WOMEN's MENTAL HEALTH AS WHOLE PERSON HEALTH

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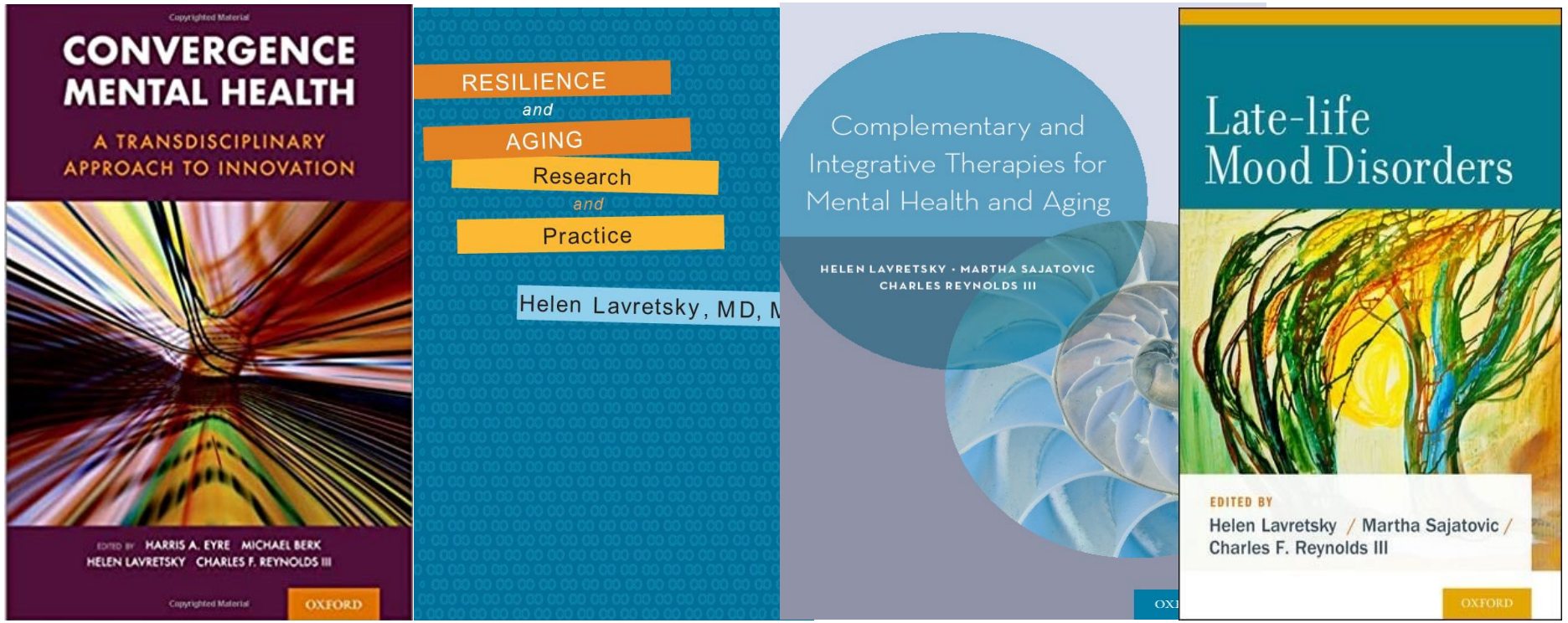
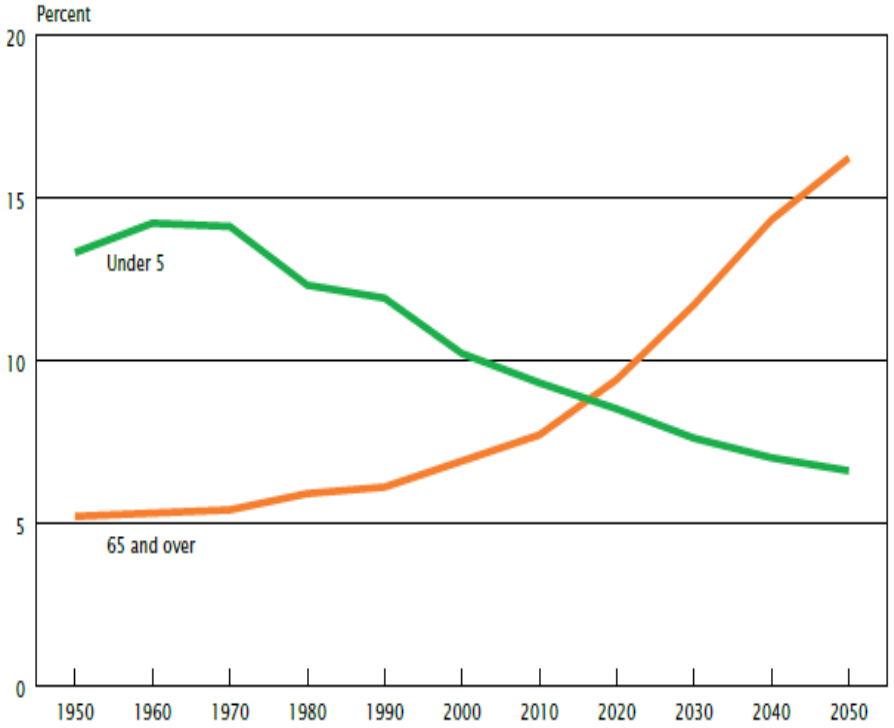
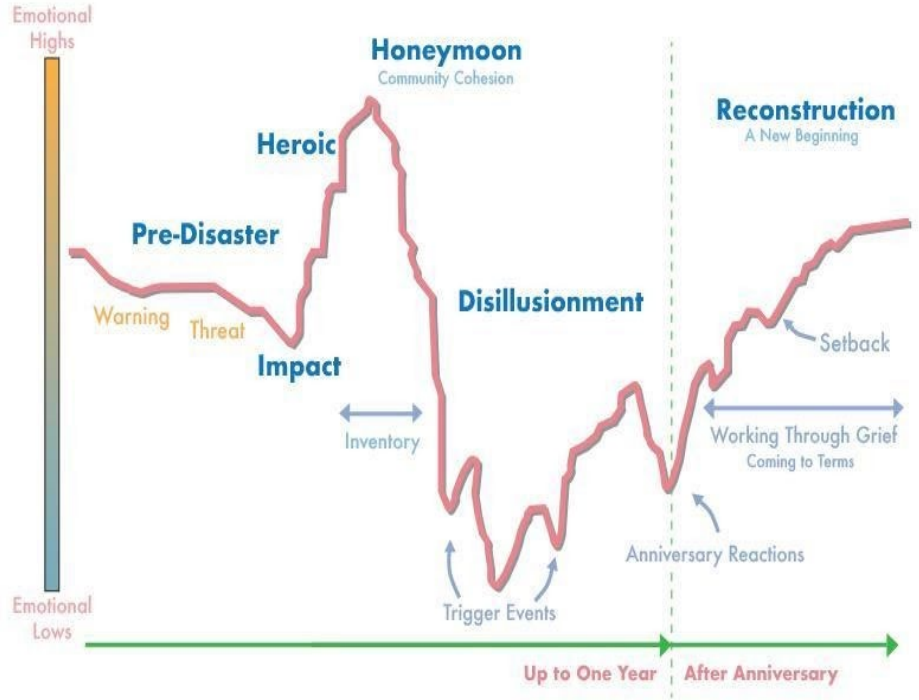


Hard Problem:
Global Population is Aging and is Chronically Stressed



Source: United Nations Department of Economic and Social Affairs, 2007b.



