetine (Cymbalta), and aerobic exercise in female C57Bl/6 mice

The Effects of Running and Antidepressants on Cell Survival and Neurogenesis

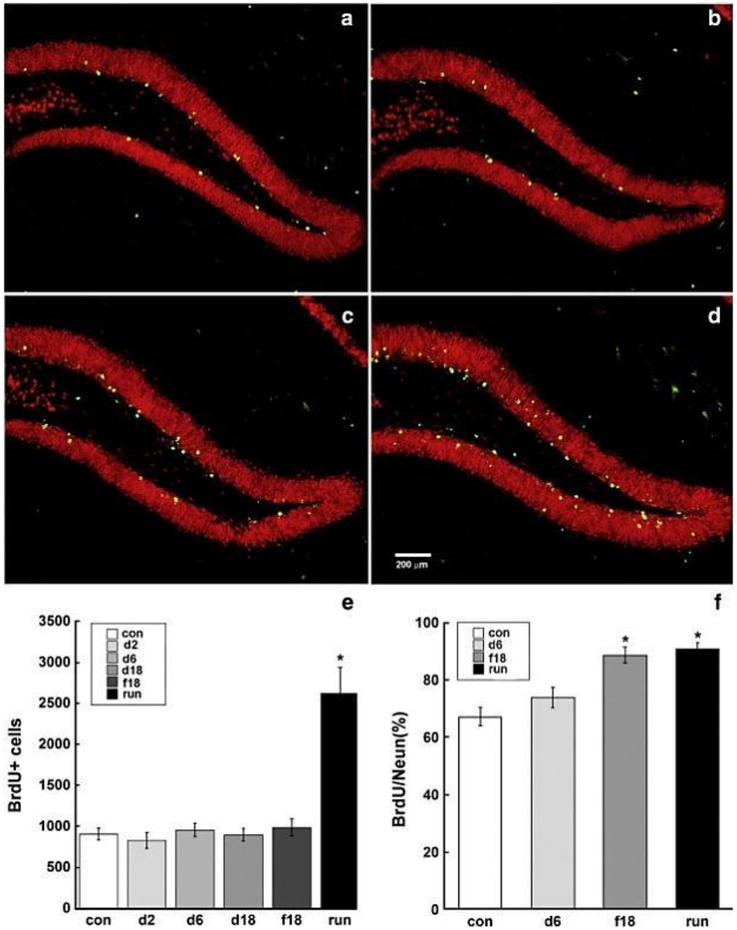


Figure 12. The effects of running and antidepressants on cell survival and neurogenesis.

(Marlatt, Lucassen, & van Praag, 2010)

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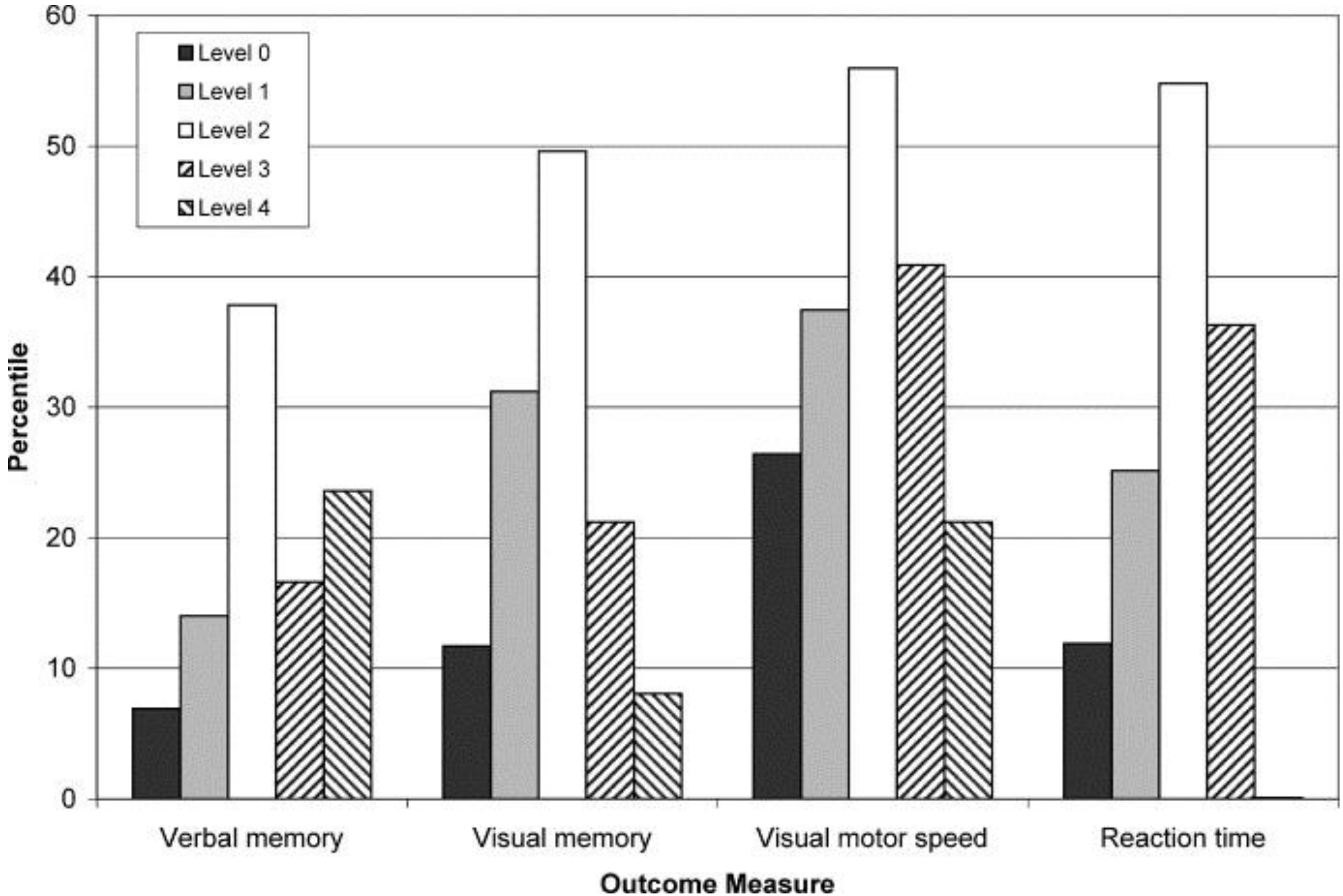
Neurocognitive Performance and Activity

- Retrospective cohort study
- 95 athletes, 15 females
- Outcome measure included performance on ImPACT testing (multiple domains)
- Accounted for activity levels

(Majerske et al., 2008)

Effects of Exertion on Recovery



(Majerske et al., 2008)

Figure 13. Neurocognitive performance

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Mood, TBI, and Exercise

- A randomized controlled trial of exercise to improve mood after traumatic brain injury
- Participants were patients with chronic TBI (> six months to five years post-injury)
- Weekly supervised exercise sessions – included warm up time, 30 minutes of aerobic exercise (60% of maximum heart rate) and cool down

(Hoffman et al., 2010)

Comparison of Control and Exercise Groups by Assignments

Table 2. *Comparison of outcomes based on group assignment*

	Control		Exercise			
Measure	**Baseline**	**10-Week**	**Baseline**	**10-Week**	**Statistical Test**	**Significance**
Beck Depression Inventory	24.7	21.2	21.5	16.4	Regression	.250
Exercise recall Total minutes per week	58	143	66	252	Mann-Whitney	.064
Exercise recall No. days per week	1.47	2.05	1.28	3.68	Regression	**.004**
Current pain	3.33	3.08	3.35	2.73	Mann-Whitney	.717
Worst pain	5.98	5.44	5.33	4.65	Mann-Whitney	.966
Average pain	4.33	4.10	3.68	3.14	Mann-Whitney	.194
Pain interference	3.58	3.79	4.13	3.24	Mann-Whitney	**.021**
Average fatigue	5.65	5.74	5.75	5.16	Mann-Whitney	.312
Fatigue interference	5.45	5.47	5.63	4.89	Mann-Whitney	.184
Brief Pain Inventory	3.54	3.51	3.82	3.12	Mann-Whitney	**.030**
Craig Handicap Assessment and Reporting Technique – Short Form	84.5	83.3	85.7	85	Mann-Whitney	.489
Traumatic brain injury symptom checklist (severity)	2.55	2.41	2.44	2.41	Regression	.431
Traumatic brain injury symptom checklist Total number of symptoms	11.4	11.4	11.0	11.8	Mann-Whitney	.682
Perceived quality of Life	45	49	54	58	Regression	.388
Pittsburgh Sleep	10.6	10.9	10.0	9	Regression	.106
Short Form-12 Physical	41.4	39.5	41.6	42	Regression	.224
Short Form-12 Mental	28.2	32.5	31.8	38.3	Regression	.238
Walking test	1272	1396	1343	1491	Regression	.566

Bold values indicate significance.

Figure 14. Control group outcomes

(Hoffman et al., 2010)

Comparison of Control and Exercise Groups by Minutes Exercised

Table 3. *Comparison of outcomes by groups sorted by minutes exercised*

	Baseline				Outcome			
Measure	**<90 Minutes n = 57**	**≥90 Minutes n = 23**	***t*-test**	***P* Value***	**<90 Minutes n = 33**	**≥90 Minutes n = 43**	***t*-test**	***P* Value***
Beck Depression Inventory	24.3	20.2	.089	.157	25.8	20.7	**.023**	**.033**
Current pain	3.2	3.7	.424	.382	3.7	3.0	.248	.289
Worst pain	5.6	5.8	.836	.748	5.7	5.6	.964	.941
Average pain	3.9	4.2	.741	.760	4.3	3.6	.273	.257
Pain interference	3.5	4.6	.192	.253	4.2	3.6	.399	.365
Average fatigue	5.8	5.4	.600	.720	5.8	5.5	.624	.692
Fatigue interference	5.5	5.6	.959	.747	5.9	5.2	.303	.271
Brief Pain Inventory	3.4	4.3	.195	.203	3.9	3.5	.524	.560
Craig Handicap Assessment and Reporting Technique – Short Form	84.6	86.2	.592	.651	82.1	86.7	.100	**.028**
Traumatic brain injury symptom checklist (severity)	2.5	2.5	.834	.936	2.5	2.4	.747	.710
Traumatic brain injury symptom checklist (total number of symptoms)	11.3	11.0	.783	.666	11.2	11.0	.901	.992
Perceived quality of life	48.1	52.5	.367	.341	43.5	53.4	**.028**	**.034**
Pittsburgh Sleep	10.4	10.2	.858	.773	11.4	9.2	**.030**	**.023**
Short Form-12 Physical	43.1	37.5	.086	.119	42.8	41.6	.692	.675
Short Form-12 Mental	28.1	34.7	**.022**	**.029**	26.0	32.6	**.015**	**.024**
Walking test	1319	1277	.682	.885	1217	1376	.089	**.036**

*MWU = Mann-Whitney U test.

Figure 15. Control group outcomes

(Hoffman et al., 2010)

Summary

- Bed rest most likely not helpful
- Cognitive rest not well studied
- Animal studies support aerobic exercise
- Exercise may be helpful but not in acute phase
- Need to better study timing and types of exercise

(Hoffman et al., 2010)

Relaxation Exercises

- Help address stress response
- May affect the cortisol response

Prevalence of Complementary Alternative Medicine (CAM)

