The use of mind-body interventions (Tai Chi and Yoga/Meditation) for Mental Health and Aging

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Disclosure

- **Grant funding** – Forest Research Institute, NIMH, NCCIH, Alzheimer’s Research & Prevention Foundation

- **Advisory Board** – Alzheimer’s Research & Prevention Foundation
Objectives

- To review the studies of Tai Chi / Qi Gong and yoga/meditation use for mood and cognitive disorders in later life
- Complementary use of Tai Chi to improve outcomes in geriatric depression (NCCAM / NCCIH)
- The use of daily yogic meditation to reduce stress and improve cognition in informal (family) dementia caregivers and in older adults with mild cognitive impairment
Sociodemographic Characteristics of the Elderly

- Population Growth
  - 12.6% of US pop. in 1990 to 12.4% in 2000 to 20% by 2030
  - Oldest-old age (>85 y.o.) group is growing fastest (4.2%)

- Gender
  - More women than men

- Age is a risk factor for many acute and chronic diseases

- INCREASED POLYPHARMACY AND COST OF MEDICAL CARE

- Psychiatric disorders
  - Dementia
  - Depression
  - Delirium
Projected Increase of Mentally ill Elderly Population

- By 2030, more than 15 million elderly, mentally ill Americans¹
- Mentally ill elderly increasing because of:
  - ↑standard of living
  - ↑treatment of physical and mental disorders
  - Cohort effect

¹ Jeste et al. 1999
What Is CAIM?

... medical and health care practices outside the realm of conventional medicine, which are yet to be validated using scientific methods

**Complementary:** in addition to conventional practices

**Alternative:** in place of conventional practices

**Integrative:** used together for targeted interventions
CAIM as a backlash against Western Medicine

- Whole person versus biological reductionism in assessment and treatment (particularly in psychiatry);
- Environment, physical, emotional, mental (cognitive); social; spiritual wellbeing
- System approach, ecology of a person, relationship with environment (child and geriatric psychiatry traditions)
- CAIM use is high among Babyboomers and following generations!
Priority Setting – A Challenge for Aging Research

- Enhance physical & mental health
- Manage pain, sleep, symptoms, disabilities
- Impact health and cognition
- Prevent disease
Need for more research

- Late-life mood and cognitive disorders, insomnia, pain, and cognitive aging are the most common reasons for using complementary and alternative therapies.
- The amount of rigorous scientific data to support the efficacy of complementary therapies in the treatment of depression is extremely limited.
- Most evidence for beneficial effects for exercise, herbal therapy (Hypericum perforatum), the use of fish oil, and acupuncture, and relaxation therapies.
- Need for further research with randomized controlled trials to investigate the efficacy of CAIM therapies for treatment of mood, insomnia, and cognitive disorders in late-life.
- This research may lead to the development of effective treatment and preventive approaches for these serious conditions.

Lavretsky, Aging Health, February 2009
Mind-Body Medicine

- Yoga
- Guided imagery
- Meditation
- Hypnotherapy
- Spirituality
- Tai Chi
- Art, dance, music therapies
Identify the common and specific features of widely used mind-body medicine practices by studying …

- their effects on brain mechanisms, physiology and psychology, as well as on clinical outcomes.
Model of Stress and Health:

- Environmental stressors (work, home, neighborhood)
- Major life events
- Trauma, abuse

- Perceived stress (threat, helplessness, vigilance)

- Individual differences (genes, development, experience)

- Physiologic responses

- Allostasis

- Behavioral responses (fight or flight; personal behavior — diet, smoking, drinking, exercise)

- Adaptation

- Allostatic load
Bi-directional interactions between the brain, autonomic, neuroendocrine, and immune systems

Targeting therapies for the stress-disease diathesis

Physiological basis for modulating brain-autonomic-immune pathways
RESILIENCE
and
AGING
Research
and
Practice

Helen Lavretsky, MD, MS
Theoretical model of resilience

**Stressors**
- Adversity
- Trauma

**Biopsychosocial Homeostasis**

**Individual Resources:**
- Self-esteem
- Optimism
- Coping
- Social support
- Personality and appraisals
- Spirituality
- Genetic influences (e.g., 5-HTTLPR)