Post-Pandemic Mental Health Crisis

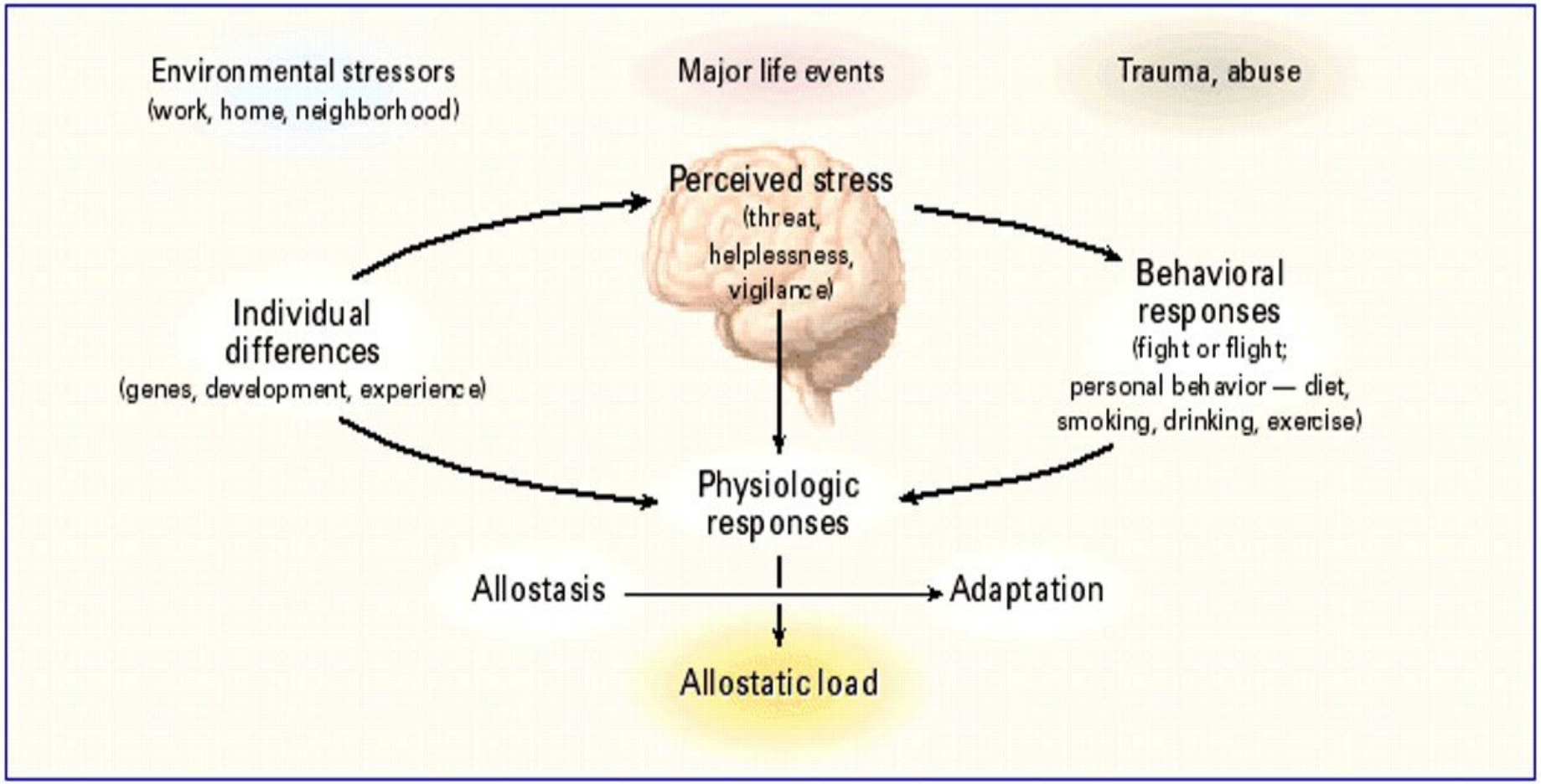
- One out of every 5 people in the United States had a mental illness in 2019 -total of 51.5 million people.
- At the height of the pandemic, 40% of adults reported symptoms of anxiety or depression — compared with 11% pre-COVID. Over time, this percentage dipped to 33% in June 2022, still higher than pre-pandemic
- Long COVID affects nearly twice as many women as men, with **6.6% of women reporting long COVID compared with 4% of men** (CDC)
- 80-90% of Long COVID have neuropsychiatric symptoms- anxiety fatigue, brain fog, depression
- Burden of COVID-19 and Long-COVID, and ongoing mass disasters increased rates of mental disorders and dementia and will reduce expected lifespan and increasing cost of morbidity and disability

