

Looking forward: Long-term Perspectives on Recovery, Risk-Reduction, and Research

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• **Chronic Symptom Management
(Recovery)**



• **Aging with a Vulnerable Brain
(Risk-Reduction)**



• **Emerging Technologies (Research)**

Mounting Evidence for a Lifetime of Change

- “The propensity for experience dependent plasticity throughout life can be more or less potentiated by diverse factors including individual genetic, cellular, molecular, and environmental differences. **These findings have lead us to understand that the rules that regulate plasticity are not only more intrinsically variable than were previously thought, but can also be shaped in mature brains.**”
- “As with many medical and health related fields where personalized and precision medicine are increasingly becoming mainstream, **neurotherapeutic interventions targeting mechanisms of plasticity and cognition should also follow an individualized approach by harnessing individual differences to best utilize the brain’s innate capacity to change.**”
 - See Patrice Voss, Maryse E. Thomas, J. Miguel Cisneros-Franco, & Étienne de Villers-Sidani. (2017). Dynamic Brains and the Changing Rules of Neuroplasticity: Implications for Learning and Recovery. *Frontiers in Psychology, 8*.

An aerial photograph showing a paved road with a yellow center line running through a dry, yellowish-brown landscape. To the right of the road, a series of irrigation canals branch out, creating a complex network of water channels. The terrain is flat and appears to be a semi-arid region. The sky is blue with some light clouds.

A Trio of Challenges



Post-Traumatic Headaches (PTH or PTHA)

- **Chronic** post-traumatic headache=12+ months after injury
 - Rates reach up to 95%
 - 71% after moderate/severe TBI and 91% after mild TBI (mTBI) at 1 year (Lucas, 2015)
 - 61% daily headaches, 39% migraine (26% had new onset of a migraine-like disorder) and 9% tension-type headaches (Kuczynski, Crawford, Bodell, Dewey, & Barlow, 2013)

Why and How

- Cervicogenic strain
- Neuro-inflammation
 - *“Inflammatory-evoked enhancement of peripheral cranial nociception, rather than changes in supraspinal pain mechanisms play a role in the initial emergence of CPTH” (Benromano, Defrin, Ahn, Zhao, Pick & Levy, 2014)*
- Damaged pain pathways?
 - *“Damage to pain modulatory systems along with chronic cranial sensitization underlies the development of CPTHA” (Defrin, Riabinin, Feingold, Schreiber, & Chaim, 2015)*
- Cardiovascular compensation
 - Increase in peripheral artery stiffness (decline of stroke volume) during the transition from rest to activity (La Fontaine, Toda, Testa, Hill-Lombardi, 2016)
- Pre-injury headaches
- Psychology
 - Conditioned pain avoidance, stress



Treatment

- There are no evidence-based treatment guidelines for PTH management (Kacperski & Todd, 2016)
- Manual therapies (e.g. neck strengthening, osteopathic manipulation)
- Cognitive Behavioral Therapy (CBT), Acceptance and Commitment Therapy (ACT)
- Biofeedback
- Aerobic exercise
 - “Active rehabilitation” (Gagnon, Friedman, & Iverson, 2016)
- Medication
 - Antidepressant, antiepileptics, triptans, OTC options
- Invasive techniques: e.g., Occipital Nerve Surgery, botox, nerve blocks, etc.
 - See: Tassorelli, C., Tramontano, M., Berlangieri, M., Schweiger, V., D’ippolito, M., Palmerini, V., et al. (2017). Assessing and treating primary headaches and cranio-facial pain in patients undergoing rehabilitation for neurological diseases. *The Journal of Headache and Pain*, 18, 1-18.

Anxiety

- Up to 50% of people report **clinically significant** anxiety after TBI (Osborn, Mathias, & Fairweather-Schmidt, 2015)
 - Increased rates of post-traumatic stress disorder, generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, specific phobia, and social anxiety disorder (Sasha, Sutherland, Syb, Mainland, & Ornstein, 2015)
- Suicidal ideation reported by more than 40% of persons after TBI
 - 4 times more likely to die “intentionally” (Kalle, Jussi, Sami, Seppo, & Matti, 2015)
 - See also Dreer, Tang, Nakase-Richardson, Pugh, Cox, Bailey, . . . Brenner. (2018). **Suicide and traumatic brain injury: A review by clinical researchers from the National Institute for Disability and Independent Living Rehabilitation Research (NIDILRR) and Veterans Health Administration Traumatic Brain Injury Model Systems. *Current Opinion in Psychology*, 22, 73-78.**
- Anxiety is related to suffering, poor psychosocial and occupational functioning, benzodiazapene abuse and increased and health care usage (Haller, Cramer, Lauche, Gass, & Dobos, 2014)
- Anxiety has a greater impact than cognitive impairment on social and occupational functioning following brain injury (Bertisch et al., 2013)