**Disruption**
- Psychological distress
- Physiological responses

**Biomarkers**
- BMI
- Cortisol levels/HPA axis
- Catecholamine levels
- Pro/anti-inflammatory cytokines / nfkappaB/ CRP
- Chol/HDL levels
- DHEAs levels
- HbA1c levels
- Telomerase/ telomere length
- Brain regional volumes: amygdala, anterior cingulate; hippocampal volumes on MRI
- Emotional processing on fMRI (e.g., emotional reactivity to human faces)
- BDNF
- Epigenetics-gene expression

**Outcomes**
1. Resilient reintegration at a higher level of adaptation
2. Reintegration back to baseline homeostasis
3. Reintegration with loss from baseline
4. Dysfunctional reintegration
5. Disease
   - Disability
   - Mortality

**Disruption**
- Psychological distress
- Physiological responses
<table>
<thead>
<tr>
<th>Yoga</th>
<th><strong>Mechanisms</strong></th>
<th><strong>Mood</strong></th>
<th><strong>Cognition</strong></th>
<th><strong>Side-effects</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Postures, breath, meditation-rebalancing the mind-body connections</td>
<td>Reduces depression and enhances wellbeing in a few studies</td>
<td>A few uncontrolled studies showed improved attention and memory in nondemented adults</td>
<td>None</td>
</tr>
<tr>
<td>Biofeedback</td>
<td>Retraining of the autonomic nervous system or alpha-brain waves</td>
<td>No data available</td>
<td>Alpha peak in brain waves is associated with enhanced cognitive performance</td>
<td>None</td>
</tr>
<tr>
<td>Spirituality</td>
<td>Lowers stress and enhances cognition via church attendance and prayer</td>
<td>Improves depression in practitioners</td>
<td>Enhances cognitive performance in those who attend church</td>
<td>None</td>
</tr>
<tr>
<td>Aerobic Exercise</td>
<td>Improved cardiovascular function, release of endorphins, increased energy, mental stimulation</td>
<td>Improved mood and wellbeing, especially in minor depression</td>
<td>Modest improvement in cognition in dementia</td>
<td>None</td>
</tr>
</tbody>
</table>
Difficulties in Performing Research Studies

- Diagnostic approaches in the Eastern and Western Medicine are principally different
- Categorical DSM diagnoses are not consistent with the Eastern diagnoses (by pulse, tongue, miridians), and therefore, recommended therapeutic approaches should be different (=many depressions, anxieties, insomnias)
- Differences in practices and the lack of standardization among trained CAM professionals
- Difficult to translate into the accepted research design, and Western outcomes
- Self-selected bias in the volunteers
- Placebo effect maybe inflated in CAM

Lavretsky, Aging Health, February 2009
While there is a genuine inability of an individual to control much of the environment, there may be an advantage to the development of adjunctive methods of treatment for mental health disorders that will provide tools to manage environmental stressors over the life course.
Tai Chi and Qi Gong

- In 2002, over 2.5 million Tai Chi users and 500,000 Qi Gong users in the United States
- low-impact, traditional Chinese exercises with a low risk of side-effects and a lack of drug interactions.
- improve health-related quality-of-life in physical and mental health conditions.
- may be effective in reducing depressive symptoms, stress, anxiety, and mood
- evidence is promising but limited for Parkinson’s disease, traumatic brain injury, sleep disturbance, substance abuse, and impaired cognitive functioning.
Putative mechanisms