Sex differences in mental disorders

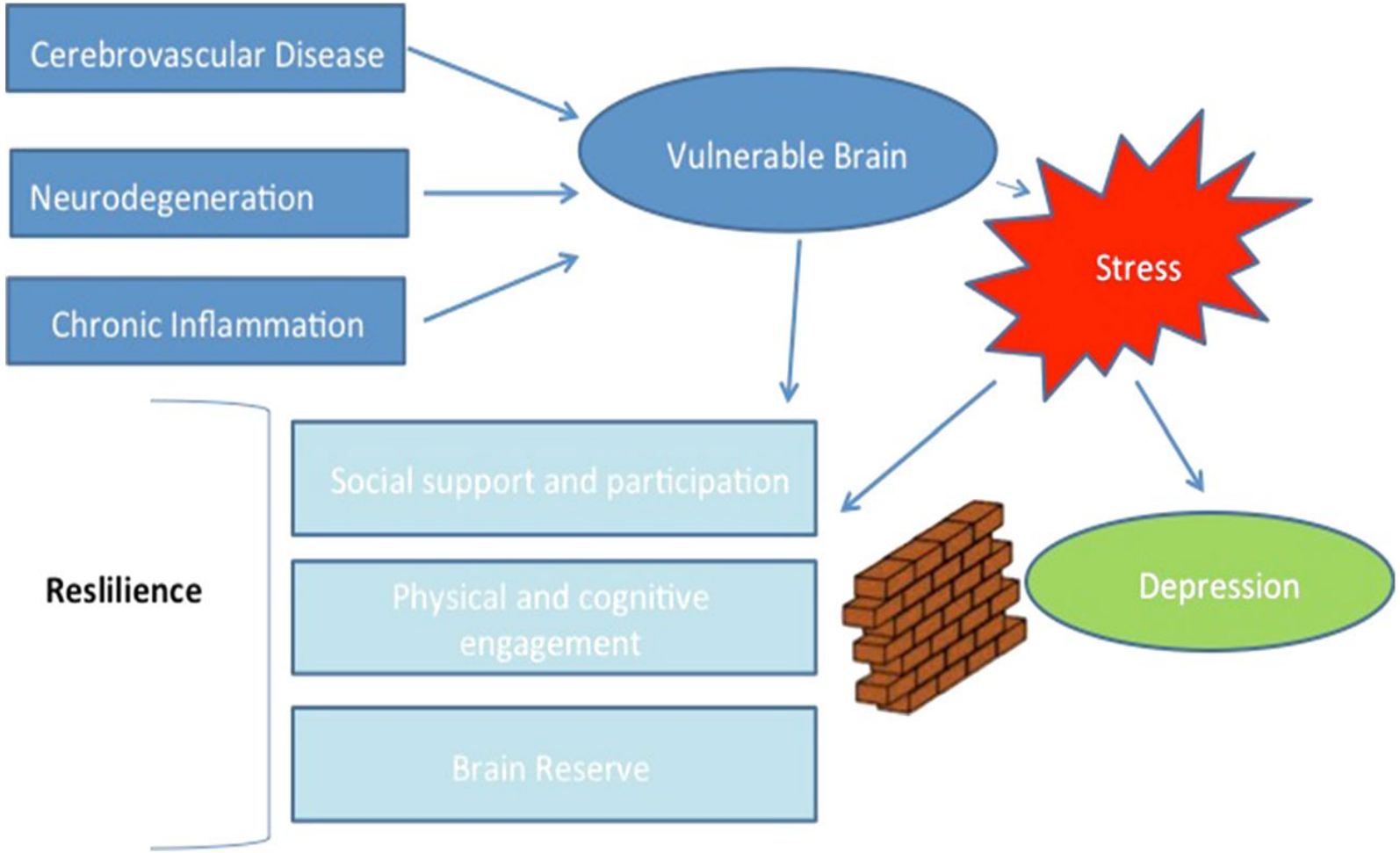
More common in women

- Depression, seasonal depression
- Anxiety
- Eating disorders
- Chronic pelvic pain (0.6 mo)
- Post-partum
- PMS and Premenstrual dysphoric disorder (80% some symptoms)
- Perimenopause-related mood disorders
- Caregiver burden and stress
- Alzheimer’s disease and related dementias more common in women

Model of Stress and Health: Relevance to Mood and Anxiety Disorders



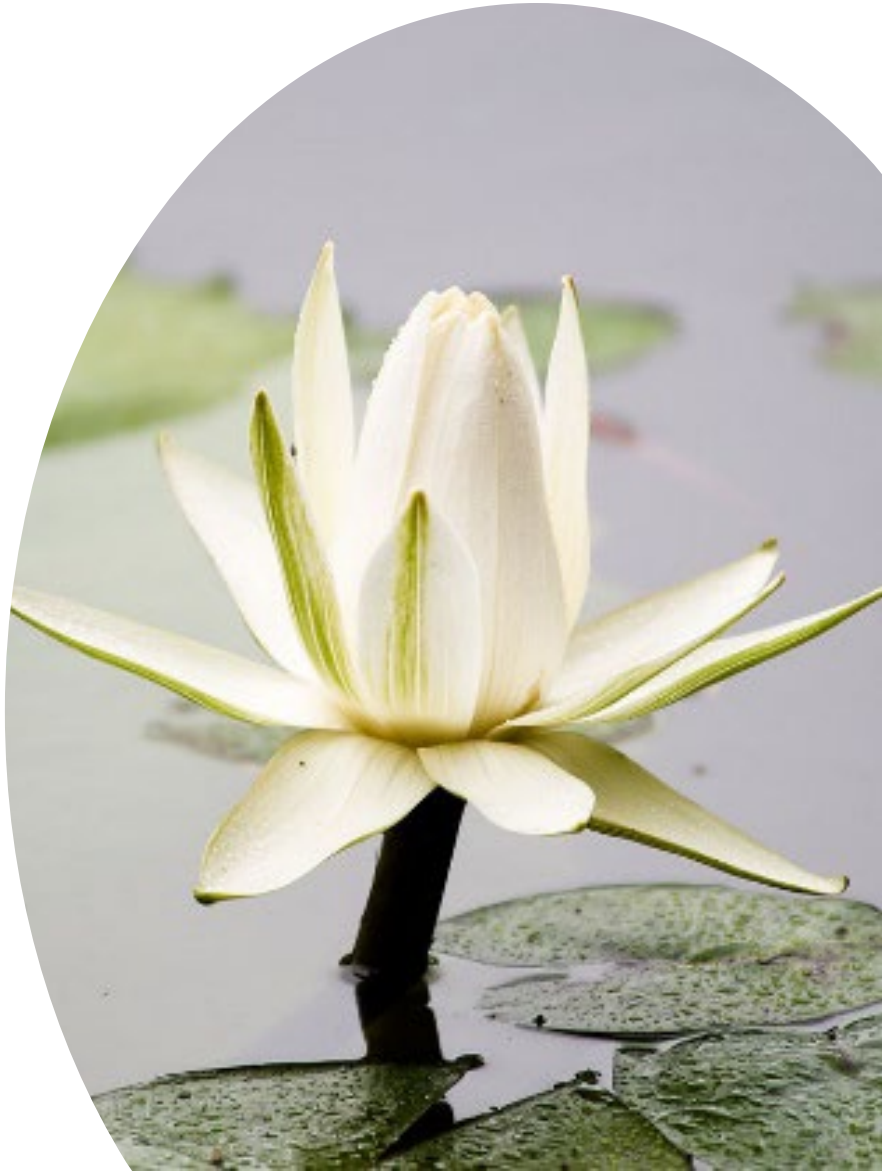
Risk and Resilience Factors in Aging Brain