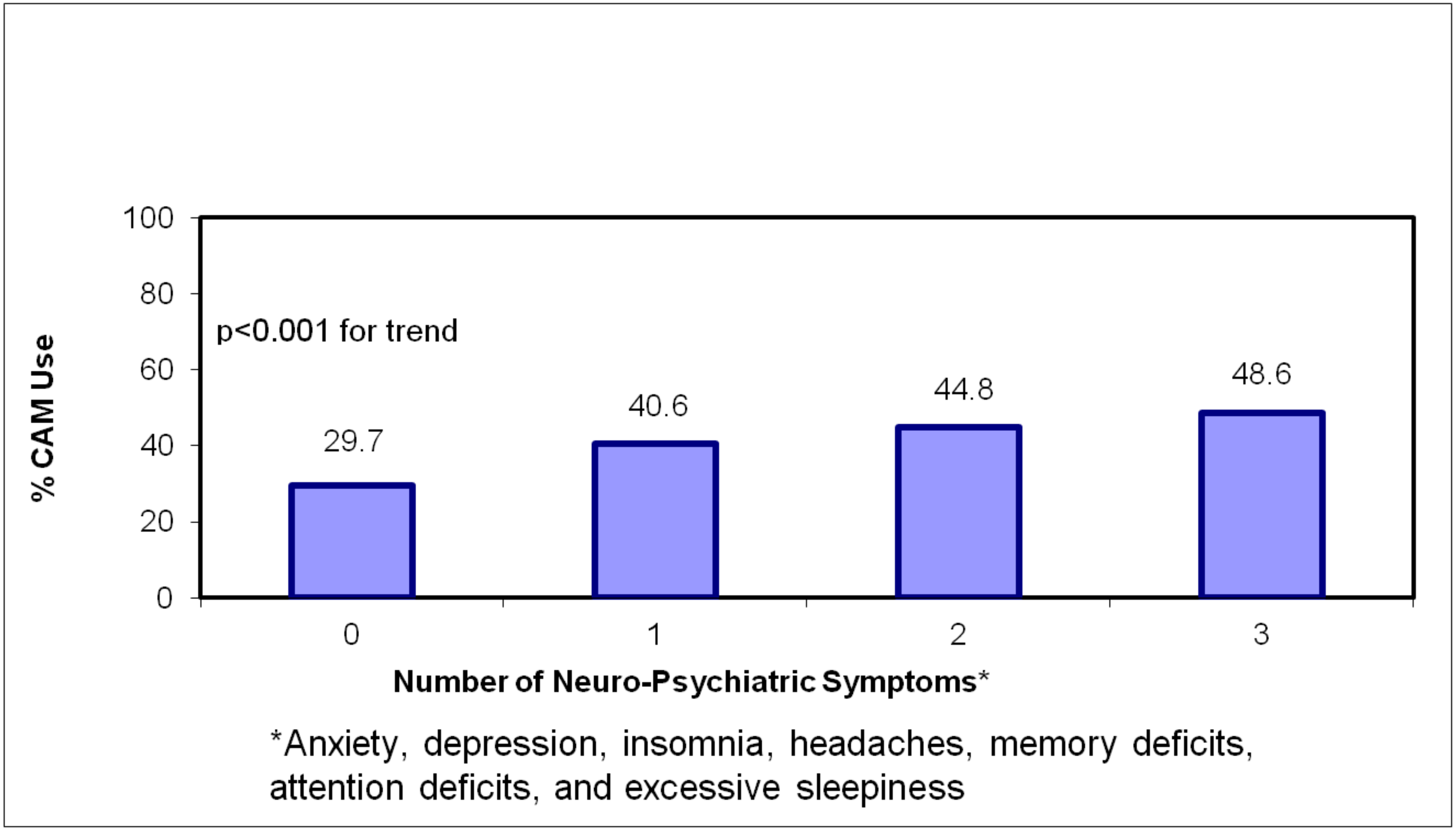


Figure 16. CAM

(Purohit, Wells, Zafonte, Davis, & Phillips, 2013)

Likelihood of CAM Use

Number of Symptoms	Odds Ratio (95% CI)
No Symptoms (Reference)	1.00 (ref)
1 Symptom	1.42 (1.31, 1.55)
2 Symptoms	1.69 (1.50, 1.90)
≥3 Symptoms	1.85 (1.64, 2.09)

Figure 17. Adjusted for sociodemographics, chronic medical conditions, neurological disorders, and baseline health habits

(Purohit et al., 2013)

CAM Usage by Modality

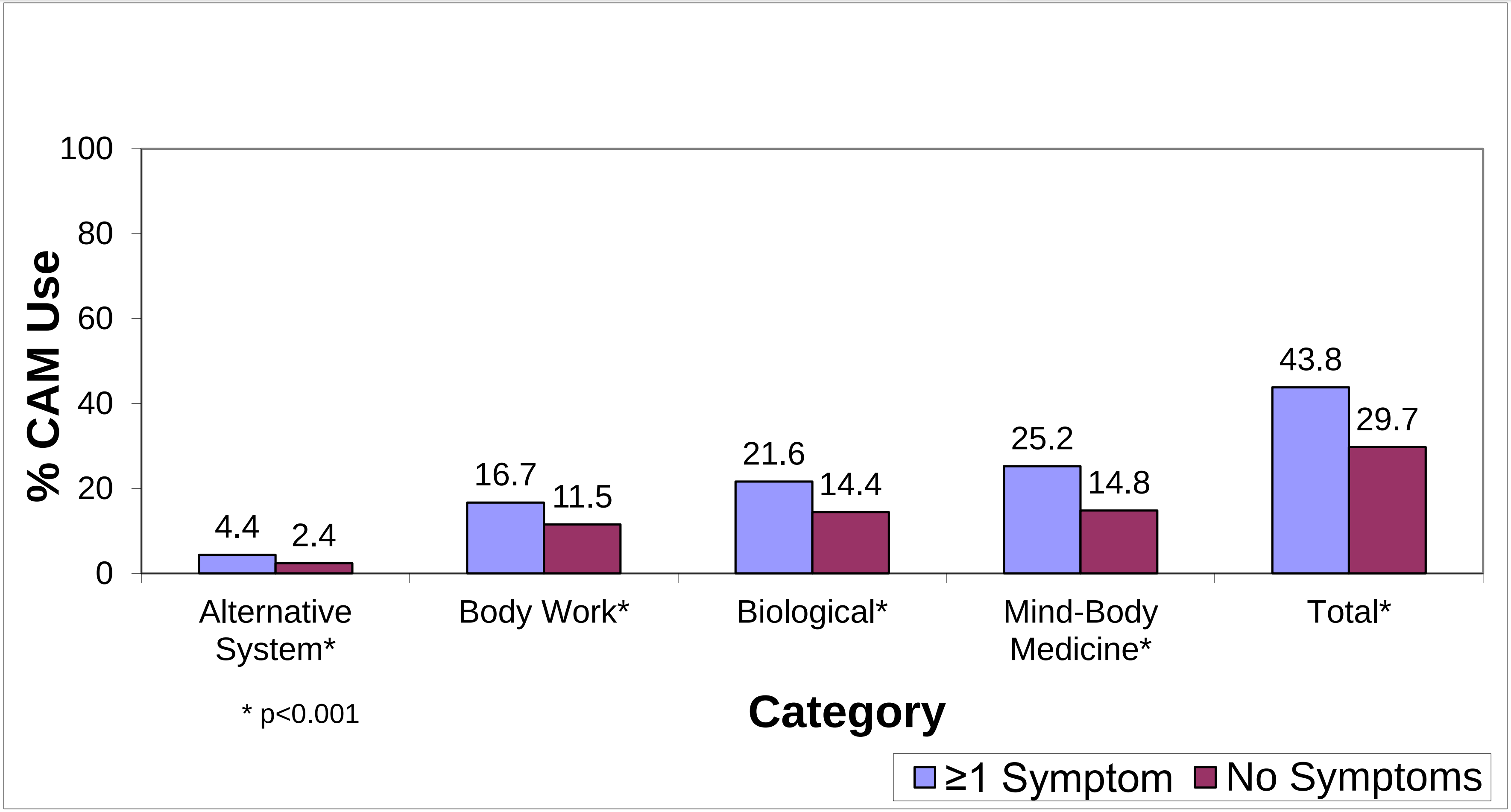


Figure 18. CAM Modality

(Purohit et al., 2013)

Reasons for Use

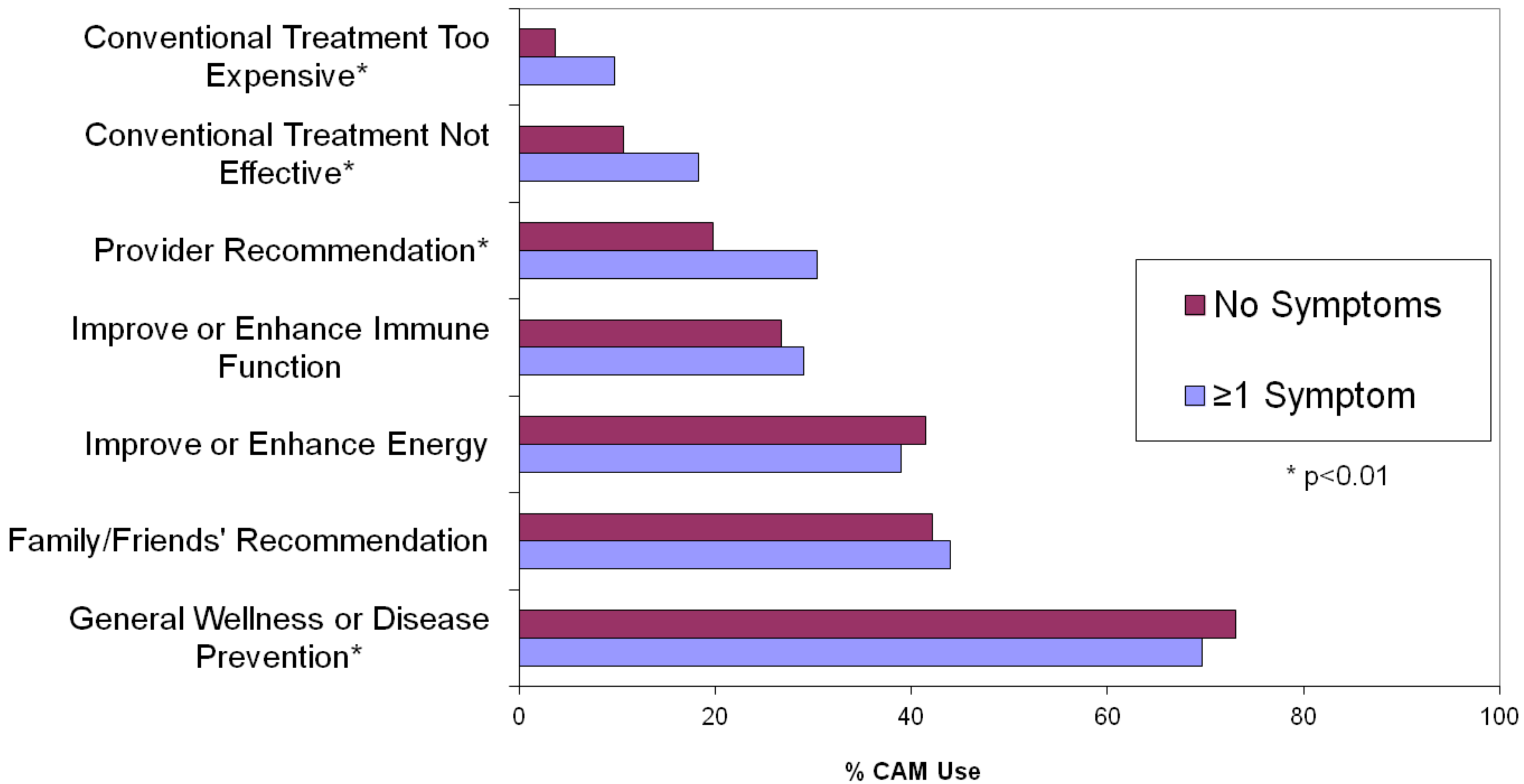


Figure 19. CAM use

(Purohit et al., 2013)

CAM Expenditure Per Capita by Therapy Category

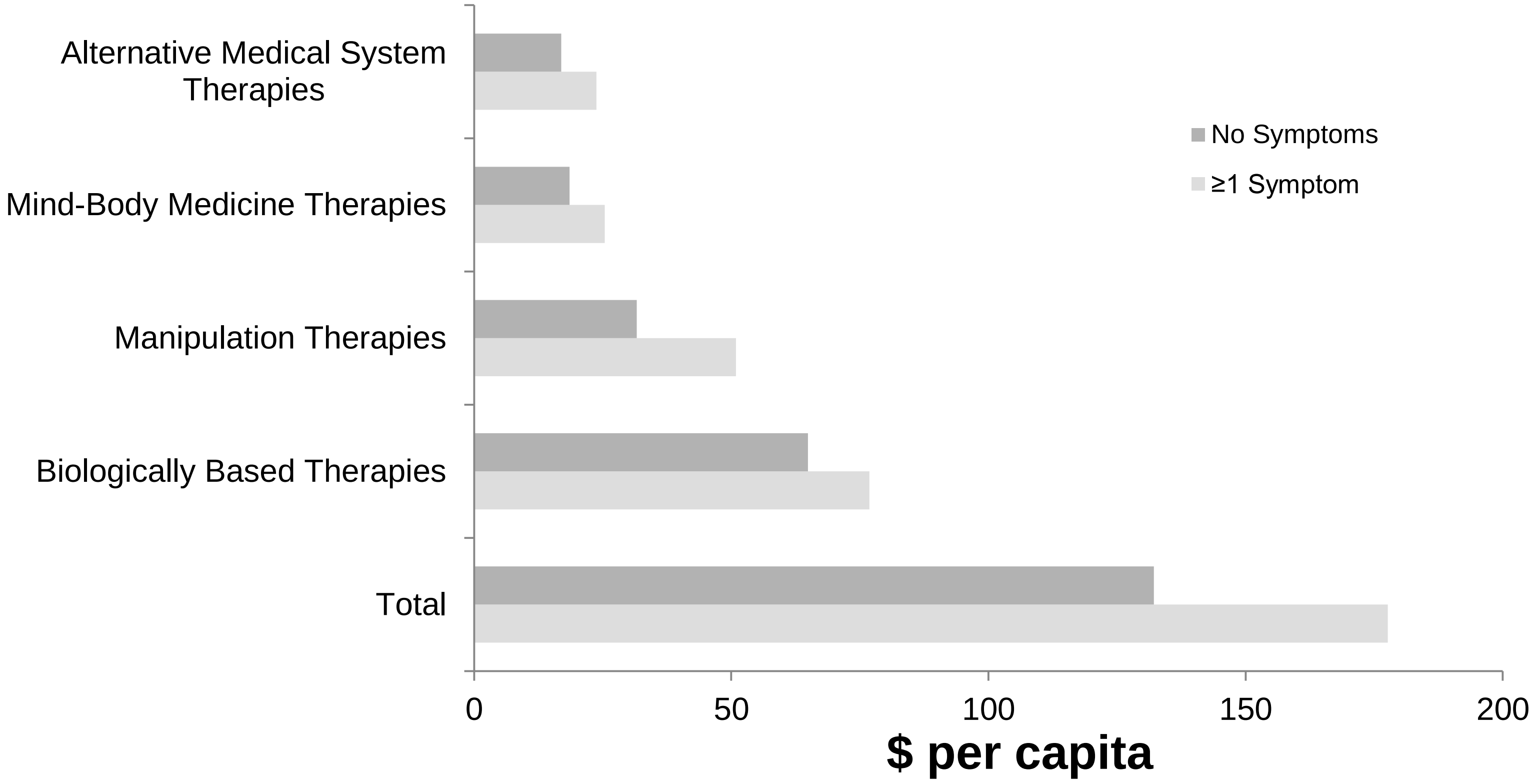


Figure 20. CAM costs

(Purohit, Zafonte, Davis, & Yeh, in press)