- promotes relaxation and decreases sympathetic output
- reduces clinical somatic symptoms, and benefits anxiety, depression, blood pressure, and recovery from immune-mediated diseases
- reduces levels of inflammatory markers (CRP), improves immune function and vaccine-response.
- reduces stress hormones of the HPA axis
- increases in peak oxygen uptake
- increases blood levels of endorphins and baroreflex sensitivity, and
- Electroencephalopathy (EEG) studies have found increased frontal EEG alpha, beta, and theta wave activity, suggesting increased relaxation and attentiveness
<table>
<thead>
<tr>
<th>Mental Disorder</th>
<th>Positive Findings</th>
<th>Negative Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>13 studies with significant positive findings, Only two with clinically diagnosed depression populations.</td>
<td>One study did not find effect on depressive symptoms.</td>
</tr>
<tr>
<td>Stress</td>
<td>4 studies with significant positive findings subjective stress measures, body temperature, and salivary cortisol levels.</td>
<td>One study did not find effect on subjective stress measures.</td>
</tr>
<tr>
<td>Anxiety</td>
<td>8 studies with significant positive effects</td>
<td>One study had negative findings on anxiety</td>
</tr>
<tr>
<td>Mood and psychological wellbeing</td>
<td>7 studies with significant positive effects.</td>
<td>One study did not find positive effect on mood.</td>
</tr>
<tr>
<td>Self-Esteem</td>
<td>1 study with significant positive</td>
<td>Two without positive effect.</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td>3 studies with significant positive effects.</td>
<td>None reported</td>
</tr>
<tr>
<td>Sleep Disturbance</td>
<td>3 studies with significant positive effects.</td>
<td>None reported</td>
</tr>
<tr>
<td>Substance Abuse</td>
<td>1 study with significant positive effects.</td>
<td>None reported</td>
</tr>
<tr>
<td>Cognitive Functioning</td>
<td>2 studies with significant positive effects.</td>
<td>None reported</td>
</tr>
</tbody>
</table>
Meta-analyses and review of yoga in older adults

- A systematic review with both narrative synthesis and meta-analysis.
- Original studies from 1950 to November 2010 were sought, evaluating the effects of yoga on older adults. The search was restricted to randomized controlled trials of yoga in subjects ≥ age 60, and published in English.
- The search yielded 18 eligible studies (N=649). The studies reported on older adults across a range of settings, intervention intensity, and outcome measures. The majority of the studies had <35 participants (range 9-77).
- The benefits of yoga may exceed those of conventional exercise interventions for self-rated health status, aerobic fitness, and strength.
- However, the effect sizes were modest, and the evidence was mixed for yoga's effect on depression, sleep, and bone-mineral density.
- Studies did not find an effect on cognition.
## Positive Findings

### Hypertension
- 22 pooled showed decline in both systolic and diastolic blood pressure ($-4.17$ and $-3.26$ mmHg, respectively)

### Osteoporosis
- In 2 studies, yoga practice increases muscular strength of specific groups, and muscle endurance for repetitive tasks, and delay bone loss and prevent fractures.

### Insomnia
- One cluster randomized trial of Silver yoga

### Stroke
- Several studies for emotional lability, poststroke hemiparesis improves

### Dementia
- 1 study with Preventing Loss of Independence through Exercise (PLIÉ) (Tai Chi, yoga, Feldenkrais, and dance movement)- improved memory
  - Functional changes included increasing body awareness, movement memory and functional skills. (2) Emotional changes included greater acceptance of resting, and a positive attitude towards exercise. (3) Improved coherent social interactions

### Diabetes
- 2 studies with significant positive effects. decrease in glucose, HbA(1c), lipids, cortisol, ferritin, MDA and a significant increase in catalase activity

### Osteoarthritis
- Several smaller studies for OA

### Healthy aging
- Prevention of depression, cognitive decline, osteoporosis in high risk groups

## Uncertainty

### Hypertension
- The type of yoga but not duration- yoga with postures, meditation, and breathing had larger reductions of $-8.17$ (systolic) and $-6.14$ (diastolic) mmHg

### Osteoporosis
- Anecdotal reduction in osteopenia

### Insomnia
- Unclear benefit for comorbid features like pain

### Stroke
- Unclear benefit for prevention

### Dementia
- 1. Functional changes included increasing body awareness, movement memory and functional skills. (2) Emotional changes included greater acceptance of resting, and a positive attitude towards exercise. (3) Improved coherent social interactions