How and Why

- White matter abnormalities
 - “Overall, anxiety was associated with more restricted diffusion and greater anisotropy in regions of crossing/diverging fibers” (Davenport, Lim, & Sponheim, 2015)
- Pituitary dysfunction
 - Growth hormone (GH) is the most common hormone lost after TBI, followed by ACTH, gonadotropins (FSH and LH), and TSH (Tanriverdi, Schneider, Aimaretti, Masel, Casanueva, & Kelestimur, 2015)
 - Growth hormone deficiency has adverse effects on executive abilities and mood=anxiety (Ioachimescu, Hampstead, Moore, Burgess, & Phillips, 2015)
 - See also: Ewing-Cobbs, Prasad, Cox, Granger, Duque, & Swank. (2017). Altered stress system reactivity after pediatric injury: Relation with post-traumatic stress symptoms. *Psychoneuroendocrinology*, 84, 66-75.
- Psychology
 - Expectancies, role changes, subjective vs. objective deficits, relationship changes
 - Premorbid psychopathology/existing vulnerability

Treatment

- Improving caregiver psychological health (Raj et al., 2014)
- Psychobiotics
 - Microbiota-gut-brain axis (Zhou & Foster, 2015)
 - "The current narrative suggests that certain neuropsychiatric disorders might be treated by targeting the microbiota either by microbiota transplantation, antibiotics or psychobiotics." (February, 2016)
- CBT
 - Thought stopping
 - Relaxation techniques

Progressive Muscle Relaxation

Our bodies respond automatically to stressful situations thoughts by becoming tense. The opposite relationship also works: a good way of relaxing the mind is to deliberately relax the body.

In a progressive muscle relaxation each muscle group is tensed in turn, and the tension is then released. This relaxes the muscles and allows you to notice the contrast between tension and relaxation.

Relaxaton should be enjoyable so if any part of the exercise is too difficult skip it for the moment. If you have any injuries you may wish to leave out that part of the exercise.

Preparation

Lie down flat on your back, on a firm bed, a couch, or on the floor. Support your head and neck with a pillow or cushion. Alternativety sit in a comfortable chair with your head well-supported. Close your eyes if you are comfortable doing so.

Instructions

Focus your attention on different parts of your body in sequence. Go through the sequence three times:

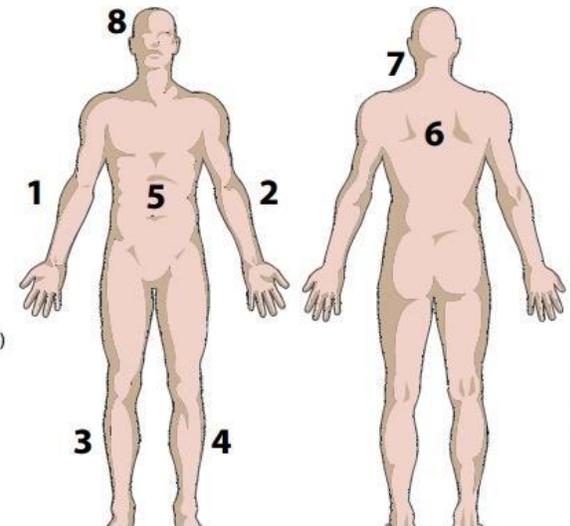
1) *Tense & release:* Tense that body part, hold it for a few moments, then relax

2) *Lightly tense & release:* Tense that body part with just enough tension to notice, then relax

3) *Release only:* Just pay attention to each muscle group and decide to relax it

Recommended sequence

- 1 Right hand & arm
(clench the fist & tighten the muscles in the arm)
- 2 Left hand & arm
- 3 Right leg
(tense the leg, lifting the knee slightly)
- 4 Left leg
- 5 Stomach & chest
- 6 Back muscles
(pull the shoulders back slightly)
- 7 Neck & throat
(push the head back slightly into the pillow/surface)
- 8 Face
(scrunch up the muscles in your face)





Sleep

- Up to 80% of people report sleep problems after injury (Mathias & Alvaro, 2012)
 - 85% report daytime sleepiness and changes in their sleep-wake cycle
 - See also Imbach, L., Buchele, F., Valko, P., Li, T., Maric, A., Stover, J., . . . Baumann, C. (2016). Sleep-wake disorders persist 18 months after traumatic brain injury but remain underrecognized. *Neurology*, 86(21), 1945-1949.
- The most common disturbances are insomnia, pleisomnia, increased sleep need, and excessive daytime sleepiness
 - Also sleep apnea, narcolepsy, periodic limb movement disorder, and parasomnias (related to brain injury; Ouellet, Beaulieu-Bonneau, & Morin, 2015; Viola-Saltzman & Musleh, 2016)
- *“Poor long-term recovery may be better understood when fatigability is taken into consideration.”* (Maruta, Spielman, Yarusi, Wang, Silver, & Ghajar, 2016)