Weisenbach, Kumar 2014

Resilience

- **Resilience** = Ability to recover from adversity / stress
- **Brain neuroplasticity and neuroprotection**
- **Mental, emotional, cognitive, physical health**
- **Lifestyle medicine-** sleep, diet, exercise, stress reduction with mind-body interventions, social and intergenerational relationships
- **Prevention of mental and medical disorders**
- **Building Brain Capital!**



Resilience-Building interventions

- **Resilience= ability to “bounce back” from adversity**
- **Resilience enhancing interventions** include wellbeing therapy, learned optimism training, hardiness training, all of which focus on positive aspects of difficult experiences thereby promoting more positive perceptions of challenges.
- **Lifestyle factors** such as diet, exercise, spirituality can enhance resilience by creating physical and mental wellbeing.
- **Complementaryc and Integrative Medicine and Health (CIH)** is a holistic and integrative approach to wellness which encompasses varied approaches to wellness and stress reduction

Domain	Examples of the interventions	Comments
Biologically based therapies	Herbal (botanical) medicines, vitamins, nonvitamin/nonmineral natural products (e.g., omega-3 fatty acids; adaptogens)	Nonvitamin/nonmineral natural products are used by 18% of U.S. adults.
Mind-body medicine	Biofeedback, meditation techniques, yoga, tai chi, energy therapies (e.g., light therapy, qi gong, healing touch)	Focuses on interactions among brain, mind, body, and behavior to affect physical function and promote health.
Manipulative and body-based practices	Chiropractic spinal manipulation, massage therapies, movement therapies (e.g., Pilates)	Focuses on structural and functional systems of the body, i.e., skeleton, soft tissues, circulatory, and lymphatic systems.
Alternative medical systems	Acupuncture, Ayurveda, homeopathy/naturopathy, traditional healers (e.g., Native American healers)	Focuses on achieving optimal health and well-being.
Other complementary and alternative medicine (CAM) practices	Spirituality, pastoral care, expressive therapies	Approaches not formally categorized, but easily accepted by individuals

Complementary and Integrative Health Interventions

Animal Assisted Therapy	Facilitate social interaction Anxiety, Depression	Increases in b-endorphin, oxytocin, prolactin, dopamine phenylacetic acid & a decrease in cortisol.	One visit in 3 weekly sessions/long-term exposure (aquarium)	Allergies/infections from live animals.	Edwards et al., 2014; Kraemer et al., 2009; Odendaal, 2000; O'Haire, 2010
Music Therapy & Social Interaction	Anxiety Depression Enhance Mental Well-being and Social Engagement Communication	Modulation of attention, memory and emotion (via limbic & paralimbic system).	One interactive performance. Weekly sessions from 4-24 weeks	No adverse effects reported	Guetin et al., 2009; Koelsch, 2009; Sung et al., 2006; Van der Vleuten et al., 2012
Movement Therapy	Mood Concentration Sleep	Modulation of serotonin and dopamine	4-10 weekly sessions	No adverse effects reported	Hamill et al., 2001; Jeong et al., 2005; Siddartha et al., 2013
Light Therapy with Melatonin	Limited Support: Mood, Sleep, Agitation Depression	Entrainment of circadian/ melatonin rhythm	2500 to 10,000 lux, am or pm. One to two hours for 10 days to two months.	Increased agitation in subgroups	Barrick et al., 2010; Burns et al., 2009; Diamond et al., 2003; Forbes et al., 2014;Hickman et al., 2007
Acupuncture	Cognition, Mood	Increased activity in temporal and prefrontal lobes. Enhanced hippocampal connectivity.	One session	Organ and tissue injury, infection, & syncope have been reported. Frequency of adverse events are low.	Hempel et al., 2013; Kwok et al.,2013; Rodriguez-Mansilla et al., 2013; Wang et al., 2014;Zeng et al., 2013
Aroma Therapy (lavender, hops, melissa essential oils)	Behavioral and psychological problems, agitation	Stimulates olfactory bulb, modulates limbic system, Influences pyriform, right amygdala, anterior cingulate & left insular cort	5–10 drops (inhalation) 4 days-4 weeks	Contact dermatitis	Ballard, 2002; Diamond et al., 2003; Lin et al., 2007

Complementary and Integrative therapies in Menopause

- **6000 women reach menopause daily (population >51 yo = 50 mln)**
- **Phytoestrogens,** Black cohosh, red clover, and soy, Vitamins B 6 and 12, D3
- **Mind and body practices** such as **yoga, tai chi, Qi Gong, hypnosis,** and **acupuncture** and Traditional Chinese Medicine (TCM)
- **Hypnosis** and self-hypnosis for hot flashes
- **Social prescribing-** Forest bathing, mind-body therapies, volunteering, intergenerational programs, music and expressive arts
- For more information, see the National Center for Complementary and Integrative Health (NCCIH)

Johnson A et al. J Evid Based Integr Med. 2019

Chiaramonte et al. Integrative Women's Health. Med Clin North Am. 2017

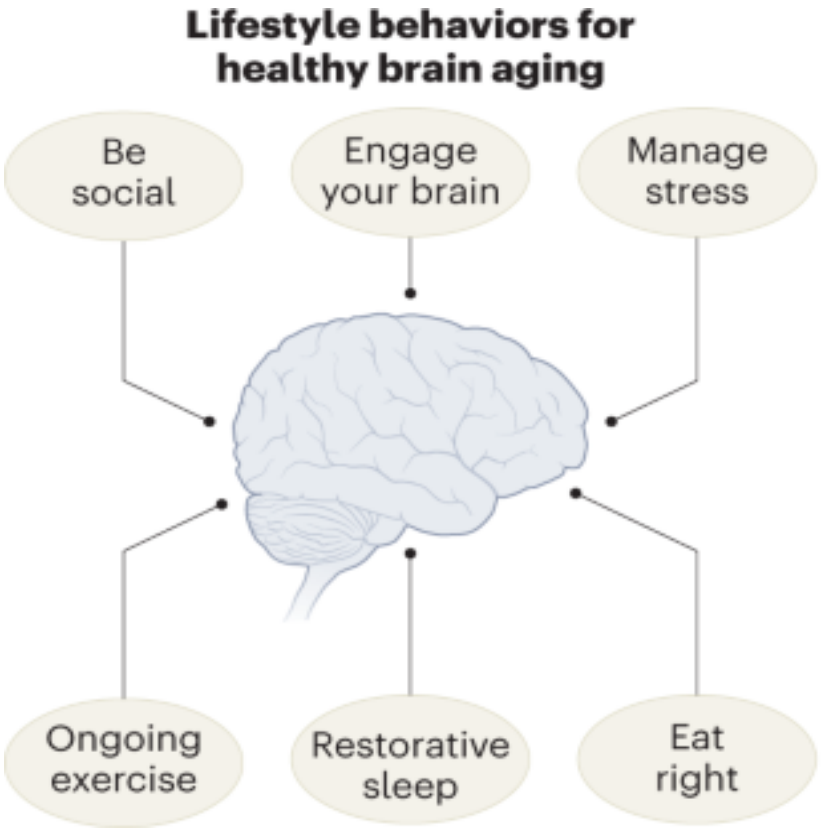
WHOLE WOMAN'S HEALTH: Wellbeing, Flourishing, and Brain Health

-Human Flourishing is a path towards complete physical and mental all-around wellbeing, both for individuals and communities. We flourish when we live with purpose; when we practice gratitude, forgiveness, and open-mindedness.