### Diabetes
- Very few studies

### Osteoarthritis
- 1. Sleep improved but not pain.

### Healthy aging
- Yoga has a very important role to play in this as it influences physical, intellectual, emotional and spiritual dimensions of life.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Design and interventions</th>
<th>Outcome</th>
<th>Adverse events related to yoga</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Broota &amp; Dhir, 1990</strong></td>
<td>30 depressed psychiatric outpatients</td>
<td>3-arm RCT: Broota relaxation technique (based on yoga, includes four postures and pranayama) vs. progressive muscle relaxation vs. no treatment. Length of intervention: 3 days.</td>
<td>At endpoint, yoga group had fewer depressive symptoms than no treatment group on a depression symptom checklist.</td>
<td>Not discussed</td>
</tr>
<tr>
<td><strong>Janakiramaiah et al., 2000</strong></td>
<td>45 hospitalized patients with DSM-IV melancholic depression</td>
<td>3 arm RCT: Sudarshan Kriya Yoga (SKY) which includes pranayama and yoga nidra vs. electroconvulsive therapy (ECT) vs. imipramine. Length of intervention: 4 weeks.</td>
<td>At endpoint, ECT was superior to SKY; SKY and imipramine not significantly different on HRSD.</td>
<td>“No clinically significant side effects (e.g., seizures, confusion, cardiovascular accidents, hypomanic switch”</td>
</tr>
<tr>
<td><strong>Rohini, et al, 2000</strong></td>
<td>30 patients with DSM-IV MDD</td>
<td>2 arm RCT: Full SKY vs. “partial” SKY (which did not include a key breathing component). Length of intervention: 4 weeks.</td>
<td>At endpoint, no differences between groups on BDI.</td>
<td>Not discussed</td>
</tr>
<tr>
<td>Study</td>
<td>Sample Description</td>
<td>Study Design</td>
<td>Intervention Details</td>
<td>Results</td>
</tr>
<tr>
<td>-----------------------</td>
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<td>---------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Sharma et al., 2005</td>
<td>30 patients with DSM-IV MDD</td>
<td>2 arm RCT: Sahaj yoga (meditation) vs. attention control (sitting quietly). All participants received antidepressants. Length of intervention: 8 weeks.</td>
<td>Over 8 weeks, yoga &gt; control group in changes in depressive symptoms (on HRSD) over time.</td>
<td>“No significant clinical side effects (confusion, cardiovascular accidents, hypomanic switch, etc.)”</td>
</tr>
<tr>
<td>Butler et al., 2008</td>
<td>46 participants with chronic depression (i.e., MDD for &gt; 2 years or dysthymia)</td>
<td>3 arm RCT: Hatha yoga + meditation + psychoeducation vs. group therapy + hypnosis + psychoeducation vs. psychoeducation alone (control group). Length of intervention: 12 weeks.</td>
<td>No assessments at 12 weeks. Yoga &gt; control on % remitted at 9 months (assessed via SCID). No differences between groups in change in HRSD-26 item over 9 months.</td>
<td>Not discussed</td>
</tr>
<tr>
<td>Kinser et al., 2013</td>
<td>27 women with MDD or dysthymia</td>
<td>2 arm RCT: Gentle hatha yoga vs. health and wellness program. Length of intervention: 8 weeks.</td>
<td>No differences between groups in change over time on PHQ-9.</td>
<td>Not discussed</td>
</tr>
<tr>
<td>Sarubin et al., 2014</td>
<td>60 inpatients with MDD</td>
<td>2 x 2 RCT: Hatha yoga vs. no yoga; quetiapine vs. escitalopram. Length of intervention: 5 weeks</td>
<td>No differences between hatha yoga and no yoga group in rates of response (50% reduction in HAMD)</td>
<td>Not discussed</td>
</tr>
</tbody>
</table>
Yoga, Meditation and Cognition

- Chiesa et al 2011—compared to the control group, meditators showed improved in:
  - sustained attention
  - conflict monitoring
  - working memory
  - domains of memory- meta-awareness and in specific autobiographical memories.

- Age-related cognitive decline, suggested due to the regulation of glucocorticosteroids, inflammation and serotonin metabolism, or directly neuroplastic

Meditation (MBSR) Programs for Psychological Stress and Well-being: A Systematic Review and Meta-analysis
Goyal, et al 2014

- Meta-analyses- after 18 753 citations, included 47 trials with 3515 participants.