Why and How

- Complex interplay between pathophysiological processes (structural, neuroelectrical, or neurochemical levels), psychological factors (e.g., sleep-related habits or TBI-related psychopathology), environmental factors (e.g., noises, light, or pain), and social factors (e.g., social roles related to work or family)
- Decreased secretion of hypocretin
 - A neuropeptide involved in sleep-wake regulation (**Baumann et al., 2015; Jaffee, Winter, Jones, & Ling, 2015**)
- Existing vulnerability



Treatment

- Diagnosis and specific treatment (Viola-Saltzman & Musleh, 2016)
 - See next slide (from Viola-Saltzman & Watson, 2012)
- Strategic napping
- Blue light therapy (Sinclair, Ponsford, Taffe, Lockley & Rajaratnam, 2014; Vanuk, et al., 2018)
- Melatonin
 - Antioxidant, anti-inflammatory, neuroprotective
 - See Lin, Chao, Chao, Honglu, Li, Zheng, Xu, Xiupeng, Liu, Yinlong, Hou, Lijun, . . . Ji, Jing. (2016). Melatonin attenuates traumatic brain injury-induced inflammation: A possible role for mitophagy. *Journal of Pineal Research*, 61(2), 177-186 and Grima, N., Ponsford, J., St. Hilaire, M., Mansfield, D., & Rajaratnam, S. (2016). Circadian Melatonin Rhythm Following Traumatic Brain Injury. *Neurorehabilitation and Neural Repair*, 30(10), 972-977.
- CBT-I
 - See Sleep Hygiene worksheet



Insomnia

Psychological/
behavioral
therapies

Sleep aids/
hypnotics

Accupuncture/
mindfulness
meditation

Hypersomnia/ narcolepsy

Stimulant
medications

Strategic caffeine
and naps

Sleep apnea

CPAP or related
device

Weight loss

Mandibular
advancement
device

Surgical
procedures

Nasal expiratory
positive airway
pressure

Guidelines For Better Sleep

Sleeping well is a habit that you can learn! Small changes can have big effects. Start today by following these rules:



Take care of your body

- Do not drink caffeine: no tea, coffee, or coca-cola after 4 o'clock
- Do not eat a big or spicy meal late in the evening
- Do not go to bed hungry
- Avoid alcohol as it interferes with sleep

Physical exercise, such as a brisk walk, in the late afternoon can help to make your body tired and help you to sleep. Try to do some exercise every day.

Sleep only at night-time and do not have day-time naps, no matter how tired you feel. Naps keep the problem going by making it harder for you to get to sleep the next night.

Having a regular bedtime routine teaches your body when it's time to go to sleep.

- Have a soothing drink like camomile tea or a milky drink
- Have a bath, or a routine of washing your face and brushing your teeth
- Go to bed at same time each night
- When in bed think of nice things (e.g. think of 5 nice things that happened that day – they might be big or small, such as a nice conversation, seeing the sunshine, or hearing nice music on the radio)
- Do a relaxed breathing exercise (one hand on stomach the other on your chest, deliberately slow your breathing, breathe deeply in your stomach instead of high in your chest)
- Try and wake up the same time every day, even if this is tiring to begin with