TBI and Mindfulness-based Stress Reduction (MBSR)

- MBSR as an intervention for TBI
- MBSR is an eight week protocol of yoga and meditation
- Weekly group training and daily home practice with CD
- Total of seven participants, pilot randomized controlled trial design

(Purohit, Zafonte, Davis, & Yeh, in press)

Results

- Hippocampus
  - 1% increase in size in bilateral hippocampus
- Amygdala
  - 2% increase in left amygdala volume
- Right orbito-frontal white matter (uncinate fasciculus)
  - 5.8% increase in volume

(Purohit, Zafonte, Davis, & Yeh, in press)

Increased Cortical Thickness

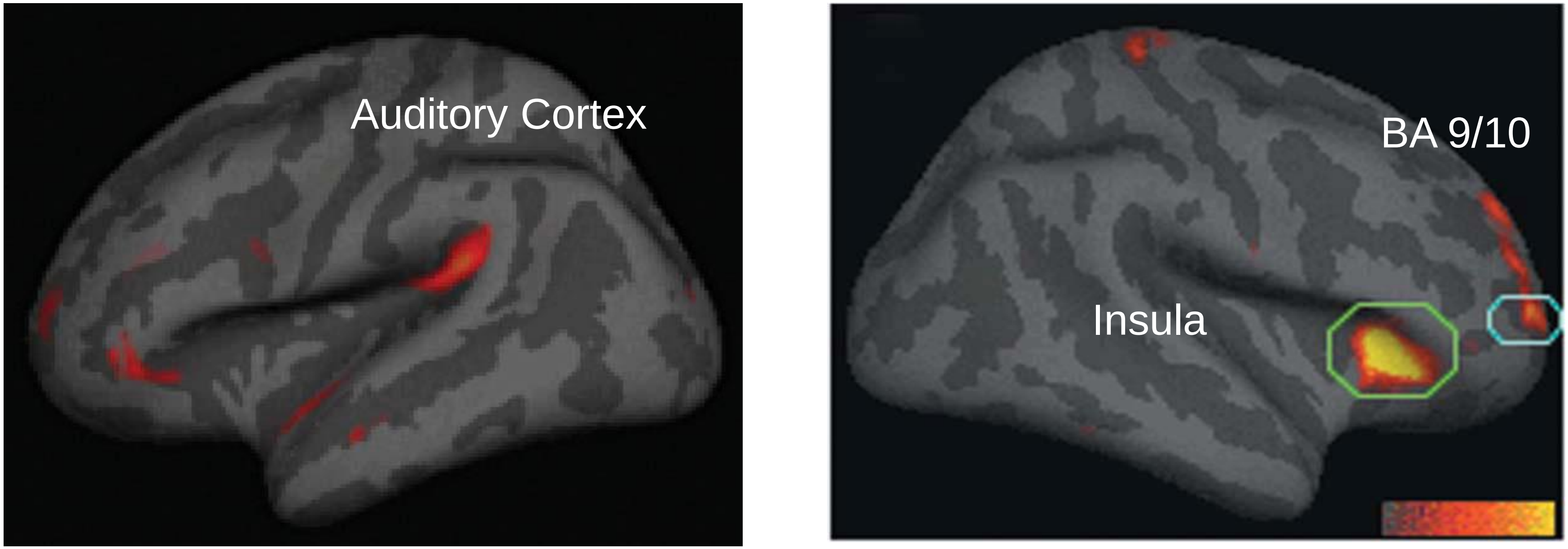


Figure 21. Cortisol effects

- Study of 20 participants who regularly meditated vs. 20 control patients
- Increased cortical thickness in specific areas

(Lazar et al., 2005)

Functional Changes

Meditation group had stronger brain activation in anterior cingulate cortex and medial prefrontal cortex

$p = 0.01$

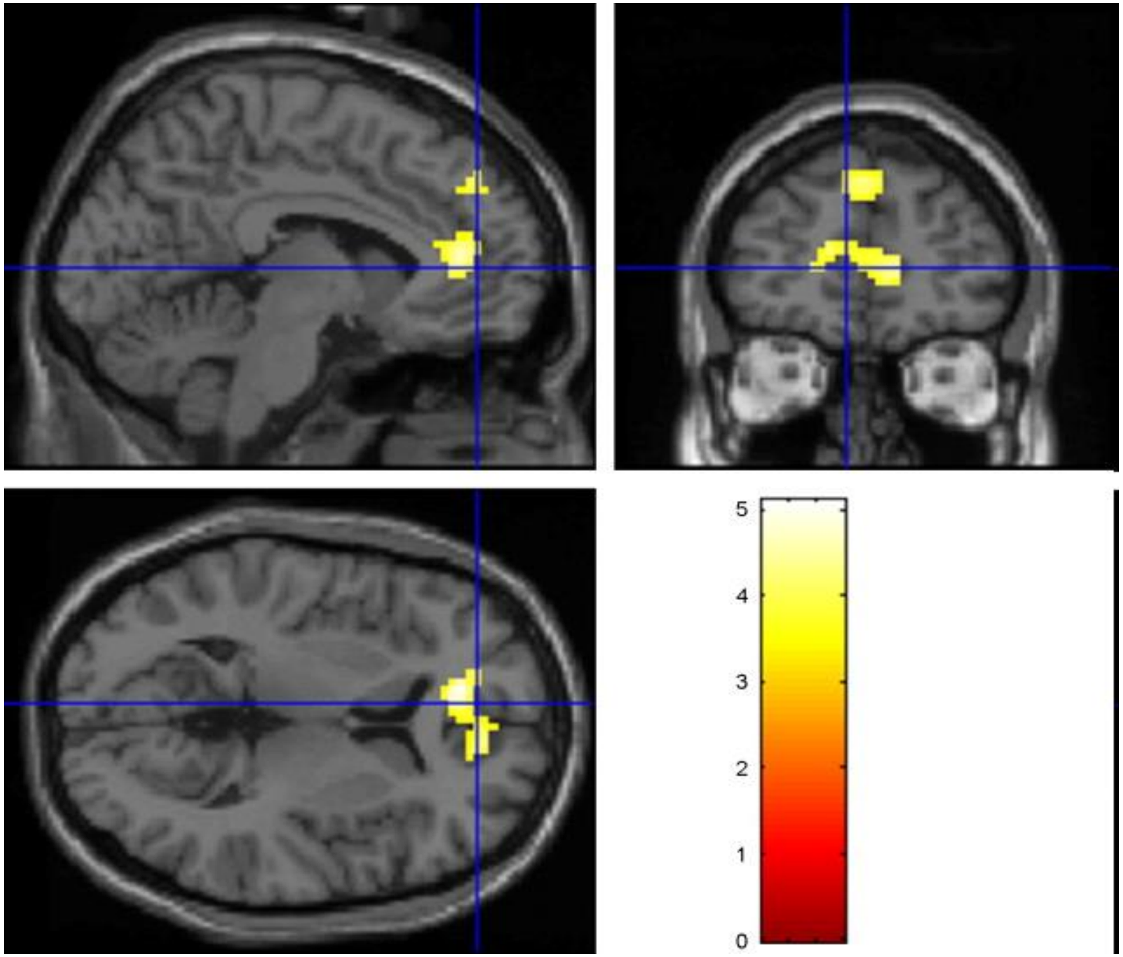


Figure 22. Meditation results

(Hölzel et al., 2007)

DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury

Genetic Changes

- N_1= Control
- M = Long-term yoga/ meditation practice
- N_2 = Underwent eight week yoga/meditation course

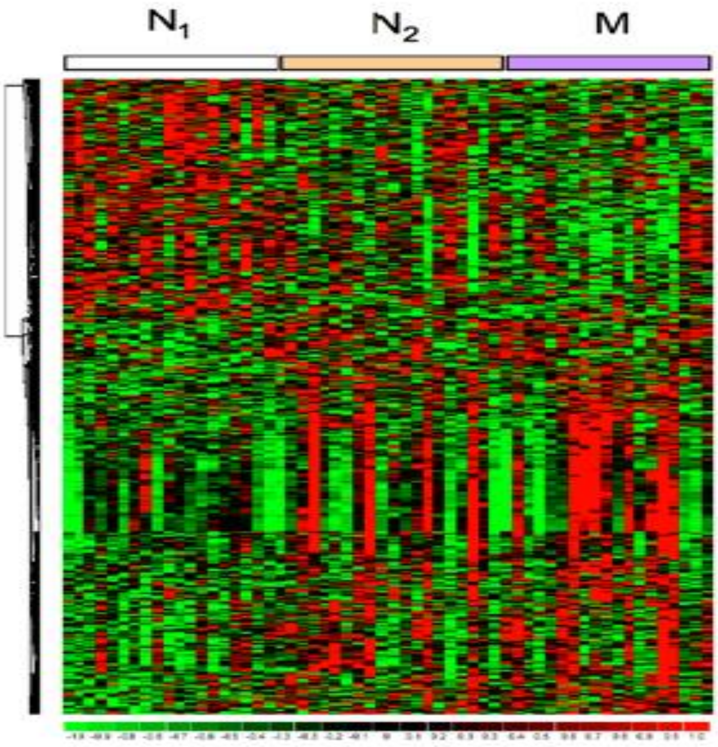


Figure 23. Genetics

(Dusek et al., 2008)

Outline

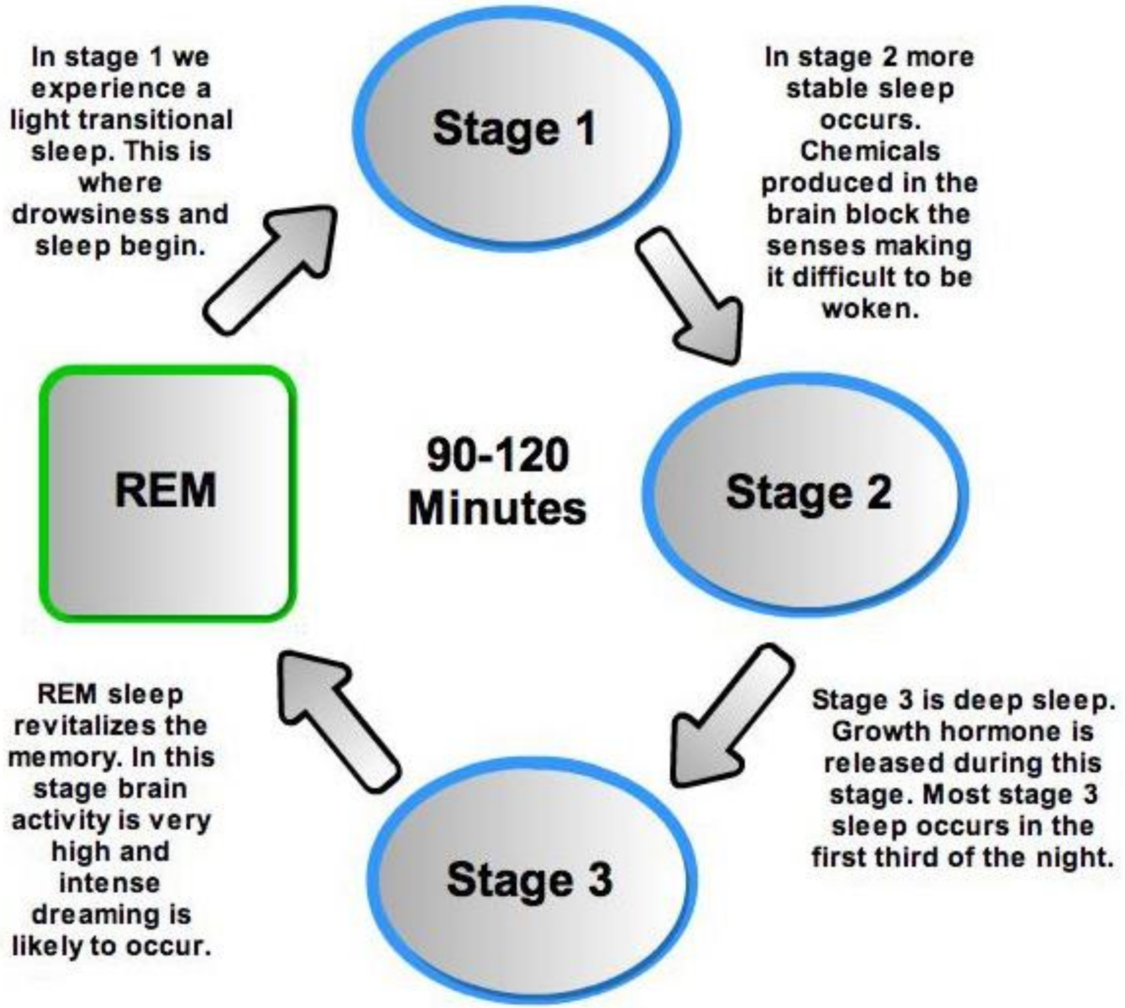
- TBI Background
  - Role of stress
- Exercise
  - Background
  - Traditional
  - Relaxation and mind-body medicine
- **Sleep**
  - Background
  - TBI and sleep
  - Treatments