- Mindfulness meditation programs had moderate evidence of improved anxiety (effect size, 0.38 [95%CI, 0.12-0.64] at 8 weeks and 0.22 [0.02-0.43] at 3-6 months), depression (0.30 [0.00-0.59] at 8 weeks and 0.23 [0.05-0.42] at 3-6 months), and pain (0.33 [0.03- 0.62])

- Low evidence of improved stress/distress and mental health–related quality of life, positive mood, attention, substance use, eating habits, sleep, and weight.

- Clinicians should be aware that meditation programs can result in small to moderate reductions of multiple negative dimensions of psychological stress.
Long-term concentrative meditation and cognitive performance among older adults.
Ravi Prakash et al, 2014

- In a cross-sectional study comparing the cognitive performance of older meditators and non-meditators.

- Twenty (age > 55 years) long-term practitioners of Vihangam Yoga meditation (>10 years of practice) were compared to non-meditators on tests of short-term memory, perceptual speed, attention, and executive functioning.

- Vihangam Yogis showed significantly better performances in all these tests of attention ($p < .05$) except for the digit backward test, where a trend ($p = .08$) was found in favor of meditators.

- Conclusion: Long-term Vihangam Yoga meditators have superior cognitive abilities than non-meditators in the old age group. This technique should be studied further for its ability to prevent age-related cognitive decline.
Complementary Use of Tai Chi Improves Resilience, Quality of life, and Cognitive Function in Depressed Older Adults.
METHODS

■ 112 older adults with major depression age 60 years and older were recruited and treated with 10 mg of escitalopram for the first 6 weeks.

■ 73 partial responders (Ham-D >6 and more than 30% improvement) to escitalopram continued to receive 10 mg of escitalopram per day and were randomly assigned to 10 weeks of either complementary intervention:

■ 1. Tai Chi Chih for 2 hours per week; or 2. Health Education Program for 2 hours per week.
Results

- Both Tai Chi (TC) and Health education (HE) participants demonstrated improvement in the severity of depression, but TC subjects >HE

- Tai Chi group demonstrated significantly greater improvement compared to HE group in:
  - Resilience
  - Energy and psychomotor retardation
  - Physical functioning
  - Cognitive measures of executive cognitive function, attention, and memory
% Responders at Week 16
(HAM-D_{24} \leq 10)

- HE
- TCC
DEPRESSION: HAM-D_{24}

- Health Ed
- Tai Chi Chih

Week
## Physical and Cognitive Functioning

<table>
<thead>
<tr>
<th></th>
<th>esCIT+ TC (N=36) Mean (SD)</th>
<th>esCIT+ HE (N=37) Mean (SD)</th>
<th>t; P DF=1, 57</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women**</td>
<td>23 (63.9%)</td>
<td>22 (59.9%)</td>
<td>0.6; 0.8</td>
</tr>
<tr>
<td>Age (years)</td>
<td>69.1 (7.0)</td>
<td>72 (7.4)</td>
<td>-1.7; 0.09</td>
</tr>
<tr>
<td>Education (years)</td>
<td>16.1 (2.5)</td>
<td>15.1 (2.5)</td>
<td>1.8; 0.07</td>
</tr>
<tr>
<td>SF-36 physical functioning at week 16</td>
<td>97.3 (4.1)</td>
<td>91.1 (13.1)</td>
<td>2.6; 0.012</td>
</tr>
<tr>
<td>SF-36 role emotional at week 16</td>
<td>83.9 (25.2)</td>
<td>71.2 (28.3)</td>
<td>1.9; 0.056</td>
</tr>
<tr>
<td>CVLT long delayed recall at week 16</td>
<td>11.6 (3.2)</td>
<td>9.7 (4.0)</td>
<td>2.1; 0.043</td>
</tr>
<tr>
<td>Stroop 3 errors at week 16</td>
<td>0.03 (0.2)</td>
<td>0.32 (0.6)</td>
<td>-2.8; 0.008</td>
</tr>
<tr>
<td>Trail A errors at week 16</td>
<td>0.2 (0.5)</td>
<td>0.6 (1.0)</td>
<td>-1.8; 0.07</td>
</tr>
</tbody>
</table>
HRQOL: SF-36 Physical Functioning

- Health Ed
- Tai Chi Chih

Baseline vs Week 16 comparison.
What else did I learn?