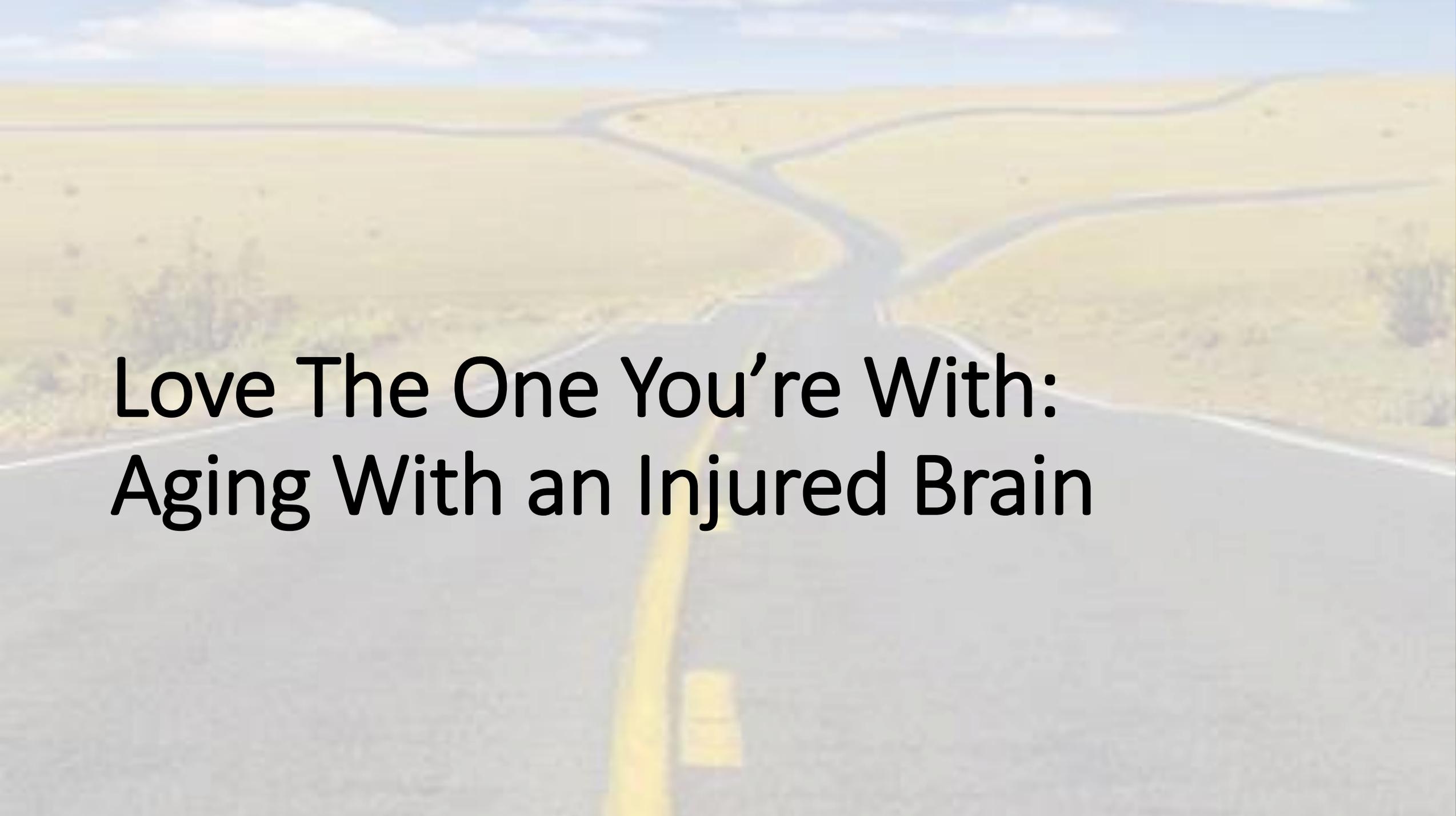
Coping with bad dreams can be difficult. Some people don't like relaxation before going to sleep, or are scared of letting go. If that is you, try these preparation techniques instead:

- Prepare yourself in case you have bad dreams by thinking of a bad dream then think of a different ending for it. Practice this new ending many times before going to sleep.
- Before going to sleep prepare to re-orient yourself when you wake from a bad dream.
- Remind yourself that you are at home, that you are safe. Imagine your street, buses, local shops.
- Put a damp towel or a bowl of water by the bed to splash your face, place a special object by the bed, such as a photograph, or a small soft toy.
- Practice imagining yourself waking up from a bad dream and reorienting yourself to the present, to safety by splashing your face, touching special object, having a bottle of rose or lavender essential oil to sniff, going to window to see surroundings.
- When you wake up from a bad dream- move your body if you can and reorient yourself immediately (touching an object, wetting face, going to the window, talk to yourself in a reassuring way)

Make your bedroom a pleasant place to be

- Get a nightlight
- Keep it clean and tidy
- Introduce pleasant smells such as a drop of lavender oil onto the pillow
- Get extra pillows
- Make sure that your home is safe e.g. doors locked, windows closed.

REMEMBER: Bed is for sleeping, so if you cannot sleep after 30 minutes, get up and do another activity elsewhere such as reading or listening to music (try and avoid TV as it can wake you up). After 15 minutes return to bed and try to sleep again. If you still can't sleep after 30 minutes get up again. Repeat this routine as many times as necessary and only use your bed for sleeping in.

An aerial photograph of a winding asphalt road through a dry, hilly landscape. The terrain is yellowish-brown with sparse vegetation. The road curves through the hills, and a yellow center line is visible in the foreground. The sky is blue with some light clouds.

Love The One You're With: Aging With an Injured Brain

Consume Fatty Acids

- Omega-3 polyunsaturated fatty acids (n-3 PUFA) improve cognition, provide neuroprotection/neurorestoration), reduce neuroinflammation and influence neuronal function
 - See Kerdiles, Layé, & Calon (2017). Omega-3 polyunsaturated fatty acids and brain health: Preclinical evidence for the prevention of neurodegenerative diseases. *Trends in Food Science & Technology*
- Framingham Heart Study and Women's Health Initiative Memory Study
 - A higher omega-3 index was correlated with larger total normal brain volume and hippocampal volume in postmenopausal women
- Eat fish not tablets
 - See Fish Oil Contaminated with Persistent Organic Pollutants Reduces Antioxidant Capacity and Induces Oxidative Stress without Affecting Its Capacity to Lower Lipid Concentrations and Systemic Inflammation in Rats *Journal of Nutrition* 2015