Sleep and TBI

- 97.4% with subjective sleep complaints
- 55.2% with objective insomnia
- 34.5% with sleep apnea
- 85.2% with day time hypersomnia
- 54.3% with sleep fragmentation (sleep cycle disturbance)
- Blunt trauma more likely to induce sleep apnea
- Blast injury more likely to induce insomnia
- Current presentation will not discuss nightmare disorder et al; large topic of its own deserving separate attention

(Collen, Orr, Lettieri, Carter, & Holly, 2012)

Sleep Architecture



(Rally, 2012)

Figure 24. Sleep Stages

REM Sleep and TBI

- Rapid Eye Movement (REM) sleep important for patients to process events, particularly traumatic events
- Patients with TBI have disturbed REM sleep components in many neural areas
- 14 Veterans with blast injury/TBI compared to 11 Veterans without history of blast injury/TBI
  - Age and gender matched
- Comparison of glucose metabolism during REM and wakefulness

(Ryan et al., 2014)

Brain Metabolic Activity

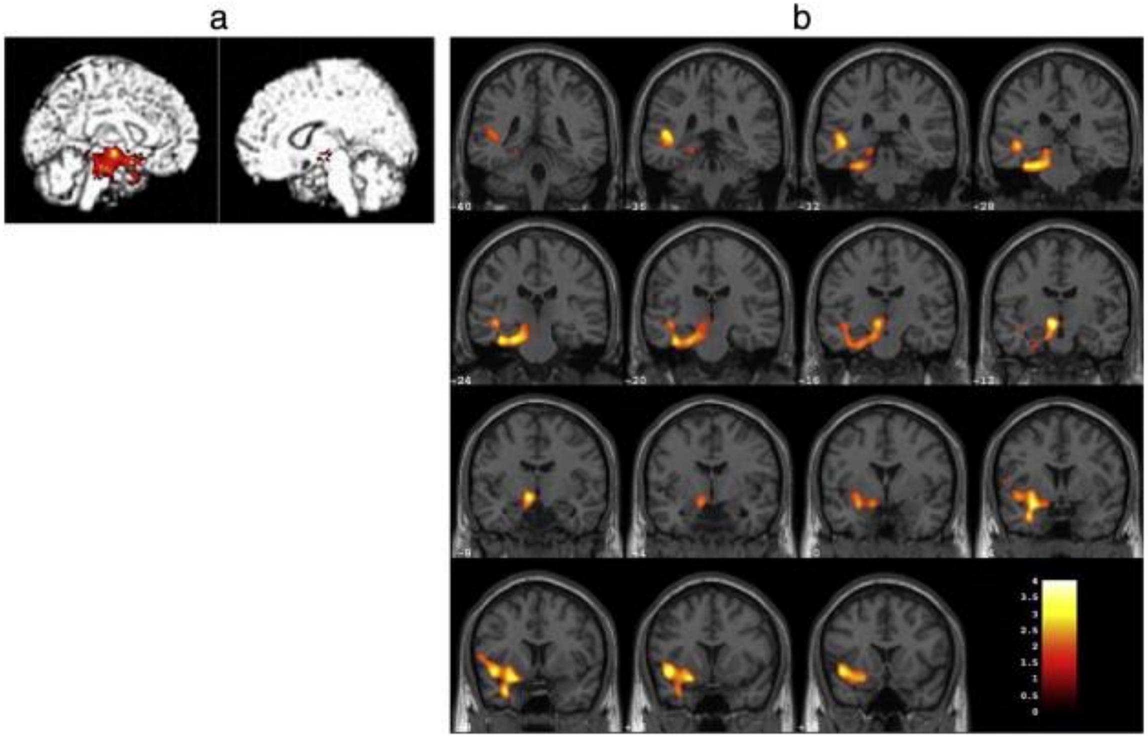


Figure 25. Areas of the brains where blast/TBI exposed veterans showed lower glucose metabolism: brainstem, basal ganglia, amygdala, hippocampus, parahippocampal gyrus, thalamus, insula, uncus, culmen, visual association cortices, and midline medial frontal cortices

(Ryan et al., 2014)

Role of Sleep

- Sleep disturbances can predict many neuropsychiatric sequelae one year after injury
- 101 patients with closed head injury evaluated within three months of injury
- Evaluated sleep with medical outcome scale for sleep
- Followed longitudinally with periodic evaluations, including six months and 12 months

(Rao, McCann, Han, Bergey, & Smith, 2014)

Sleep Dysfunction in Acute TBI and Symptoms One Year Post Injury

Adjusted for age, gender, general medical health, psychiatric symptoms in the acute TBI period			
Dependent variables	*β* (SE)	*p* Value	Adjusted R^2
Hamilton Depression Scale	0.255 (0.074)	0.002	0.417
Apathy Evaluation scale	0.153 (0.076)	0.054	0.336
Activities of Daily Living	0.001 (0.01)	0.929	0.126
Clinical Anxiety Scale	0.111 (0.033)	0.002	0.411
Social Functioning Examination	0.001 (0.001)	0.287	0.309
Mini Mental State Exam	0.041 (0.018)	0.035	0.573

Figure 26. Relationship between sleep problems in the acute TBI period and psychiatric symptoms at 1 year post-injury after controlling for confounds in persons with mild TBI.

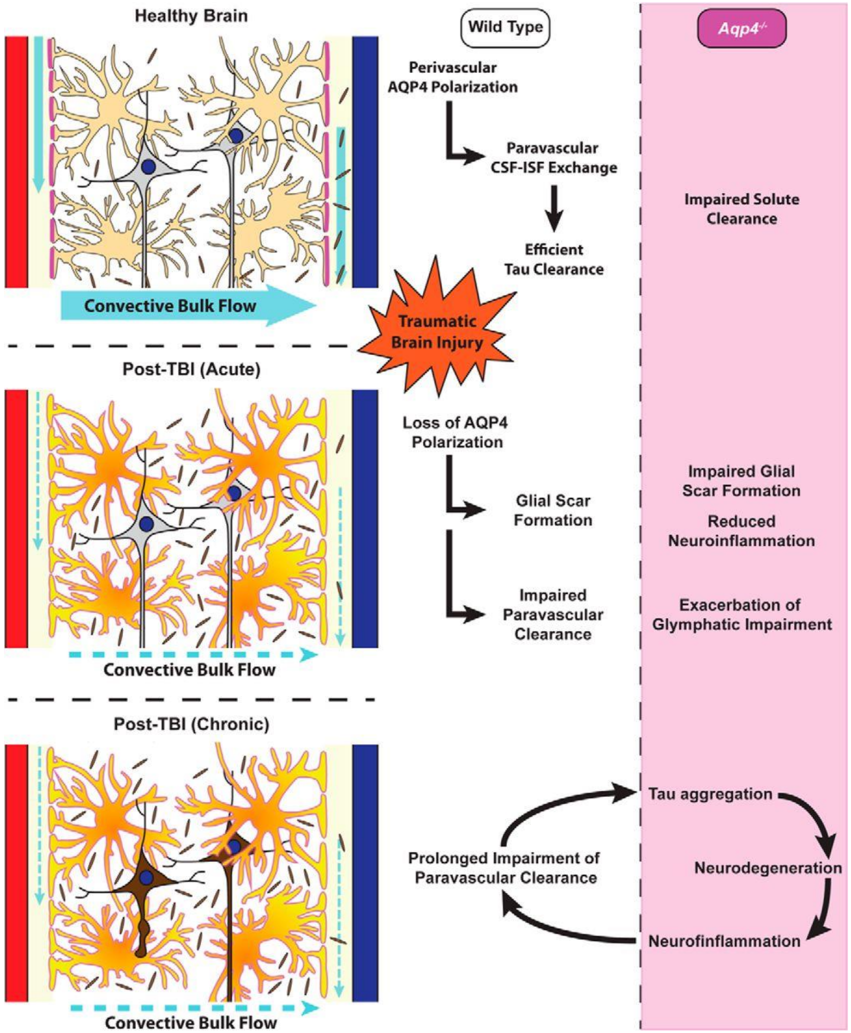
(Rao et al., 2014)

Sleep and Debris Clearance

- Brain lacks typical lymphatic system for debris and fluid clearance
- Discovery of a “glymphatic” system
- Functions similar to lymphatic system
- Involvement of glial (support) neural cells

(Iliff et al., 2014)

“Glymphatic System”



(Iliff et al., 2014)

Figure 27. Glymphatic System

Pharmacological Treatment

- Benzodiazepines
  - Disruption of normal sleep architecture
  - Cognitive impairment during peak concentration
  - Potential residual cognitive impairment after discontinuation
- "Z" drugs (zopiclone, zaleplon, zolpidem, eszopiclone)
  - Impairments in cognition and motor function
  - Concern for interfering with neuroplasticity
  - Not well studied in TBI population

Pharmacological Treatment

- Trazodone
  - May be better than benzodiazepines and “Z” drugs
  - But poorly studied in patients with TBI

- Melatonin agonists
  - Ramelteon
  - May have better side effect profile
  - But no published studies in patients with TBI
  - No long-term studies
  - Takeda withdrew approval application in Europe in 2011

Mindfulness and Sleep

- Subjects' focus group report (n = 18)
- Qualitative analysis
- Patients reported
  - Sleep quantity unaffected
  - Sleep quality improved (more restorative, less distress about insomnia)
  - *Motivated by the results*

(Hubbling, Reilly-Spong, Kreitzer, & Gross, 2014)

Sleep Neurophysiology

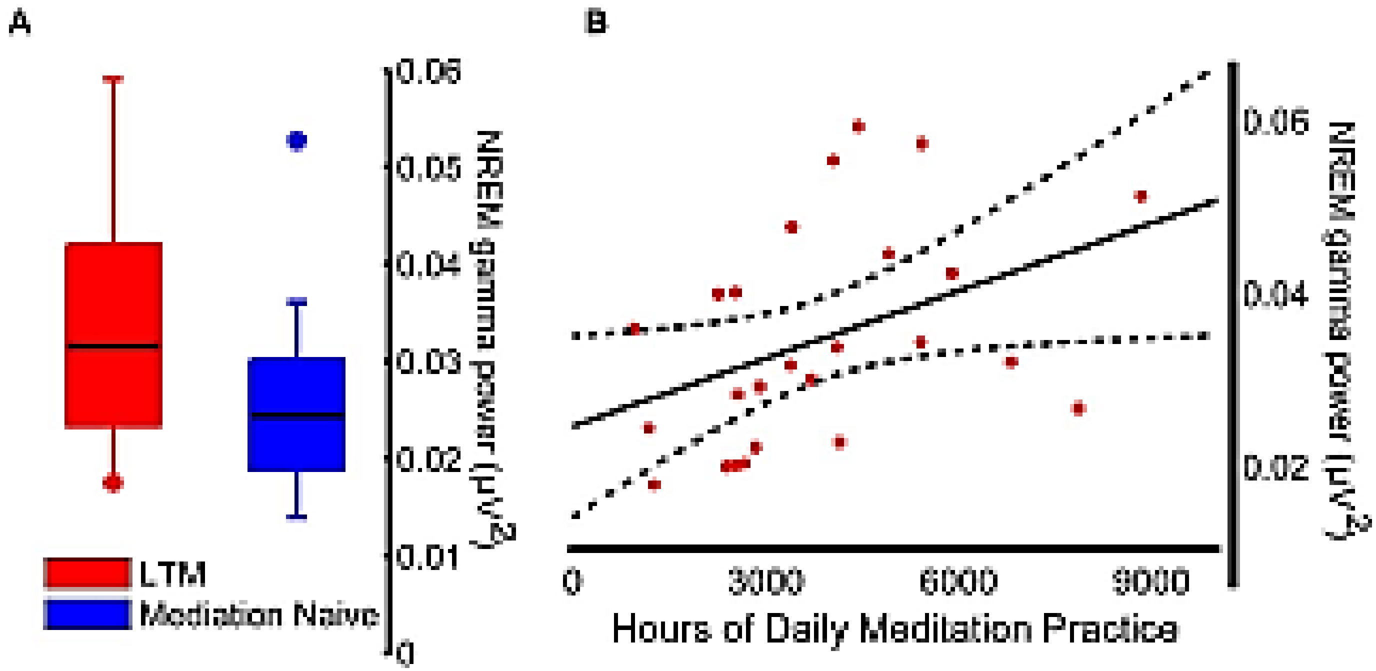


Figure 28. N=29 per group Gamma waves may correlate with enhanced consciousness and intellectual acuity in awakened state