-**Brain Health** is the state of brain functioning across cognitive, sensory, social-emotional, behavioral and motor domains, allowing a person to realize their full potential over the life course, irrespective of the presence or absence of disorders

-Optimal Brain Health optimizes Mental, Emotional, and Physical Health, and benefits individual and societal well-being

Six pillars of brain health and the societal benefits



Benefits of healthy brain aging at the population level

- Cognitive resilience
- Reduced dementia
- Reduced healthcare costs
- Reduced economic costs
- Increase in 'brain capital'
- More inclusive workforce
- Improved quality of lives
- Greater experience to share
- Expanded cultural contributions

Eyre, Lavretsky et al 2022

Brain and Mental Health and Lifestyle Habits

Sleep -7-9 hours of daily sleep is necessary for proper cognitive and behavioral function

Brain reorganizes and recharges itself and clears toxic waste byproducts which have accumulated throughout the day

Emotion regulation is disrupted with chronic sleep loss- depression, anxiety, anger, aggression, cognitive problems and behavior

Exercise- recommended 150 min of moderate aerobic activities and 2-3 days of weight training per week

Physical activity maintains healthy body and brain, provides the integrity of the blood–brain barrier, increasing clearance and degradation of aging related amyloid species, and regulating microglia activation

Endurance and aerobic training reduce cognitive impairment and have neuroplastic effects on the brain- increase in hippocampal volume

Diet: Mediterranean, DASH, MIND- Compared to SAD- reduced depression by 25-30%and improved cognition

Intermittent fasting: 12-20 hours- reduce cellular aging

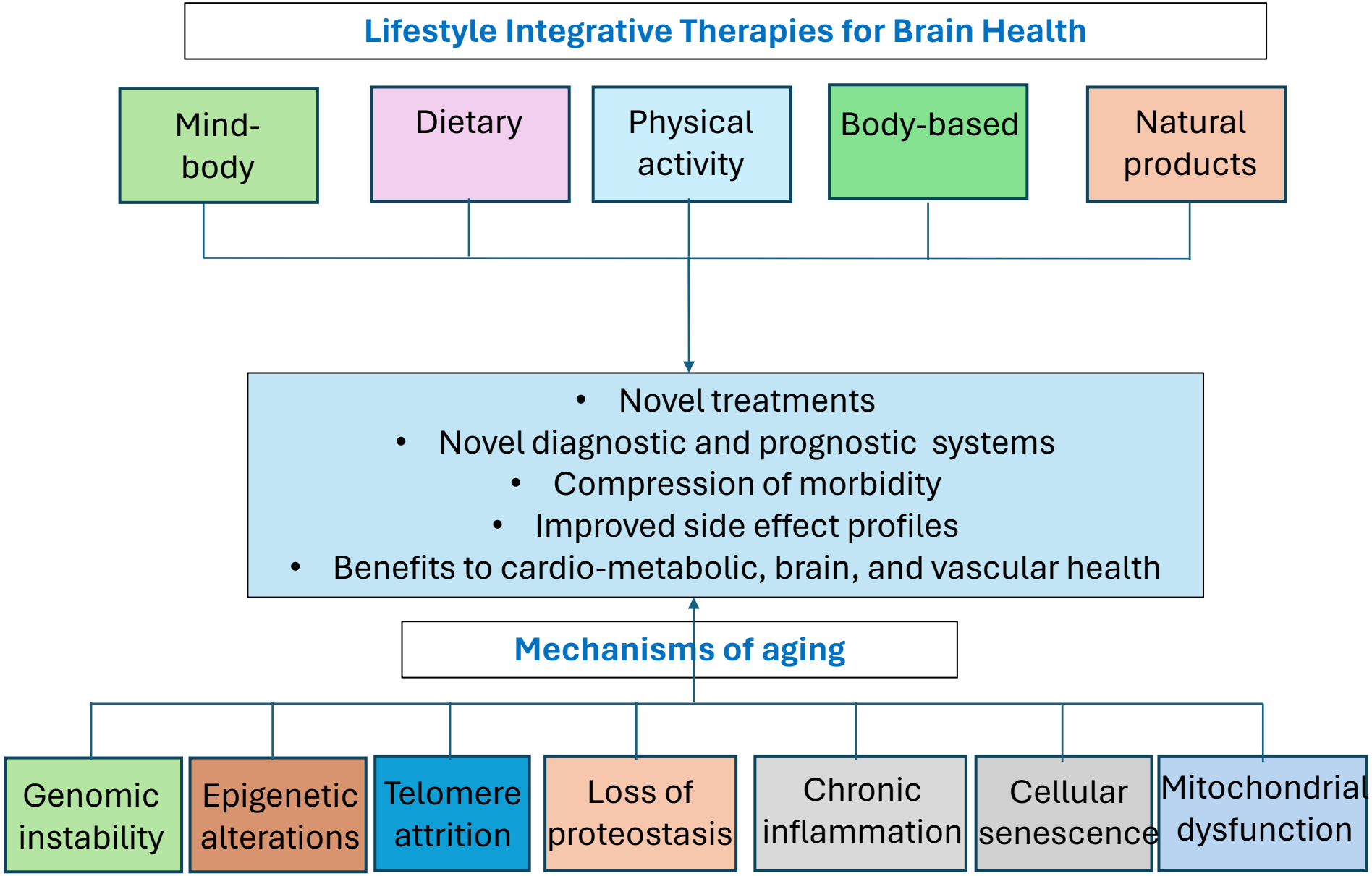
Supplements: MVI, Vitamin D, B, Omega-3 fatty acids. Probiotics, tea, coffee, alcohol

Stress-reduction: meditation, yoga, Tai Chi, Qi Gong, acupuncture, massage, breath-work, being in nature (forest bathing)

Social support vs loneliness: affects brain and mental health- reduction in depression /anxiety