Play Music

- Engagement in musical activity offsets age-related decline in cognitive skills
 - See **The Effect of Music Therapy on Cognitive Functioning Among Older Adults: A Systematic Review and Meta-Analysis** *Journal of the American Medical Directors Association* **2015** and **Musical Training as a Framework for Brain Plasticity: Behavior, Function, and Structure** *Neuron* **2012** and **Amad, A., Seidman, J., Draper, S., Bruchhage, M., Lowry, R., Wheeler, J., . . . Smith, M. (2017). Motor Learning Induces Plasticity in the Resting Brain—Drumming Up a Connection. *Cerebral Cortex*, 27(3), 2010-2021** and **Scholz, D., Rhode, S., Großbach, M., Rollnik, J., & Altenmüller, E. (2015). Moving with music for stroke rehabilitation: A sonification feasibility study. *Annals of the New York Academy of Sciences*, 13371(1), 69-76.**
- www.swallowhillmusic.org

See a Doctor

- Bloodwork=Endocrine function
 - Estradiol=neuroprotective
 - **Neuroprotective actions of estradiol revisited. *Trends in Endocrinology & Metabolism 2011***
 - Testosterone=neuroprotective
 - **Neuroprotective role of testosterone in the nervous system. *Pharmacology 2004***
 - Thyroid hormones=promotes neurogenesis
 - **Modulation of adult hippocampal neurogenesis by thyroid hormones: implications in depressive-like behavior. *Molecular Psychiatry 2006***
- Candidate for NSAIDs? (ADVIL)
 - Previous studies have suggested that people who take ibuprofen long-term had a lower risk of developing dementing disease
 - See also **Morgan A Clond, Bong-Seop Lee, Jeffrey J Yu, Matthew B Singer, Takayuki Amano, Alexander W Lamb, . . . John S Yu. (n.d.). Reactive oxygen species-activated nanoprodru of Ibuprofen for targeting traumatic brain injury in mice. *PLoS ONE, 8(4)*, E61819 and Guo, Jing-Wen, Guan, Pei-Pei, Ding, Wei-Yan, Wang, Si-Ling, Huang, Xue-Shi, Wang, Zhan-You, & Wang, Pu. (2017). Erythrocyte membrane-encapsulated celecoxib improves the cognitive decline of Alzheimer's disease by concurrently inducing neurogenesis and reducing apoptosis in APP/PS1 transgenic mice. *Biomaterials, 145*, 106-127.**

Grab Some Dragons



- “Inflamm-aging”
- Probiotics, antioxidants (e.g. essential fatty acids, coenzyme Q10, and creatine), anti-inflammatory foods (e.g., curcumin)
 - See Westfall, S., Lomis, N., Kahouli, I., Dia, S., Singh, S., & Prakash, S. (2017). Microbiome, probiotics and neurodegenerative diseases: Deciphering the gut brain axis. *Cellular and Molecular Life Sciences*, 74(20), 3769-3787.
- Glutathione research with Craig Hospital (Linseman, Gerber & Gorgens)
- Red Dragon fruit

Get Moving



- Framingham Heart Study, Boston University School of Medicine
 - Those with lower fitness levels in midlife also had lower brain tissue levels in later life
- Aerobic fitness selectively affects hippocampal function
 - *Journal of Cognitive Neuroscience 2014*
- Aerobic exercise preserved capacity of the aging human hippocampus for functionally relevant vascular plasticity (which decreases with age)
 - **Vascular hippocampal plasticity after aerobic exercise in older adults** *Molecular Psychiatry 2014*
- Brain-derived neurotrophic factor (BDNF)=increases after *voluntary* exercise
 - Neuroprotection
 - Dendritic arborization
 - Suppressed by stress (cortisol)
 - Decreased BDNF levels=atrophy and neuronal death
 - Decreased BDNF are characteristically low in depression and in patients with suicidal behavior

DU Concussion Biomarker Study (Granholm, Davidson, Ledreaux & Gorgens)

Table 1. Cohort demographics by sport played

		Total participants recruited	Male/Female	Percent Male/Female
	Total	237	134/103	57/43
Sport:	Lacrosse	54	34/20	63/37
	Soccer	34	16/18	47/53
	Hockey	28	28/0	100/0
	Swim	28	20/8	71/29
	Basketball	22	10/12	45/55
	Ski	19	8/11	42/58
	Tennis	12	8/4	67/33
	Golf	11	4/7	36/64
	Gymnastics	11	0/11	0/100
	Volleyball	11	3/8	27/73
	Diving	3	2/1	67/33

Table 2. History of concussion in cohort by sport.