(Ferrarelli et al., 2013)

Mindfulness-based Stress Reduction (MBSR) Versus Lunesta

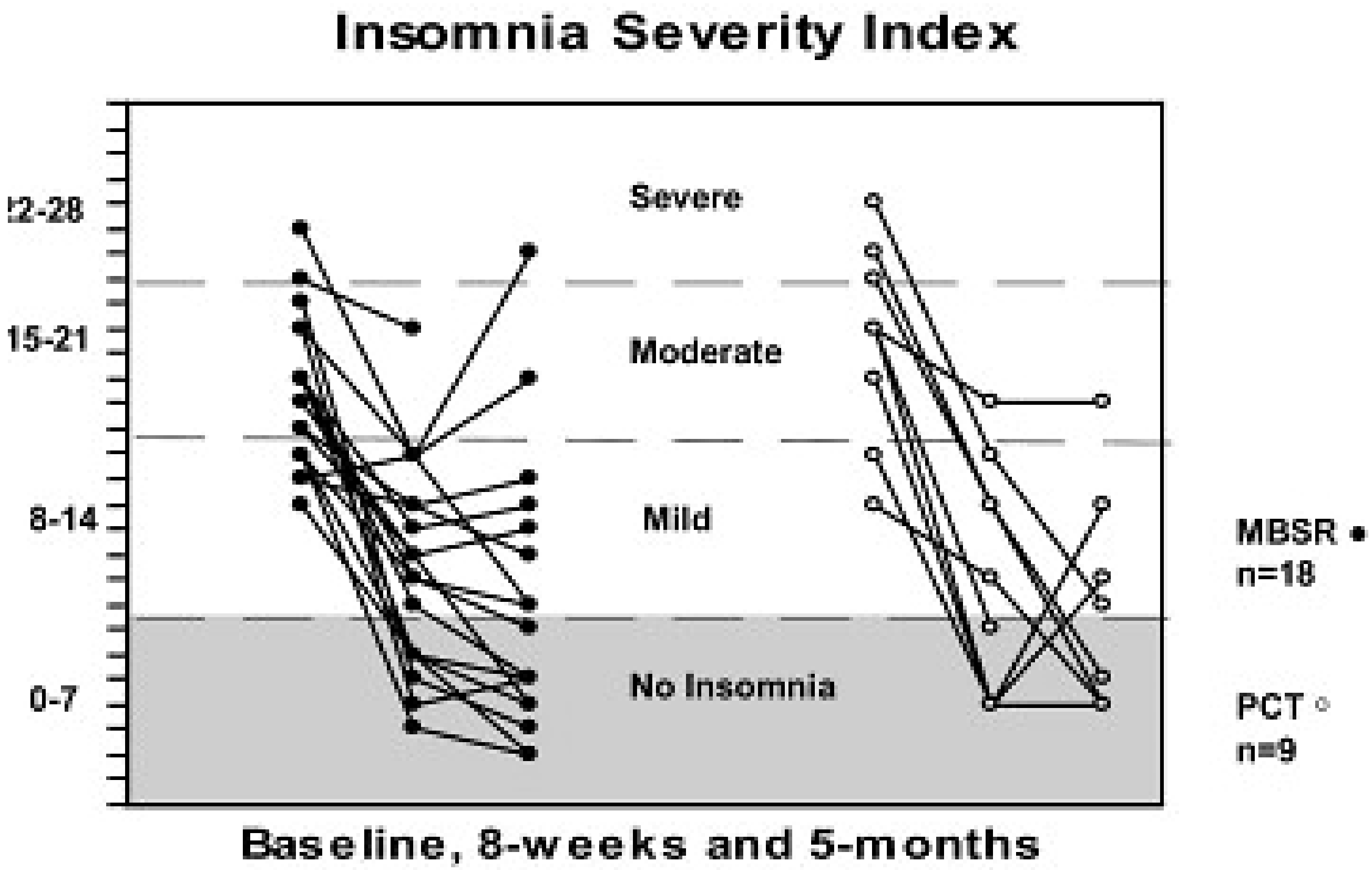


Figure 29. MBSR

(Gross et al., 2011)

Summary of Sleep

- Sleep is important for neural healing
- Poor sleep may predict worse outcomes at one year (and beyond)
- Sleep is important for neural "cleansing" with the "glymphatic" system
  - May also explain chronic effects of injury even if acute effects minimal
- Current pharmacological interventions have negative consequences
- Lifestyle measures may be best for sleep treatments

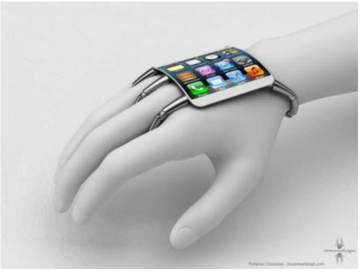
Conclusions

- Exercise has mixed results
  - Traditional exercise shows value in animal models
    - Equivalent robust benefits not demonstrated in clinical trials
  - Mind-body medicine with better promise and demand among patients

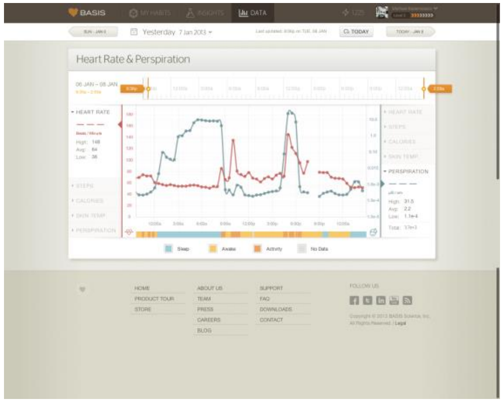
- Sleep is critical for good recovery
  - Good evaluation and treatments lacking
  - Role of mind-body medicine

Monitoring – Biowearables

www.fitbit.com



www.apple.com



www.mybasis.com

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Nutrition

Emerald Lin, MD

(Disclosure)

Nutrition: Overview

- **Sugar**
  - Free radicals, oxidative stress, inflammation,
  - Role of omega 3s
- Supplements
- Alcohol
- MREs
- Telomeres

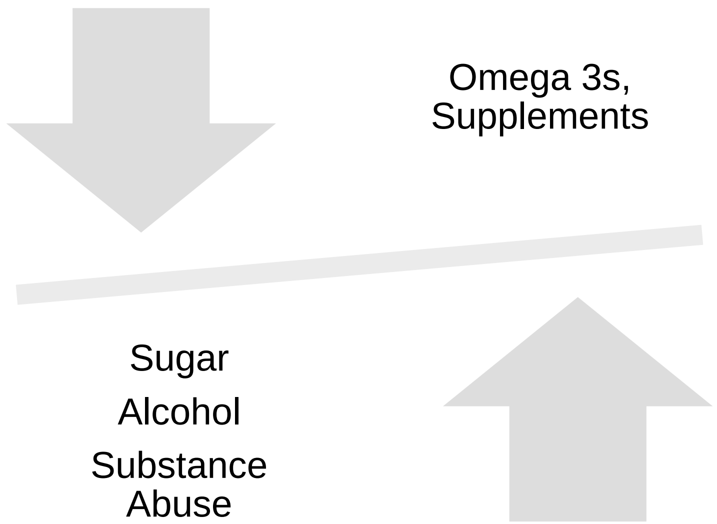


Figure 30. Nutrition Overview

(CDC, 2012)

Typical Consumption

- **2005-2008** CDC Data (Ogden) 50% of U.S. population consumes sugar drinks on any given day, and 25% consumes at least 200 kcal (more than one 12-oz can of cola).
  - Males: average of 178 kcal from sugar drinks on any given day, while females consume 103 kcal.

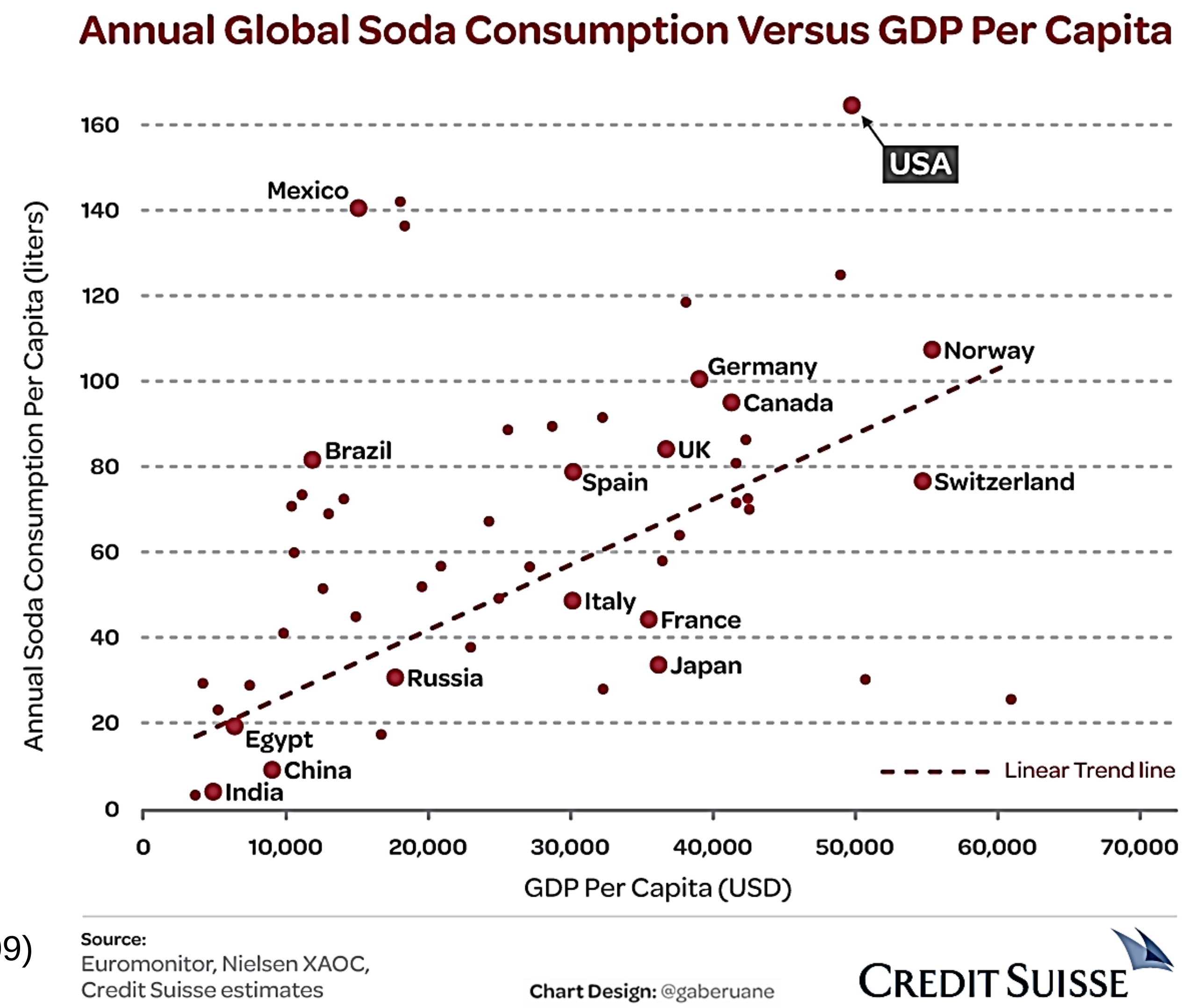
- **2009–2010** CDC: U.S. adults estimated average of 151 kcal/day of sugar sweetened beverages (SSB)
  - regular soda and fruit drinks leading sources

- **2012** Behavioral Risk Factor Surveillance System
  - 18 states surveyed, 26.3% of adults consumed regular soda or fruit drinks or both ≥1 times daily.