Meaning and purpose: Volunteering, Spirituality

Creativity: leisure activities, Expressive Arts


Lifestyle Integrative Therapies for Brain Health
Mind-body
Dietary
Physical activity
Body-based
Natural products
• Novel treatments
• Novel diagnostic and prognostic systems
• Compression of morbidity
• Improved side effect profiles
• Benefits to cardio-metabolic, brain, and vascular health
Mechanisms of aging
Genomic instability
Epigenetic alterations
Telomere attrition
Loss of proteostasis
Chronic inflammation
Cellular senescence
Mitochondrial dysfunction

Pink Brain Project

- To date, no studies of yoga have targeted women at high risk for AD (e.g., postmenopausal with SCD and cardiovascular risk factors)
- Aim: Investigate the efficacy and neurobiological mechanisms of response to KK+KY compared to MET on memory performance at 12- and 24-weeks in women at high AD risk.
- Secondary clinical outcomes examined include mood, resilience, and quality of life.
- Biomarkers- inflammatory and neuroimaging

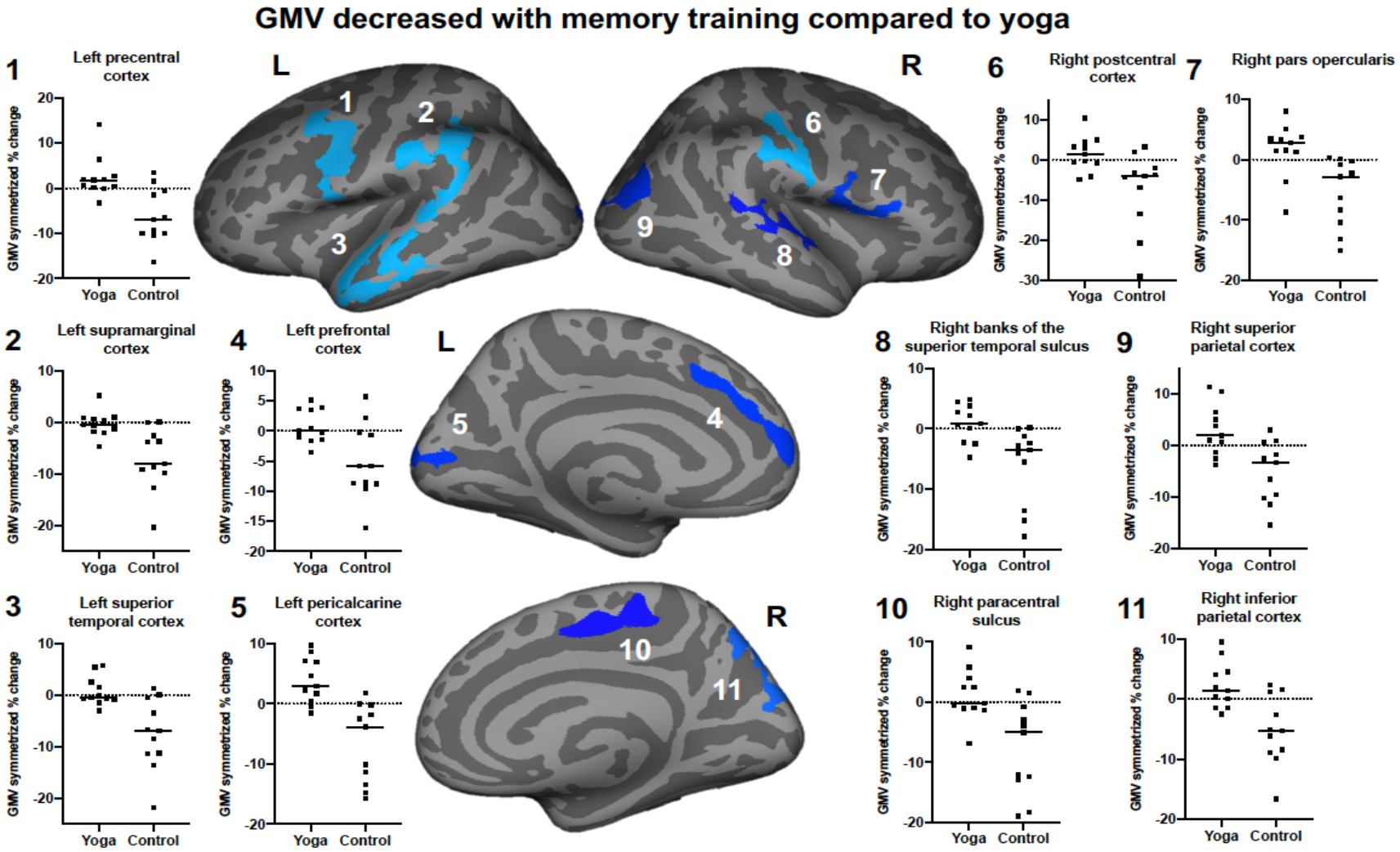
EFFECT SIZES

Measure	12-Week Follow-up Effect Size (95% CI)[1-2]	24-Week Follow-up Effect Size (95% CI)[1-2]
BDI	0.16 (-0.37, 0.68)	0.17 (-0.34, 0.69)
CD-RISC	-0.16 (-0.69, 0.36)	0.05 (-0.47, 0.57)
CVRF	-0.28 (-0.80, 0.25)	
HAM-A	0.28 (-0.24, 0.79)	-0.23 (-0.73, 0.28)
MFQ		
Frequency of Forgetting	-0.49 (-1.03, 0.05)	-0.28 (-0.80, 0.25)
Seriousness of Forgetting	-0.28 (-0.82, 0.25)	-0.73 (-1.26, -0.19)
Cognitive Domains		
Delayed recall		0.69 (0.17, 1.21)
Executive functioning		0.01 (-0.49, 0.52)

At 24-weeks follow-up, YOGA yielded a significant, large effect size improvement in subjective cognitive impairment compared to MET. But displayed a significant, large effect size decline in delayed recall at 24-weeks follow-up but no change in executive functioning.