History of concussion	Number of athletes	Percent of athletes with history of concussion	Male/Female	Percent Male/Female
Total	65	27	39/26	60/40
Lacrosse	22	41	13/9	59/41
Soccer	13	38	9/4	69/31
Hockey	9	32	9/0	100/0
Basketball	6	27	3/3	50/50
Swim	4	14	3/1	75/25
Volleyball	4	36	0/4	0/100
Ski	3	16	1/2	33/67
Tennis	2	17	2/0	100/0
Diving	1	33	1/0	100/0
Gymnastics	1	9	0/1	0/100

Table 3. Athletes with acute concussion.

Concussed	Number of athletes	Male/Female
Total	15	7/8
Lacrosse	5	3/2
Hockey	3	3/0
Soccer	2	0/2
Basketball	2	0/2
Volleyball	1	0/1
Diving	1	1/0
Gymnastics	1	0/1

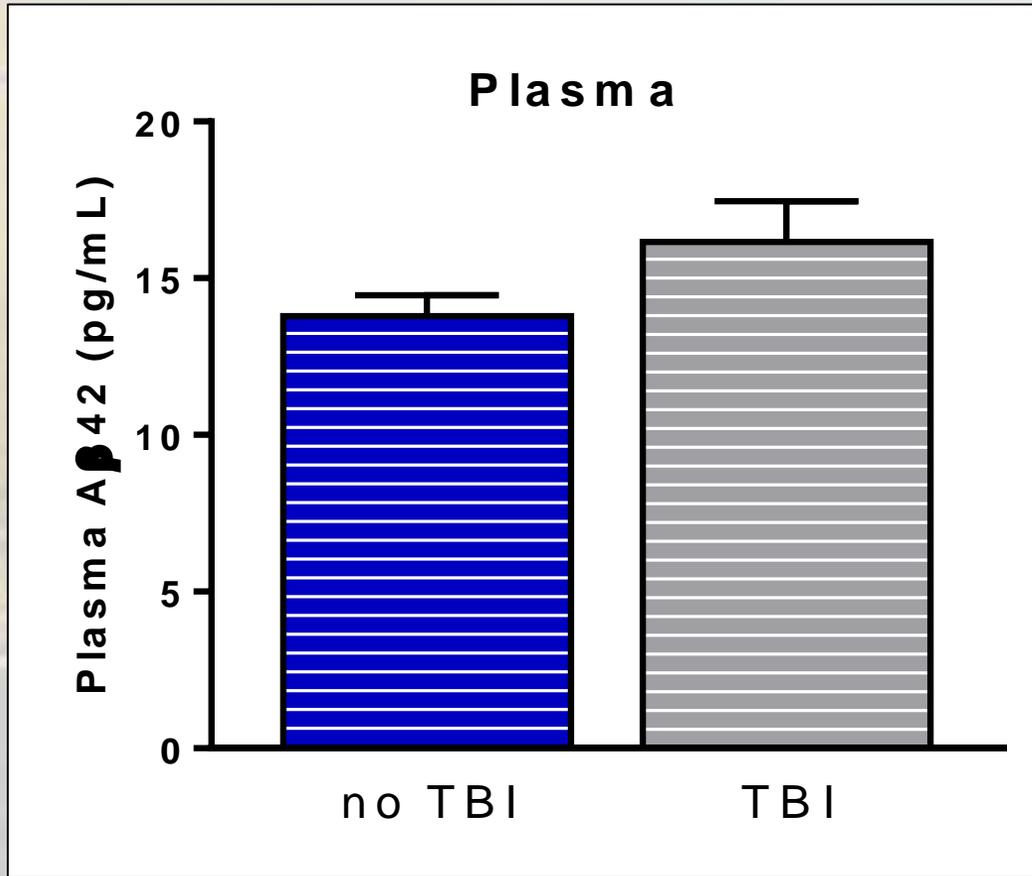


Fig. 5. $A\beta_{1-42}$ plasma levels were increased in athletes with a history of concussions