The world average daily intake of sugar and high-fructose corn syrup (HFCS) is now 70 grams (17 teaspoons). (Credit Suisse, 2013)

(CDC, 2012)

Annual Global Soda Consumption



(Euromonitor, 2009)

Figure 31. Soda Consumption

Sugar Content

Item	Grams of Sugar
Soda	2 chocolate bars (39g sugar)
Coffee/coffee based beverage	8.5 scoops ice cream (95g)
Energy drink	6 glazed donuts (62g)
“Healthy” juice	Same as soda
Sports/health drinks	Same as soda

(CDC, 2012)

Figure 32. Sugar Content

Typical Energy Drinks

Product	Per Serving: Size (fl oz)	Calories	Sugars (g)	Caffeine (mg)
AMP Energy (PepsiCo)	8	110	29	71
Red Bull Energy Drink	8.4	110	27	83
Monster Energy	8	100	27	92
Nestle Jamba	8.4	90	20	98
Arizona Energy	8	100	26	129
Full Throttle	8	220	58	210
NOS High Performance	16	220	52	224

Figure 33. Energy Drinks

(Consumer Reports, 2012)

Sugar and the Brain

- In 2012 Fernando Gomez-Pinilla & Rahul Agrawal conducted a research study that yielded the following results:
  - Animal study, compared two groups
    - Group 1 – Fructose solution
    - Group 2 – Fructose solution plus omega 3 fatty acids (flaxseed oil and docosahexaenoic acid (DHA), essential for synaptic function
  - Results: Maze performance
    - Group 1 – Slower, decreased synaptic activity, insulin resistance
    - Group 2 – Much faster
  - Significance
    - Diet high in fructose can slow brain function→ decrease in memory and learning
    - Omega 3 fatty acids can help counteract this effect

Sugar and the Brain

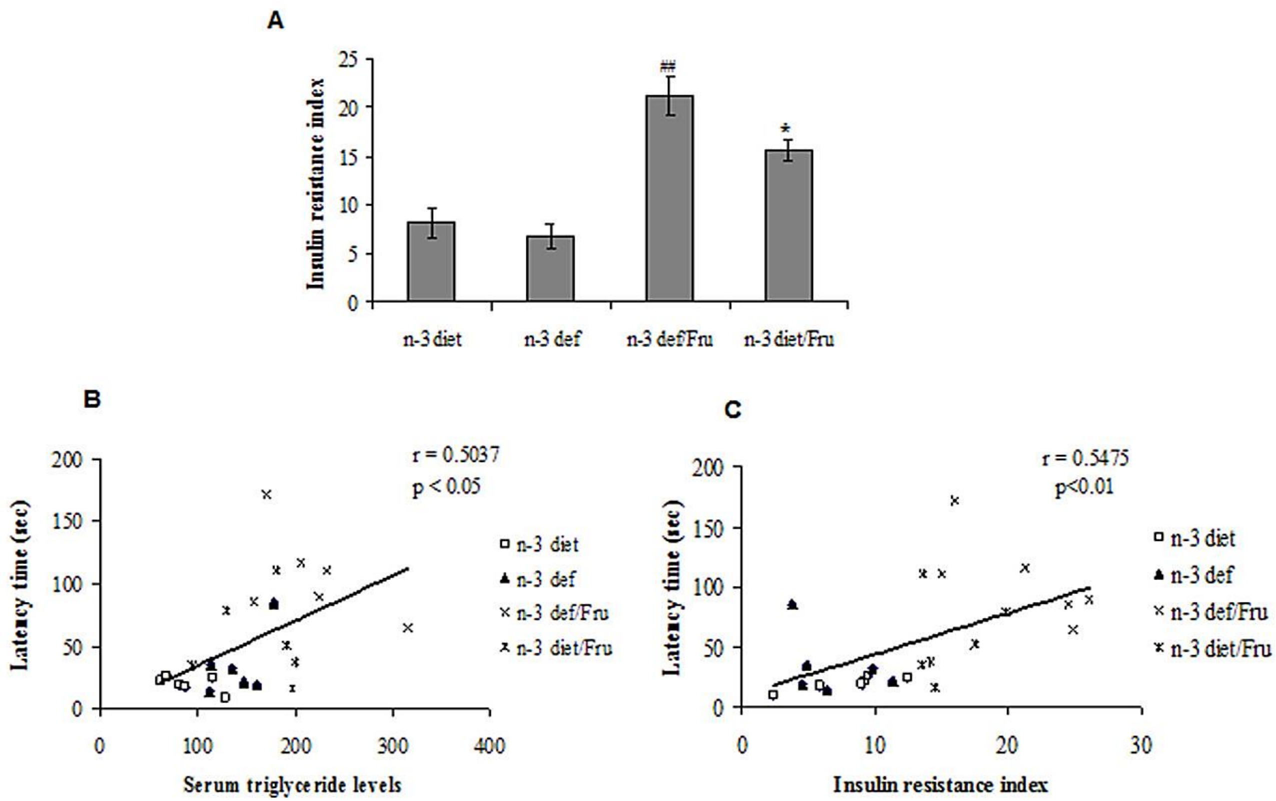


Figure 34. Metabolic Syndrome

(A) Insulin resistance index in groups subjected to n-3 and n-3 deficient diet with or without fructose water.

Correlation analysis: positive correlation between:

(B) Serum triglyceride levels and latency time

(C) Insulin resistance index and latency time on maze.

(Gomez-Pinilla & Agrawal, 2012)

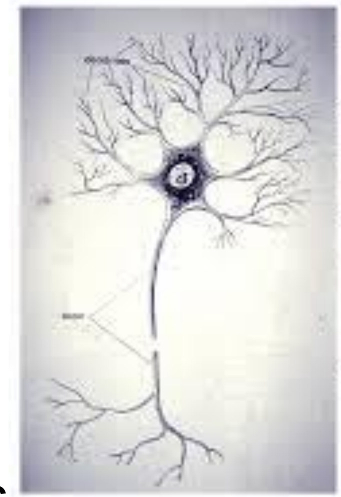
Diet and Brain Function

- Diet can affect energy metabolism and synaptic plasticity.
- Energy metabolism influences neuronal function, neuronal signaling, and synaptic plasticity.
  - Can affect and influence psychological health and therefore cognitive function.
- Oxidative stress promotes damage to phospholipids present in plasma membrane (including omega 3 fatty acid DHA), disrupting neuronal signaling.
  - Thus, dietary DHA seems crucial for supporting plasma membrane function, interneuronal signaling, and cognition.
- Dual action of brain-derived neurotrophic factor in neuronal metabolism and synaptic plasticity are crucial for activating signaling cascades.

(Gomez-Pinilla et al., 2012)

Omega 3s

- Content in standard foods
- Potential benefits
  - Beneficial neuroplastic effects
  - Support synaptic connections
  - Can counteract high sugar diet
  - Cellular level: Reduce free radicals and inflammation
  - Maintain insulin: Sugar balance
- Omega 3 fatty acids and polyphenols
  - Crucial role maintaining plasma membrane, important for neuronal signaling



Omega 3 Fatty Acid and Recovery

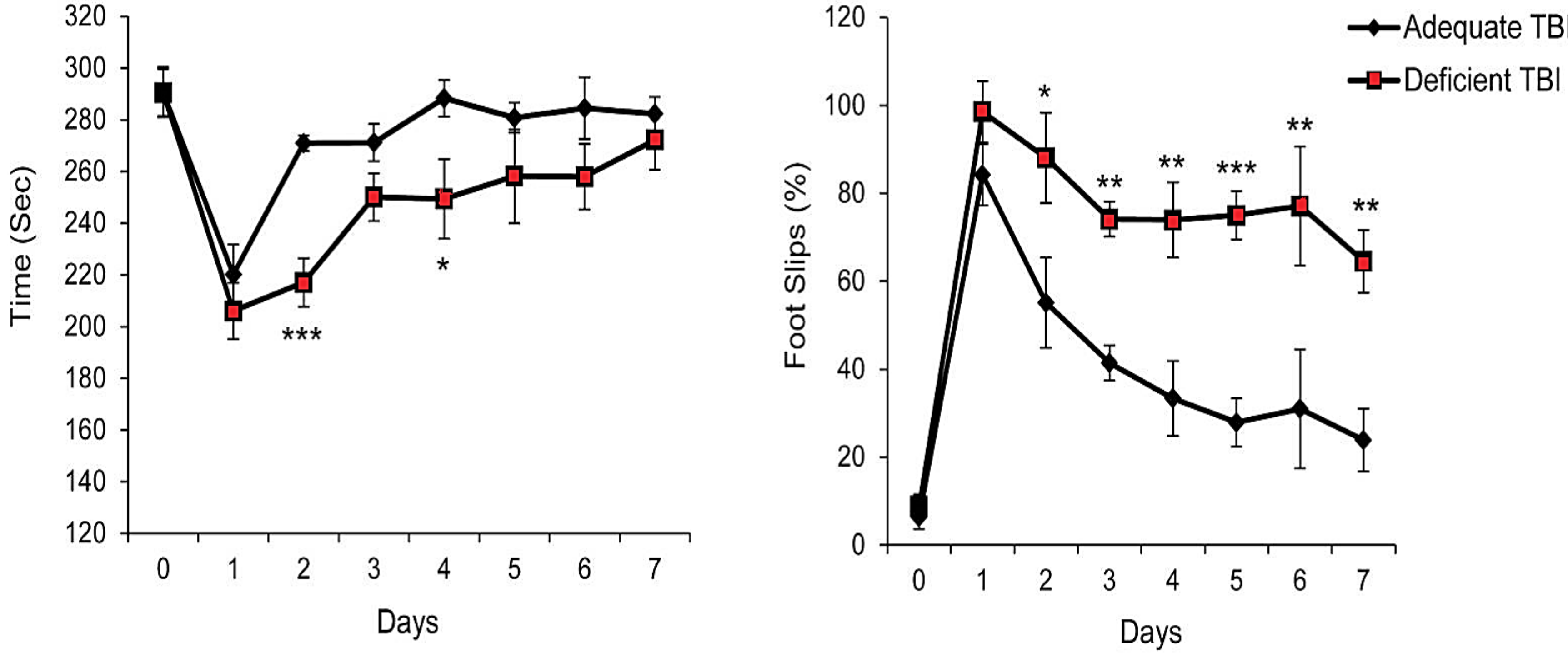


Figure 35. Omega 3 fatty acid deficiency impairs recovery from TBI-induced motor deficits.
(A) Slower recovery from TBI in Deficient TBI as compared to the Adequate TBI mice
(B) Greater hindlimb footslips in DHA Deficient mice as compared to respective Adequate controls

(Desai, Kevala & Kim, 2014)

Omega 3s: Clinical

- Human study
- Preloading
- Use as treatment?

(Hasadsri et al., 2013)

Omega 3 Fatty Acids

- Case report: Severe TBI status post motor vehicle accident
- Intervention: 15 mL twice a day (30 mL/d) of 9756 mg eicosapentaenoic acid, 6756 mg DHA, and 19212 mg total n-3FA daily via percutaneous endoscopic gastrostomy
- Progressed from Rancho Los Amigos Cognitive Scale (RLS) 1, Glasgow Coma Scale 3 to RLS 3 (Day 21), given rehabilitation, then three months later, completed high school diploma
- Two years later RLS 8
- Suggests that benefits may be possible from aggressively adding substantial amounts of n-3FA to optimize nutritional foundation of severe TBI patients.

(Lewis, Ghassemi, & Hibbeln, 2013)

Nutrition: Overview

- Sugar
  - Free radicals, oxidative stress, inflammation
  - Role of omega 3s
- **Supplements**
- Alcohol
- MREs
- Telomeres

Supplements: Creatine

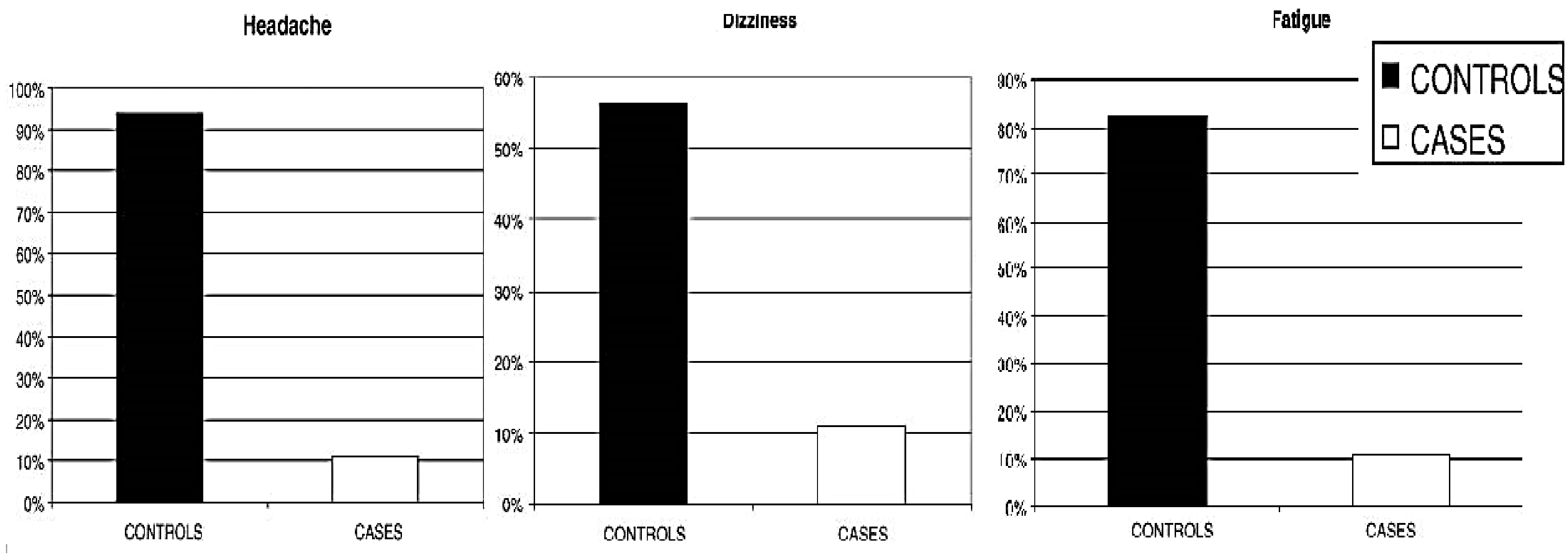


Figure 36. 39 subjects ages 1-18 years, given creatine:

- Subjects with TBI improved results in duration of post traumatic amnesia (PTA), duration of intubation, intensive care unit stay.
- Significant improvement headache ($p < 0.001$), dizziness ($p = 0.005$) and fatigue ($p < 0.001$), aspects in all patients.