- HE is an active control - boosting social support and it is easy to follow
- TCC – not everybody “gets” it
- Adherence and satisfaction did not differ
- Personalized approach of Mind-Body medicine may improve treatment response to standard antidepressants on multiple outcomes and reduce exposure to multiple drugs
Conclusions

- Complementary use of mindful exercise combined with standard antidepressants may provide additional improvement in clinical outcomes of geriatric depression such as resilience, quality of life, and cognitive function.

- The Mechanism – via stress reduction, decreased inflammation, epigenetic changes.

- Neuroplastic mechanisms are tested in the new R-01 using Tai Chi vs HE added to standard antidepressants.
Yogic meditation to reduce stress and improve functioning in family dementia caregivers

- Sponsored by the Alzheimer’s Research Prevention Foundation

Lavretsky et al 2012; Black et al 2012; Pomykala et al 2012
Objectives

- To compare psychological, cognitive, and neurobiological effects of yogic meditation versus relaxation in stressed and depressed family dementia caregivers
- Practice for 12 minutes per day for 8 weeks.
The stress/health model applied to caregiving

Primary stressors:
- Care recipient disability
- Problem Behaviors

Secondary stressors:
- Family or work problems

Appraisals of demands and adaptation

Emotional response

Morbidity/Mortality

INTERVENTIONS
- Family counseling
- Social Support
- Psychoeducation/communication
- Skills training
- Self-care prevention

2 pilot meditation studies are available

Schulz, & Martire 2004
Gene-Environment Interaction and Stress-Vulnerability Model

STRESSORS
Patient characteristics- stage of dementia, problem behaviors
Caregiver characteristics
Time in caregiving, losses

Innate characteristics
Age, sex, race, Genetic (5-HTTLPR; IL-6 genes)
Personality/affective style
Resilience

Intermediate phenotypes
Emotional processing
Negative ruminations (fMRI)
Amygdala, Subgenual Cingulate
Il6, cytokines, cortisol, DHEA

Phenotypes
1. Depression / No Depression
2. Resilience
Kirtan Kriya versus Relaxation for stressed dementia caregivers

- 39 stressed caregivers with minor depressive symptoms randomized to 12 minutes per day meditation versus passive listening to instrumental music tapes for 8 weeks

- Distress, depressive symptoms, anxiety, burden

- Cytokines, cortisol, catecholamines, cognition, PET scan, fMRI, NFkappaB, telomerase, gene expression
What is Kirtan Kriya?

• **Kirtan Kriya** is a 11-minute chanting exercise in the Kundalini yoga tradition that people have been practicing for thousands of years. This meditation involves repetitive finger movements, or mudras, plus verbal chanting and silent chanting of the mantra “Saa Taa Naa Maa.”

• **What does Kirtan Kriya mean in English?**

A **kirtan** is a song. These ancient primal sounds from Sanskrit mean “birth, life, death, rebirth.” Kriya refers to a specific set of movements or chants.

• In the yogic tradition, kriyas are used to help bring the body, mind, and emotions into balance, thus creating healing.

• **Focus of attention**
### Group comparison in 39 completers

<table>
<thead>
<tr>
<th>Variables</th>
<th>Meditation (N=23)</th>
<th>Relaxation (N=16)</th>
<th>t; P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60.5 (8.2)</td>
<td>60.6 (12.5)</td>
<td>0.03; 0.9</td>
</tr>
<tr>
<td>Education</td>
<td>16.1 (2.1)</td>
<td>15.1 (2.8)</td>
<td>-1.2; 0.2</td>
</tr>
<tr>
<td>Month of depression</td>
<td>45.1 (35.4)</td>
<td>39 (21.2)</td>
<td>-0.6; 0.5</td>
</tr>
<tr>
<td>Yrs of caregiving</td>
<td>4.7 (2.4)</td>
<td>4.2 (2.9)</td>
<td>-0.6; 0.6</td>
</tr>
<tr>
<td>Hours per week</td>
<td>47.8 (35.8)</td>
<td>63.3 (36.2)</td>
<td>-0.2; 0.2</td>
</tr>
<tr>
<td>CIRS</td>
<td>3.0 (2.3)</td>
<td>4.6 (3.1)</td>
<td>1.8; 0.08</td>
</tr>
<tr>
<td>CVRF</td>
<td>5.2 (3.7)</td>
<td>7.4 (6.4)</td>
<td>1.4; 0.2</td>
</tr>
<tr>
<td>HAMD baseline</td>
<td>11.8 (4.1)</td>
<td>11.4 (4.0)</td>
<td>-0.3; 0.7</td>
</tr>
</tbody>
</table>