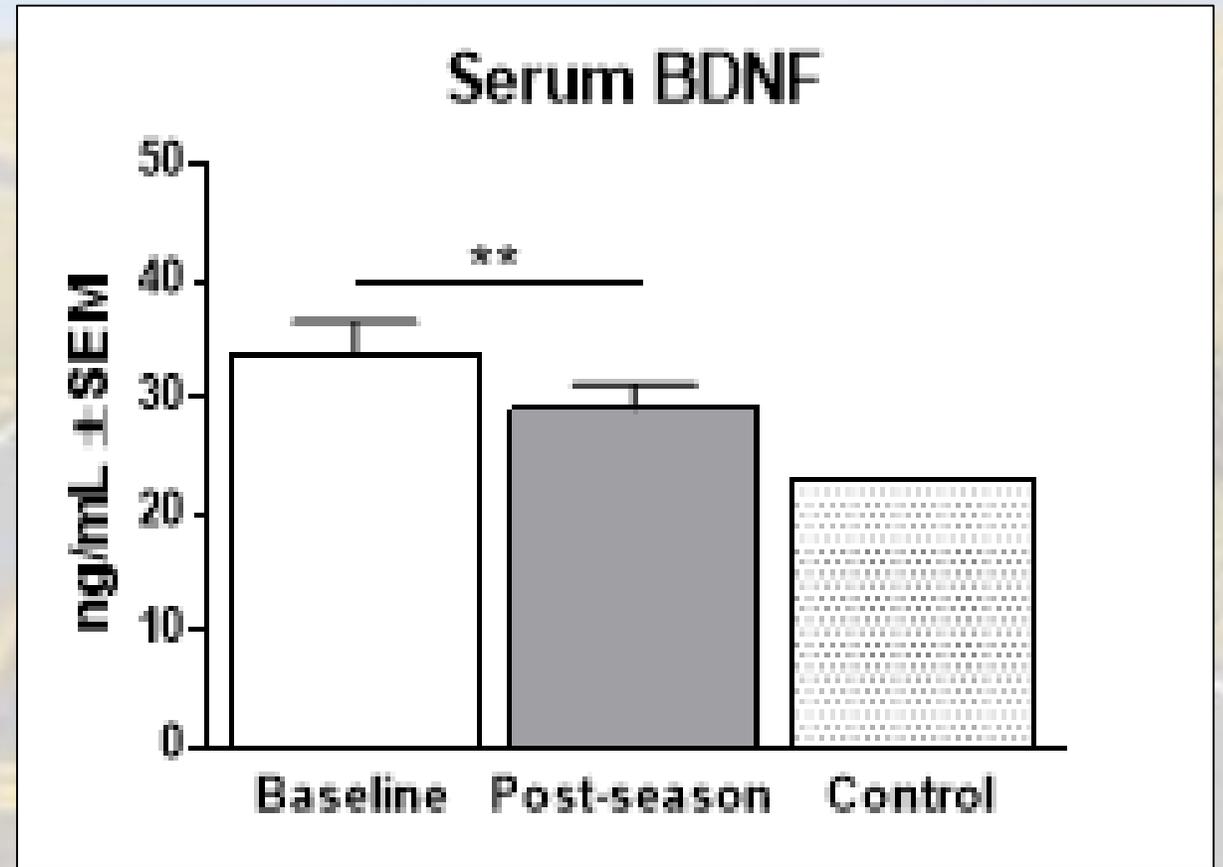
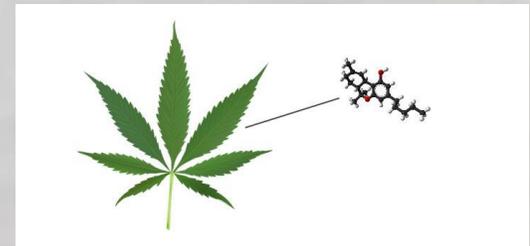


Fig. 6. BDNF levels in serum were significantly reduced in the DU ice hockey team ($n=14$) post-season, compared to pre-season baseline but were still higher than the average for non-athletic controls. Average \pm S.E.M.

An aerial photograph of a paved road with a yellow center line, winding through a dry, hilly landscape. The terrain is yellowish-brown, suggesting a semi-arid environment. A river or stream flows through the landscape, curving around the hills. The sky is blue with some light clouds.

A Few Oddities for Good Measure

- Protective effect of negative marital experiences for older adults
 - Marital Quality and Cognitive Limitations in Late Life *The Gerontological Society of America 2015*
- Brief stressful challenges appear beneficial for brain plasticity, allow adaptation, and in some instances increase neurogenesis
 - Environmental Control of Adult Neurogenesis: From Hippocampal Homeostasis to Behavior and Disease *Neural Plasticity 2014*
- Nose breathing
 - See Zelano, C., et al. (2016). Nasal Respiration Entrain Human Limbic Oscillations and Modulates Cognitive Function. *Journal of Neuroscience*, 6: 12448 –12467
- Cannabinoids
 - Known to promote both embryonic and adult hippocampus neurogenesis and to produce antidepressant-like effects
 - See Kozela, E., Juknat, A., & Vogel, Z. (2017). Modulation of Astrocyte Activity by Cannabidiol, a Nonpsychoactive Cannabinoid. *International Journal of Molecular Sciences*, 18(8), 1669.



An aerial photograph of a road intersection in a rural, arid landscape. The road is paved and has a yellow center line. The surrounding area is dry and yellowish-brown, with some sparse vegetation. The sky is blue with some light clouds. The text is overlaid on the left side of the image.