Women 50+ with cardiovascular conditions and memory complaints

The Yoga group showed either no decline or increases in GMV the left precentral (1) and lateral occipital cortices (5) compared to **Memory training.**



Krause et al 2023

Chemokine/Cytokine Assay

12-Week Follow-Up	YOGA (N=18) Estimate (SD)	Within-Group Statistics	MET (N=27) Estimate (SD)	Within-Group Statistics
Eotaxin-1	-0.07 (0.7)	t(67)=-0.99, p=0.32	-0.11 (0.6)	t(67)=-2.12, p=0.04
FGF2	-0.44 (0.2)	t(67)=-2.5, p=0.01	-0.38 (0.2)	t(67)=-2.4, p=0.02
24-Week Follow-Up	**YOGA (N=26) Estimate (SD)**	**Within-Group Statistics**	**MET (N=32) Estimate (SD)**	**Within-Group Statistics**
Eotaxin-1	0.09 (0.07)	t(67)=1.31, p=0.19	-0.16 (0.6)	t(67)=-2.75, p=0.01

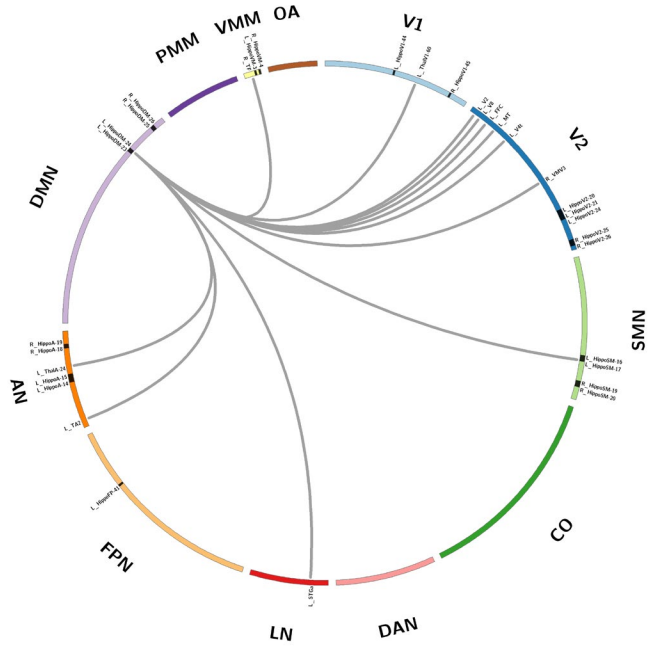
MET but NOT YOGA participants displayed higher Eotaxin-1 levels at 12- and 24-weeks follow-up. *Eotaxin-1 levels have previously been shown to increase in linear fashion with age and cognitive decline. In mouse models, higher eotaxin-1 levels correlate with impaired learning and reduced neurogenesis. Crosses the BBB to exert its effects on the brain.*

Both MET and YOGA participants showed higher FGF levels at 12- and 24-weeks follow-up. *FGF2 is neuroprotective. Decreased in the DLPFC & hippocampus in post-mortem MDD samples. Upregulated in response to anti-depressant administration.*

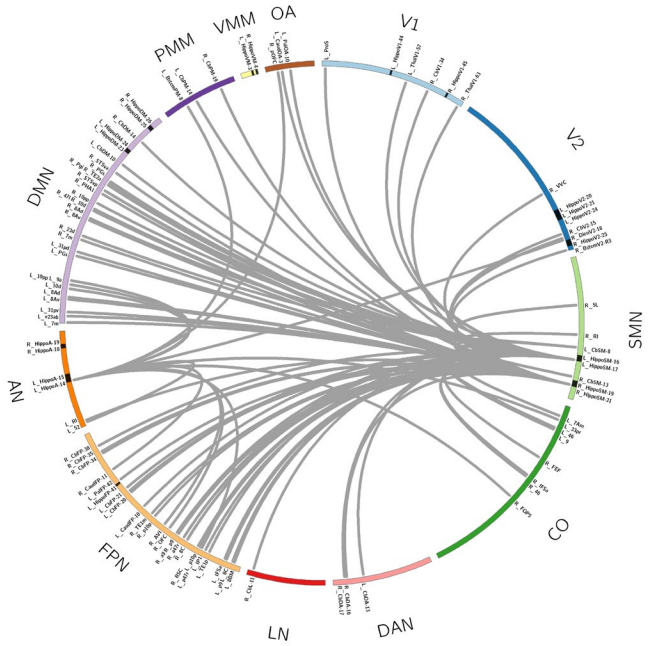
Results – Group differences in hippocampal connectivity changes

- Four hippocampal seeds showed significant differences in connectivity changes between the two groups (p<.001).
- Yoga>MET: An anterior hippocampal seed in the default mode network (DMN) showed significantly greater increases in connectivity with regions mainly in the visual system in the Yoga group than in the MET group.
- MET>Yoga: A posterior hippocampal seed in the auditory network, and two in the somatosensory network, showed significantly greater increases in connectivity with regions mainly in the DMN and frontoparietal network in the MET group than in the Yoga group.

Yoga>MET



MET>Yoga



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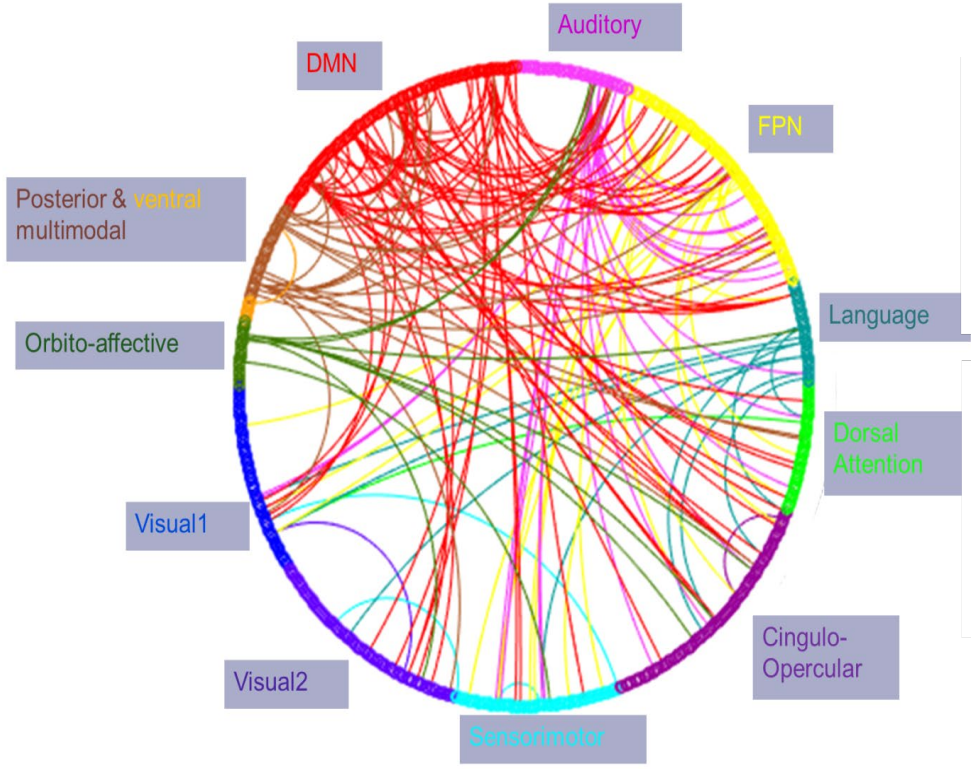
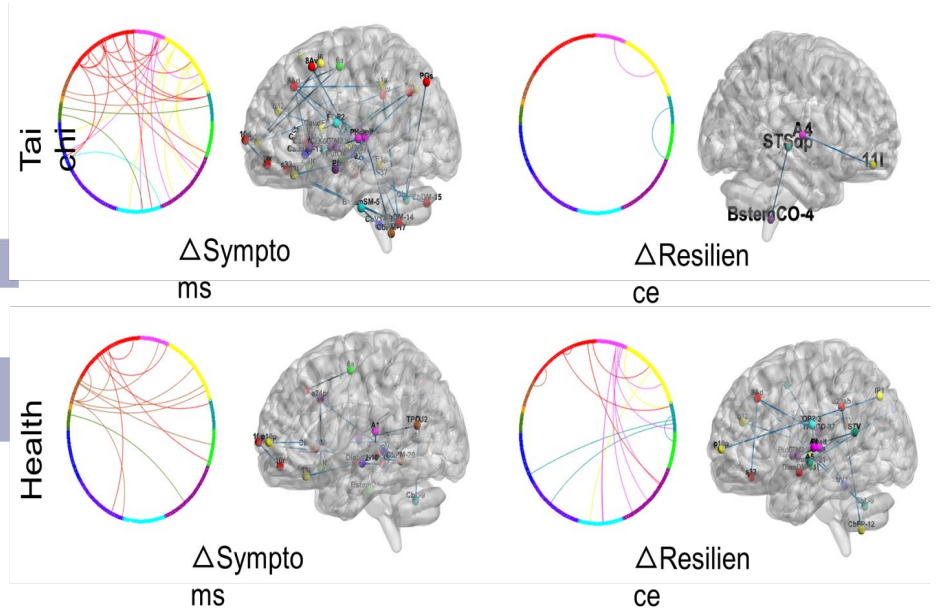
Increased Brain Connectivity in older adults with major depression with Tai Chi training vs HEW training