Lavretsky et al 2012 Int J Geriatr Psychiatry
HAMD scores over time

- Meditation
- Relaxation

Axes:
- Y-axis: Scores (0-14)
- X-axis: HAMD0, HAMD2, HAMD4, HAMD6
Resilience

Baseline

Week 8

Meditation

Relaxation
Cognition - Trail B seconds

Baseline vs Week 2:
- Meditation line (brown)
- Relaxation line (cyan)

Y-axis: 0 to 120 seconds
X-axis: Baseline to Week 2
NFkB expression

- **Nuclear Factor kappa Beta (NFkB)** has been linked to chronic stress; the body’s immune responses such as inflammation-induced carcinogenesis and anti-tumor immunity.

- NFkB expression as a measurement of stress reduction.

- NFkB expression in the monocytes was examined using intranuclear staining and flow cytometry.

- The preliminary data has shown significant increases in NFkB expression in meditation subjects, and decreases in samples stimulated to induce inflammatory effects.

Black et al PNE 2012
Mean Total Cells Under High Stimulation
Expressing NFkB Pre and Post Study

Percent Cells

Pre/Post study

Relaxation Audio
- Meditation
Telomerase activity

- **Telomere** (protective DNA sequence at the ends of chromosomes) length is a biomarker of biological age linking stress and disease.

- Greater stress and negative affect and vascular risk factors are associated with lower telomerase activity.

- Predictor of long-term cellular viability, which decreases with chronic stress.

Lavretsky et al Int J Geriatric Psychiatry 2012
Telomerase activity

![Graph showing Telomerase activity over Week 8 with lines for Meditation and Relaxation]
Microarray analyses

Controlling for age, sex, race, years of education, BMI, duration of distress and depression, and history of depression, 19 gene transcripts showed systematic up-regulation over time (Group x Time interaction ≥ 20% difference across groups) - immunoglobulin-related transcripts (e.g., IGJ, IGLL3) and multiple un-named genes of unknown function (LOC genes) 45 genes showed systematic down-regulation - transcripts included pro-inflammatory cytokines (IL8) and activation-related immediate-early genes (JUN, FOSB) Transcript origin analyses identified plasmacytoid dendritic cells and B lymphocytes as the primary cellular context of these transcriptional alterations (both p < .001) Promoter-based bioinformatic analysis implicated reduced NF-kappa B signaling and increased activity of Interferon Response Factor 1 in structuring those effects (both p < .05). Black et al PNE 2012
Promoter-based bioinformatic analysis implicated reduced NF-kappaB signaling and increased activity of Interferon Response Factor 1 in structuring those effects (both $p < .05$).
FIGURE 1. Cross sectional view shown above displays the crosshair intersection within the right inferior frontal area. This region was the most significant and largest cluster demonstrating a decrease in the meditation group compared to the control group over time (t=4.74 with p=0.001, 160 conti voxels at p<0.01).
FIGURE 2. Cross sectional view shown above displays the crosshair intersection at (-44,-74,-16), within the left associative visual cortex. This region also decreased in the meditation group compared to the control group over time ($t=4.15$, $p=0.002$).
Study Design

- 9 subjects
- Practiced Kirtan Kriya for 3 months
- Experimental Paradigm:

Block Design

| REST | MEDITATION | REST | TAP | REST | CHANT | REST | VISUAL |
(a) Block Design; (b) Kirtan Kriya meditation consists of four finger positions and corresponding chants, which are to be completed while simultaneously visualizing light.