All Together Now: Multimodal interventions

UCLA's Center for Alzheimer's Disease Research and the Buck Institute for Research on Aging, 2015

- 36-point therapeutic program that involves comprehensive diet changes, brain stimulation, exercise, sleep optimization, specific pharmaceuticals and vitamins, and multiple additional steps that affect brain chemistry
- Reduced/reversed memory decline in dementing disease
 - Eliminating all simple carbohydrates, gluten and processed food from her diet, and eating more vegetables, fruits and non-farmed fish
 - Meditating twice a day and beginning yoga to reduce stress
 - Sleeping seven to eight hours per night, up from four to five
 - Taking melatonin, methylcobalamin, vitamin D3, fish oil and coenzyme Q10 each day
 - Optimizing oral hygiene using an electric flosser and electric toothbrush
 - Reinstating hormone replacement therapy, which had previously been discontinued
 - Fasting for a minimum of 12 hours between dinner and breakfast, and for a minimum of three hours between dinner and bedtime
 - Exercising for a minimum of 30 minutes, four to six days per week

An aerial photograph of a winding asphalt road in a dry, hilly landscape. The road curves through the terrain, with a yellow dashed line down the center. The surrounding land is a mix of light brown and tan, with some sparse, dry vegetation. The sky is a pale blue with a few wispy white clouds.

Sci-Fi in Real-Time: Advances in Brain Health

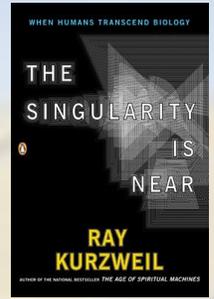
Electrical Stimulation

- Temporal Interference
 - Non-invasive deep brain stimulation
 - Better targeted than repetitive transcranial magnetic stimulation
 - See Grossman, N., *et al.* (2017). Noninvasive Deep Brain Stimulation via Temporally Interfering Electric Fields. *Cell*, 169: 1029-41.
- Transcranial Lasers
 - Infrared (IR) radiation or Low-level light therapy (LLLT) or photobiomodulation (PBM) therapy
 - Light at red and near-infrared wavelengths
 - Increasing evidence suggests that IR can carry out photostimulation and photobiomodulation effects particularly benefiting neural stimulation, wound healing, and cancer treatment
 - See Vargas, E., Barrett, D., Saucedo, C., Huang, L., Abraham, J., Tanaka, H., . . . Gonzalez-lima, F. (2017). Beneficial neurocognitive effects of transcranial laser in older adults. *Lasers in Medical Science*, 32(5), 1153-1162.

Nanotechnology/Optogenetics

- Targeted delivery of genes, drugs, or growth factors across the blood-brain barrier
 - “Carbon nano-tubules re-established the electrical activity [after CVA] in damaged neural tissues and promoted functional recovery”
 - See Hassanzadeh, Atyabi, & Dinarvand. (2017). **Application of modelling and nanotechnology-based approaches: The emergence of breakthroughs in theranostics of central nervous system disorders.** *Life Sciences*, 182, 93-103.
- Building a new brain (biomaterials)
 - See Z. Álvarez, *et al.* **Neurogenesis and vascularization of the damaged brain using a lactate-releasing biomimetic scaffold** *Biomaterials*, 35 (2014), pp. 4769-4781
- ‘Body–machine interface’
 - Optogenetics is a technology that allows precise spatial and temporal control of cells
 - Optogenetics relies on the biological activity elicited by photosensitive proteins in response to light
 - Optogenetic control of “stem cell-derived neuronal engraftment strategies”
 - See Josue D Ordaz, Wei Wu, & Xiao-Ming Xu. (2017). **Optogenetics and its application in neural degeneration and regeneration.** *Neural Regeneration Research*, 12(8), 1197-1209.

Outsourcing the CNS



- Computer Models
 - The correlation between the neurobiological mechanisms and a variety of cognitive, behavioral, and physiological phenomena may be easily explored by modelling of the neuronal systems
 - Using neural network models, the dynamics of neural circuitry or the behavior of individual neurons can be evaluated
- Micro-brains
 - See Haring, A., Sontheimer, H., & Johnson, B. (2017). Microphysiological Human Brain and Neural Systems-on-a-Chip: Potential Alternatives to Small Animal Models and Emerging Platforms for Drug Discovery and Personalized Medicine. *Stem Cell Reviews*, 13(3), 381-406.
- Singularity (when technology transcends biology)
 - Ray Kurzweil (Google) “We’ll one day find a way to download human consciousness, making bodies obsolete” (in his estimation, by 2040)
 - “Humans will most likely experience gradual conversion as portions of their brain are augmented with neural implants, increasing their proportion of non-biological intelligence slowly over time”
 - 2045 Initiative
 - “Create technologies enabling the transfer of a individual’s personality to a more advanced non-biological carrier, and extending life, including to the point of immortality”

2045

STRATEGIC SOCIAL INITIATIVE

AVATAR PROJECT MILESTONES



Avatar **D** 2040 - 2045
A hologram-like avatar

Avatar **C** 2030 - 2035
An Avatar with an artificial brain in which a human personality is transferred at the end of one's life

Avatar **B** 2020 - 2025
An Avatar in which a human brain is transplanted at the end of one's life

Avatar **A** 2015 - 2020
A robotic copy of a human body remotely controlled via BCI

Thank you BIAC!