(Sakellaris et al., 2008)

Supplements: Branched-chain Amino Acid (BCAA)

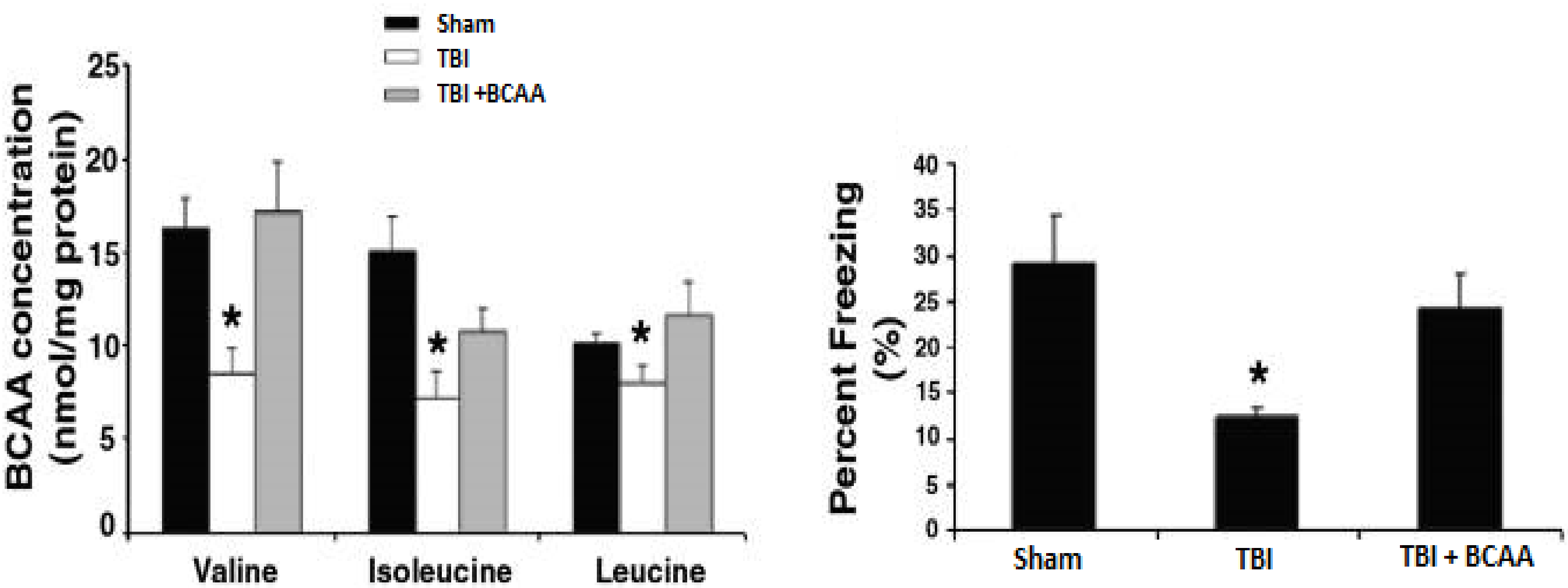


Figure 37. Supplements

- Consumption of 100 mM each of leucine, isoleucine, and valine for 5 days restored hippocampal BCAA levels.
- Contextual fear conditioning tests - significant cognitive impairment ($P < 0.05$) after TBI.
  - Completely reversed by BCAA treatment.
- Dietary BCAAs returned hippocampal BCAA concentrations to normal, reversed injury-induced shifts in net synaptic efficacy, and restored cognitive performance after concussive brain injury.

(Cole et al., 2009)

Supplements: Curcumin

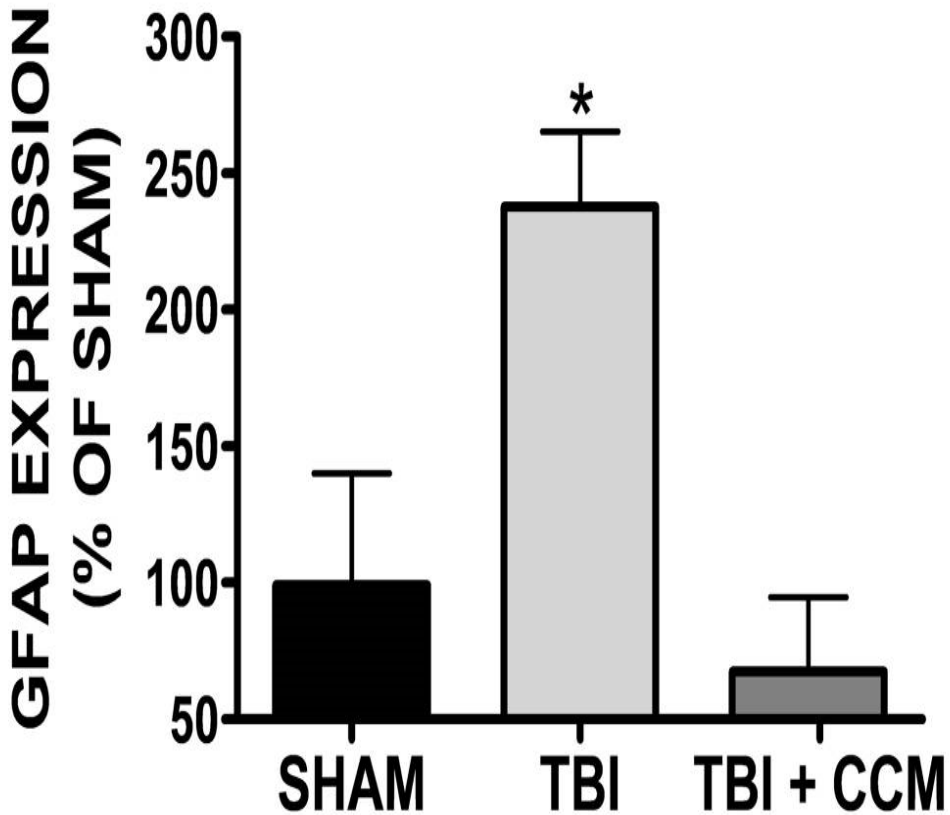


Figure 38. Curcumin

- Effect of curcumin administered 30 minutes prior to injury on glial fibrillary acidic protein (GFAP), a reactive astrocyte marker] expression in cortex at 24 hours post-TBI
- Study suggests clinically-achievable concentrations of curcumin reduce glial activation and cerebral edema following neurotrauma.

(Laird et al., 2011)

Nutrition: Overview

- Sugar
  - Free radicals, oxidative stress, inflammation
  - Role of omega 3s
- Supplements
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- MREs
- Telomeres

Alcohol

Hayes et al., 2012

- Abstinent alcoholics (31) compared to healthy controls (34)
- Results: Abstinent alcoholics with reduced whole brain thickness compared to controls
  - Cortical thickness decreased bilaterally in superior frontal, precentral, post central, middle frontal, middle/superior temporal, middle temporal and lateral occipital cortical regions
  - Most severe in frontal and temporal regions

Fortier et al., 2014

- Alcohol damages white matter tracts, thereby affecting executive function
- Compared 31 abstinent alcoholics with 20 controls
- Results: Widespread bilateral decrease in fractional anisotropy in multiple frontal, temporal, parietal and cerebellar white matter tracts
- FA in inferior frontal gyrus (decision making, inhibition) correlated with severity of alcohol
- Frontostriatal circuits mediating inhibitory control affected

Nutrition: Overview

- Sugar
  - Free radicals, oxidative stress, inflammation
  - Role of omega 3s
- Supplements
- Alcohol
- **MREs**
- Telomeres

PHOTO REFERENCE: NATICK PAM 30-25, August 2012

In the Field: MREs

ASSAULT RATIONS: First Strike Ration® (FSR™)

Photo courtesy of: NSRDEC US Army Natick Soldier Research

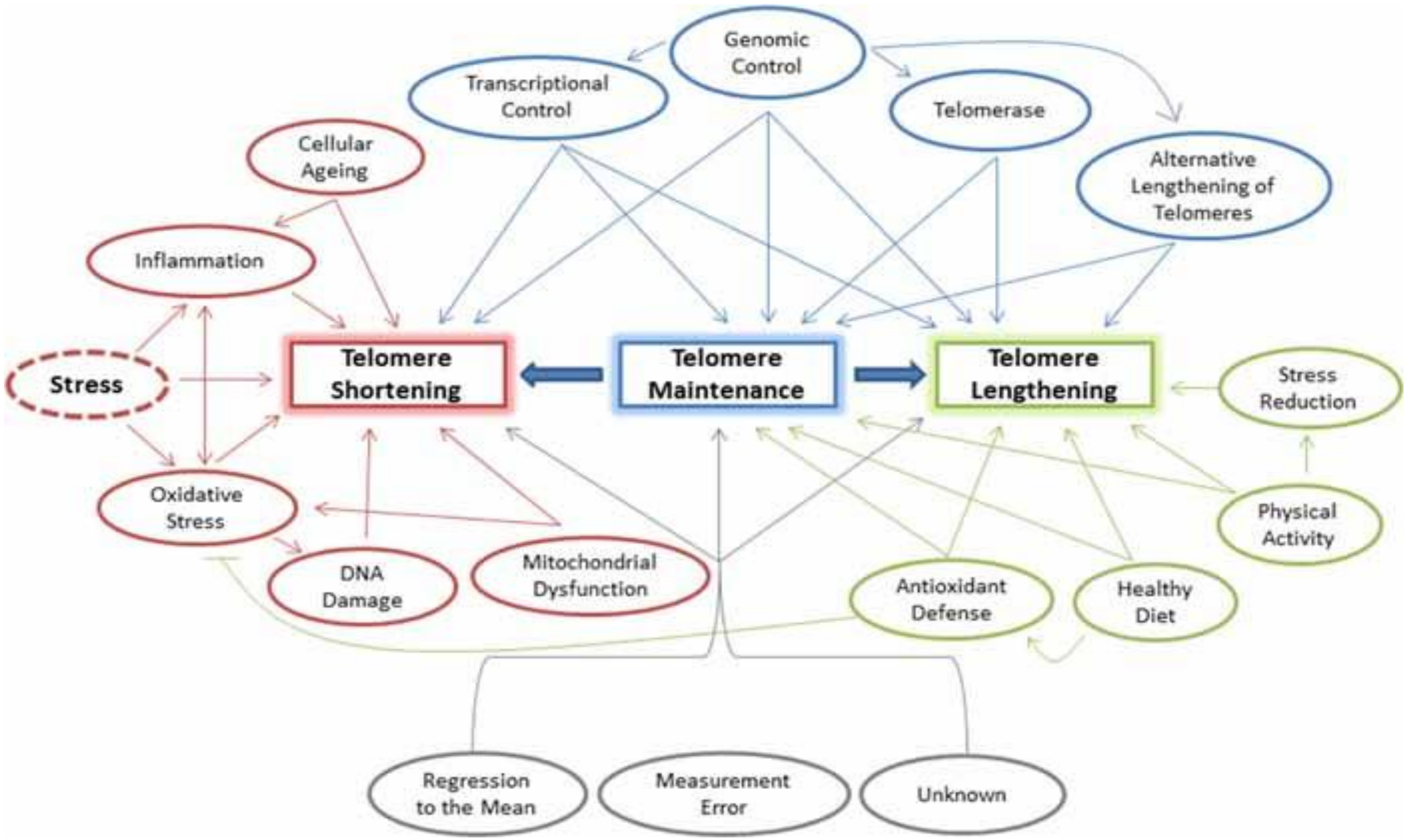
- Omega 3 content important
  - Usually low in standard MREs
- Research ongoing to create military rations that are portable, durable, nutritious, and pleasing to taste buds

DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury

Nutrition: Overview

- Sugar
  - Free radicals, oxidative stress, inflammation
  - Role of omega 3s
- Supplements
- Alcohol
- MREs
- **Telomeres**

Telomeres



(Shalev, 2012)