Increased connectivity associated with improvements in depression (as assessed by the MADRS) and resilience ($p < 0.05$).

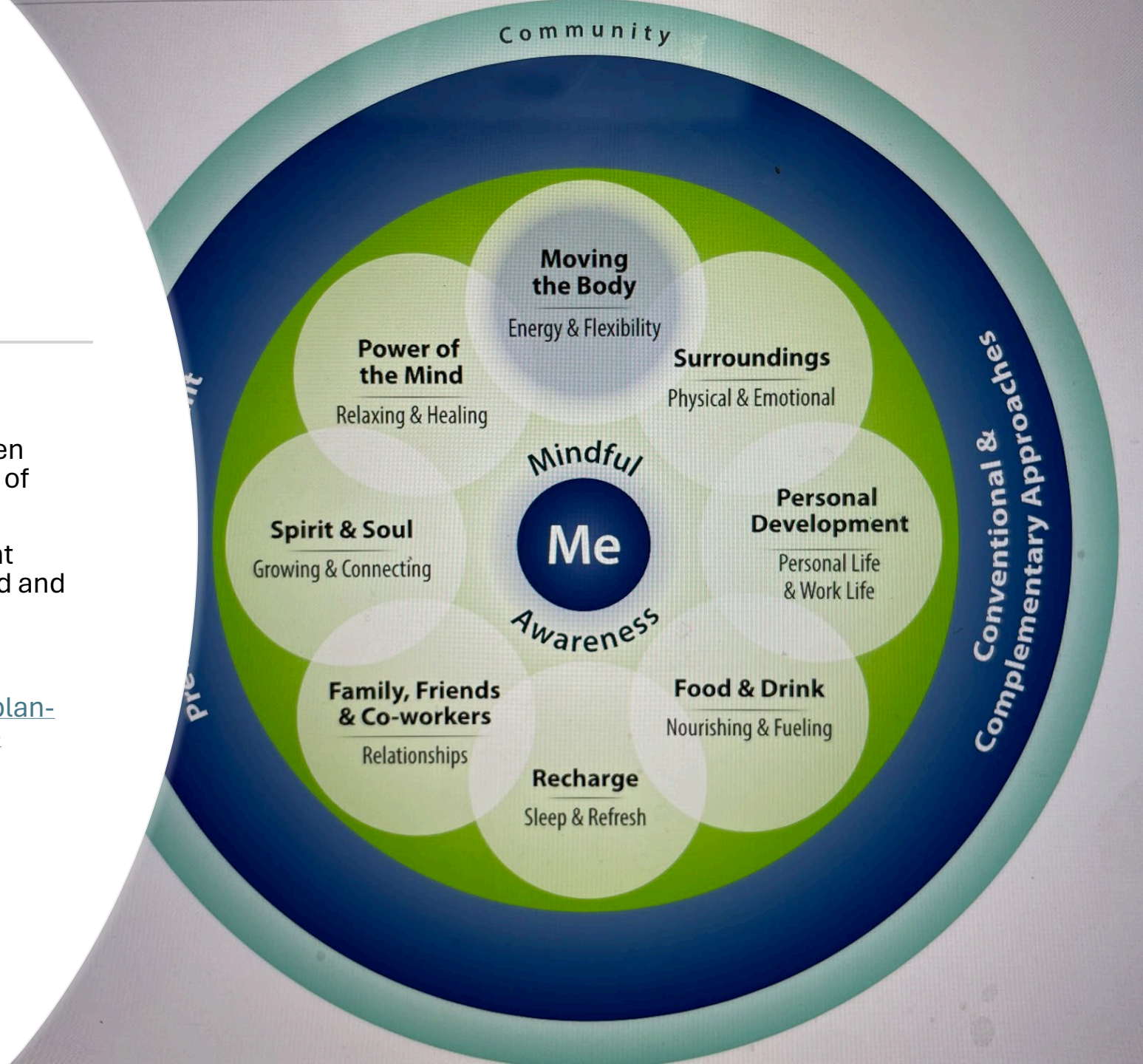
Kilpatrick et al 2022

Summary

- **WHOLE PERSON HEALTH- WELLBEING, FLOURISHING, BRAIN HEALTH – as a goal for primordial, primary, and secondary prevention**
- CIH therapies can be used in clinical care for women with mood and anxiety disorder, and for prevention of cognitive decline
- Future research needs to address multi-component interventions for treatment and prevention of mood and cognitive disorders in aging women

- https://www.nccih.nih.gov/about/nccih-strategic-plan-2021-2025/introduction/building-a-path-to-whole-person-health

- https://www.va.gov/wholehealth/



Thanks!