(c) Group level contrasts for each of the Kirtan Kriya elements > Relaxation (red/yellow), and Relaxation > Elements (blue) (image provided by Pamela Douglas).
Activation pattern

- **Tapping and chanting** activated pre- and postcentral gyrus.

- **Visualization** activated **superior lateral occipital cortex** compared to resting state.

- **Kirtan Kriya** show activity in **medial frontal cortex**, **medial occipital cortex**, and prominent activation in **bilateral temporal poles**.

- **Default mode network (DMN) map** demonstrated a large attenuation of the low frequency oscillation following the initiation of mediation.
(a) Group level results for Kirtan Kriya > Rest (red), and Rest > Kirtan Kriya (blue) 
(b and c) Default mode network IC spatial map and corresponding time course with attenuation of DMN following the onset of mediation shown in (c).
Independent Component Analysis

Group ICA (gICA)
- High variance ICs for relaxation condition resemble DMN.

(image provided by Pamela Douglas).
fMRI in meditators showed higher activity in a functional network including the anterior cingulate, fronto-orbital cortex and insula

(Light blue areas show the ACC-orbito-insular network, pink for group difference, z=1.7, p<.05)
Neural mechanisms of Kirtan Kriya

- The elements of Kirtan Kriya activated regions known to be associated with each task.
- Meditation strongly activated bilateral temporal pole, known to be involved in empathy.
- The difference between meditators and non-meditators showed higher activity in the anterior cingulate, fronto-orbital cortex and insula (self-referential, self-evaluation).
- DMN activity was largely suppressed throughout the course of Kirtan Kriya meditation, meaning that Meditation is not Rest;
- Meditation has “brain fitness effect.”
Cognition and neuroplasticity in response to yoga versus memory training in older adults with MCI

- 14 yoga and 11 MET participants compared after 12 weeks of Kundalini yoga (with Kirtan Kriya) or memory training in older adults (>54 y.o.) with MCI using resting-state fMRI.

- Yoga participants showed increased connectivity in DMN (medial frontal gyrus, subgenual and pregenual anterior cingulate cortex), salience network (right insula, frontal orbital cortex, and striatum); and decreased connectivity in the left sensory-motor network (left precentral, postcentral gyrus, and superior parietal lobe) vs. MET.

- Significant changes in DMN, salience, and sensory-motor networks observed in senior participants with yogic meditation may reflect a brain function improvement after yogic meditation.
Legend
Default Mode Network (DMN) in the yogic meditation (YOG) versus memory enhancement training (MET) groups (p < 0.05, corrected). The yellow region is the identified resting state DMN commonly engaged in the YOG and MET groups. The red regions indicate increased connectivity in the YOG than MET participants after training of 12 weeks; The light and deep blue bars indicate connectivity at baseline and followup for MET group; the light and deep green bars indicate connectivity at baseline and followup for YOG group.
Legend
Salience Network in the yogic meditation (YOG) versus memory enhancement training (MET) groups (p < 0.05, corrected). The yellow region is the identified resting state salience network commonly engaged in the YOG and MET groups. The red regions indicate increased connectivity in YOG than MET participants after training of 12 weeks; The light and deep blue bars indicate connectivity at baseline and followup for MET group; the light and deep green bars indicate connectivity at baseline and followup for YOG group.
Conclusion

- Very promising results for future studies of yoga/Tai Chi/meditation vs. drugs vs. behavioral approaches for prevention of depression in high-risk group of caregivers.

- Cognitive and neuroplastic effects can be of interest for prevention of cognitive decline.

- Acceptability is improved with the use of non-pharmacological and spiritual interventions, especially in ethnic minorities.
Sponsors and collaborators

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- **Collaborators:**
  - Michael Irwin, Liz Breen, and the Cousins Center-PNI - inflammatory markers
  - Elissa Epel and UCSF Blackburn lab - telomerase
  - Katherine Narr, Pamela Douglas, Marco Iacoboni; Hongue Yang and Brain Mapping Center (fMRI)
  - Coordinators: Natalie St Cyr; Nora Nazarian; Irena Chuchev
References


Thank you!