Figure 39. Telomeres

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Telomere Length and Diet

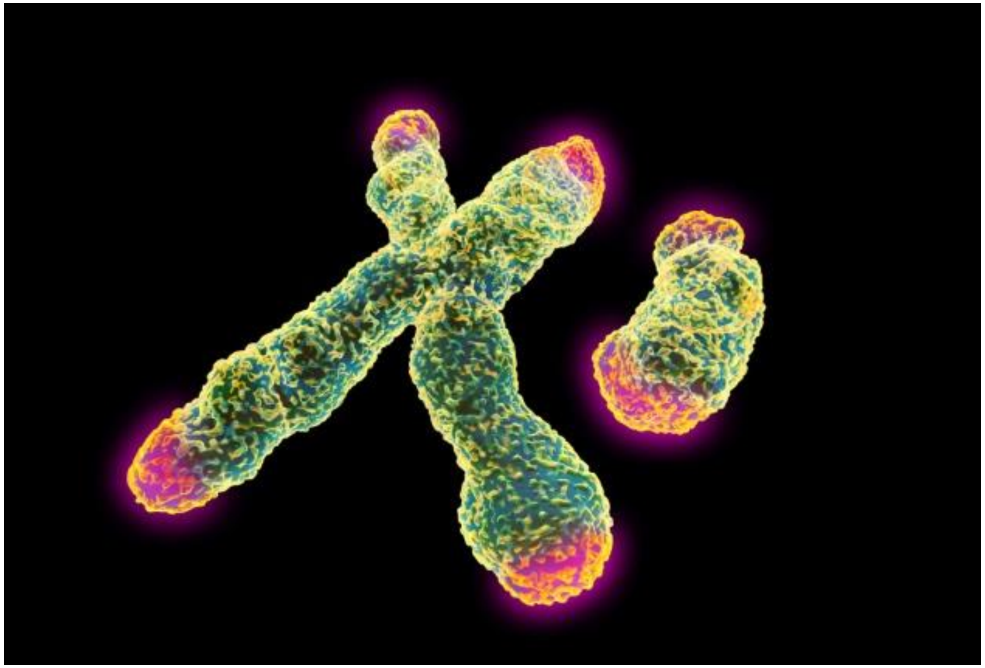


Figure 40. Mediterranean diet and telomere length in Nurses' Health Study: Population-based cohort study

(Crous-Bou, 2014)

Telomere Length and Diet

- Design
  - Prospective cohort study, N = 121, 700 female registered nurses in 11 U.S. states, aged 30-55 years at enrollment
  - 61 item semi-quantitative food frequency questionnaire, repeated every ~four years to assess diet in previous year
  - Alternate Mediterranean Diet (AMD) score
    - Vegetables (excluding potatoes), fruits, nuts, whole grains, legumes, fish, monounsaturated: saturated fatty acid ratio, red and processed meats, and moderate alcohol intake

(Crous-Bou, 2014)

Telomere Length and Diet

- Results: Telomere length measurement: Statistically significant inverse correlation between age at blood draw and telomere length:
  - Younger women – longer telomeres ($P<0.001$)

- Association between adherence to Mediterranean diet and telomere length:
  - Higher AMD scores associated with higher age adjusted mean leukocyte telomere length z scores (P for trend=0.02).
  - Association statistically significant even with inclusion of BMI, pack years of smoking, physical activity, and total caloric intake in models
  - Multivariable adjusted least squares mean leukocyte telomere length z score across AMD groups (≤2, 3, 4, 5, ≥6) was −0.038, −0.049, −0.010, 0.039, and 0.072 (P for trend=0.004)

(Crous-Bou, 2014)

Telomere Length and Diet

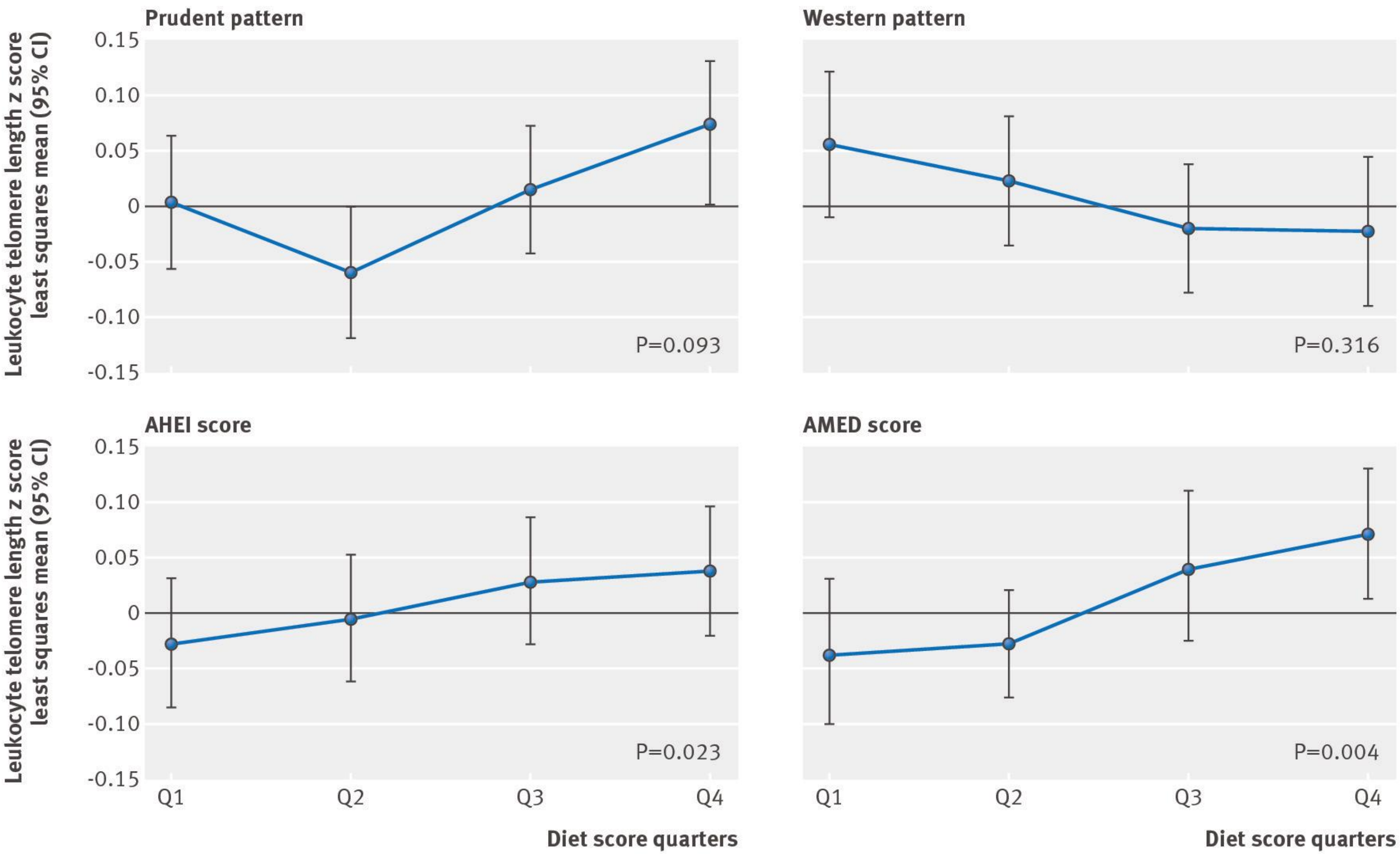


Figure 41. Telomere

(Crous-Bou, 2014)

Nutrition

- Cross sectional study, N = 4676 women from Nurses' Health Study

- Results: Greater adherence to Mediterranean diet significantly associated with longer leukocyte telomere length.

- Difference in telomere length for each one point change in Alternate Mediterranean Diet score corresponded on average to 1.5 years of aging.

(Crous-Bou, 2014)

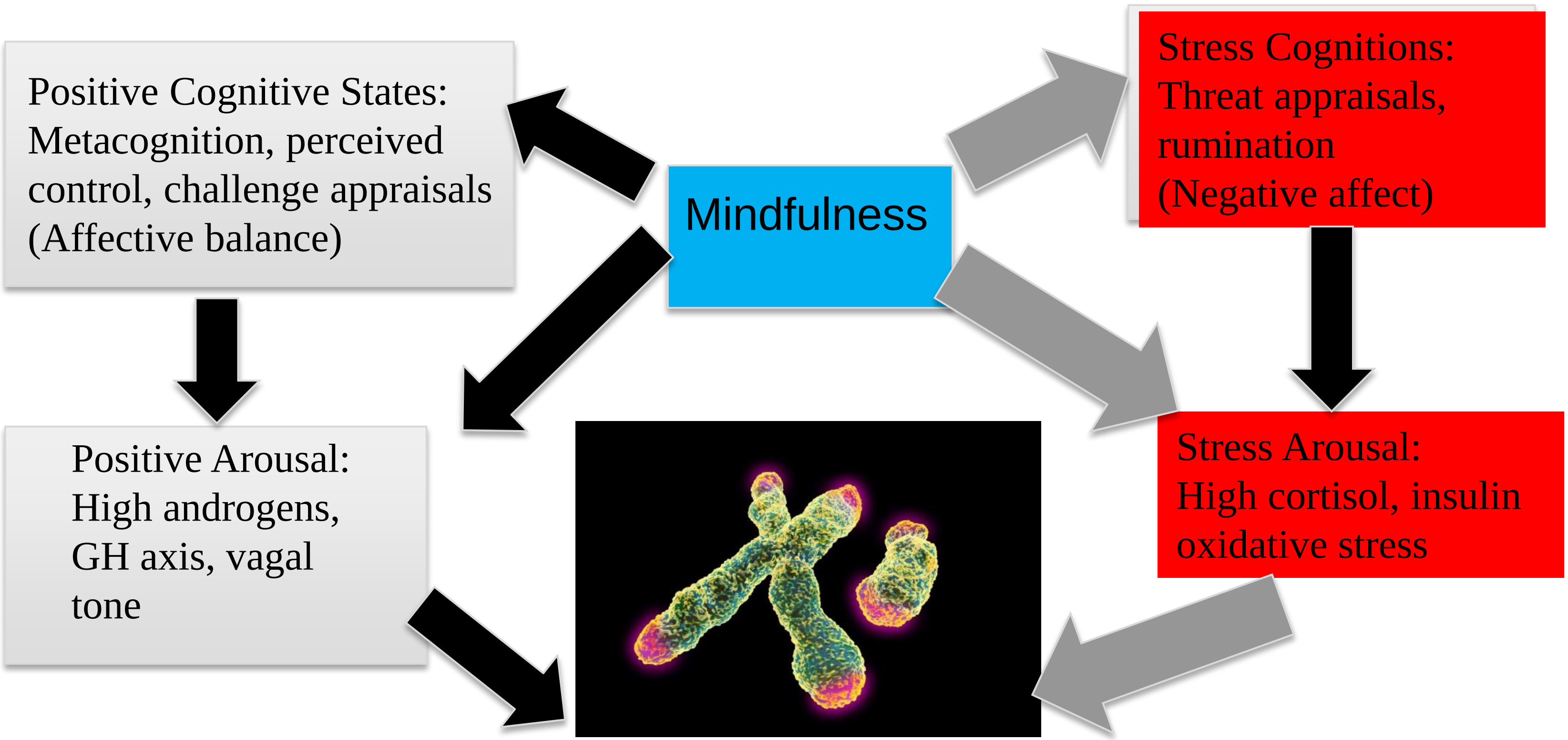
Nutrition

- A three point change in Alternate Mediterranean Diet score would correspond to on average 4.5 years of aging.
  - Comparable to difference observed when comparing smokers with non-smokers (4.6 years)
    - 35 highly active women with less active women (4.4 years)
    - 16 women with high phobic anxiety scores with women with low phobic anxiety (6 years)

(Crous-Bou, 2014)

Mindfulness and Telomeres

Can Meditation Slow Rate of Cellular Aging?
Cognitive Stress, Mindfulness, and Telomeres



(Epel, Daubenmier, Moskowitz, Folkman, & Blackburn, 2009)

Figure 42. Cellular Aging

Sugar and Athletes

Dwight Howard

- High blood glucose level: *528*gm of sugar daily
  - ≈ 24 chocolate bars
- Changed diet: Increased healthy fats/oils and decreased processed foods
- Blood glucose levels decreased 80%
- Cholesterol profile improved
- Endurance and performance improved

Nutrition: Summary and Recommendations

- Basic science
  - Cellular metabolism and synaptic connections leading to cognitive and psychological function can be affected by
    - Free radical formation and oxidative stress
    - Dietary content
    - Damage is likely partially reversible with omega 3 and antioxidants and possibly protective of future injury
- Animal studies show supplements can have positive results
- Human studies
  - Retrospective cohort positive correlations

Nutrition: Summary and Recommendations

- Lifestyle changes and incorporation with exercise and sleep are important
- Needs more clinical research
  - Extrapolate from animal studies
  - Evaluate effects of dosing and duration
  - Evaluate effects of pre- and post- event – does preloading help recovery?
  - Deployed setting
  - Different populations and prospective randomized controlled trials

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