

Rethinking Mental Health: Spirituality, Healing and Culture

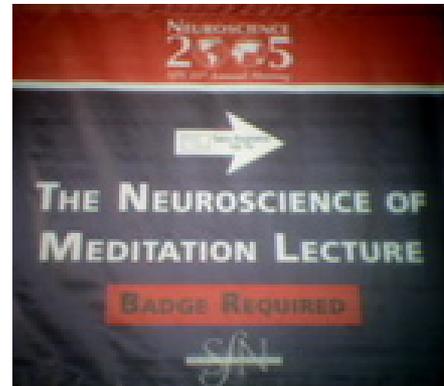
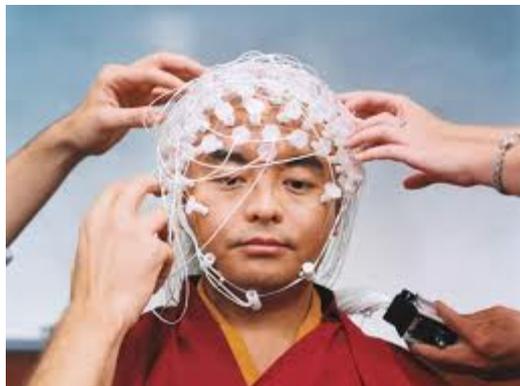
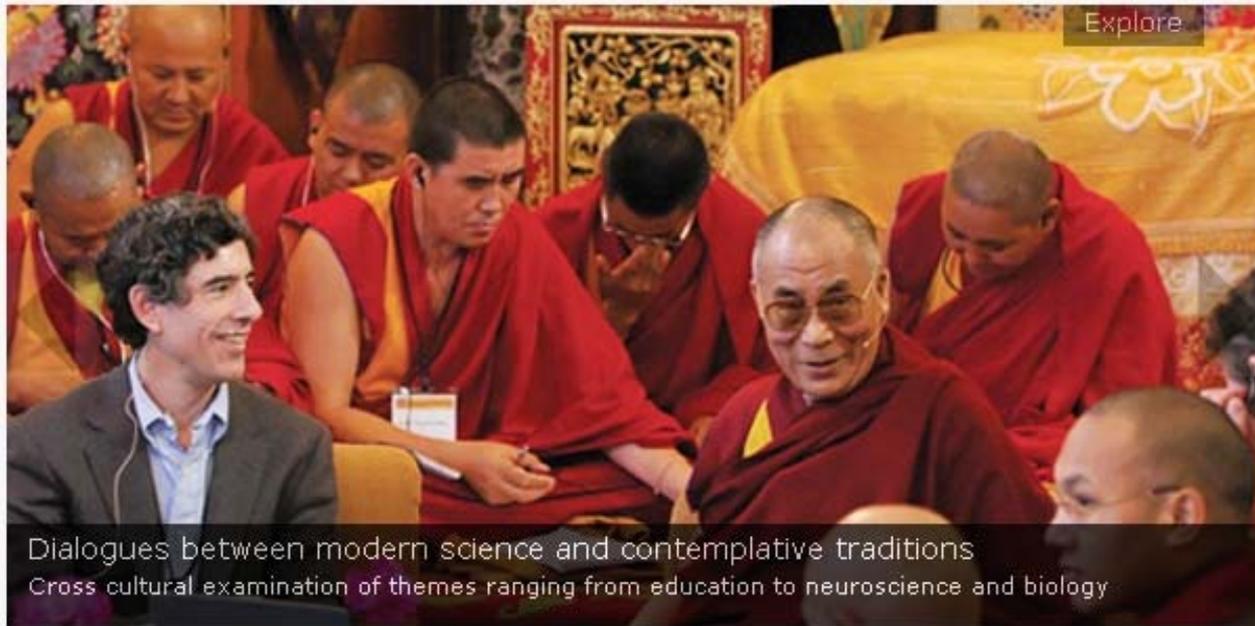
Lecture: Neuroscience and Meditation

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Boston University

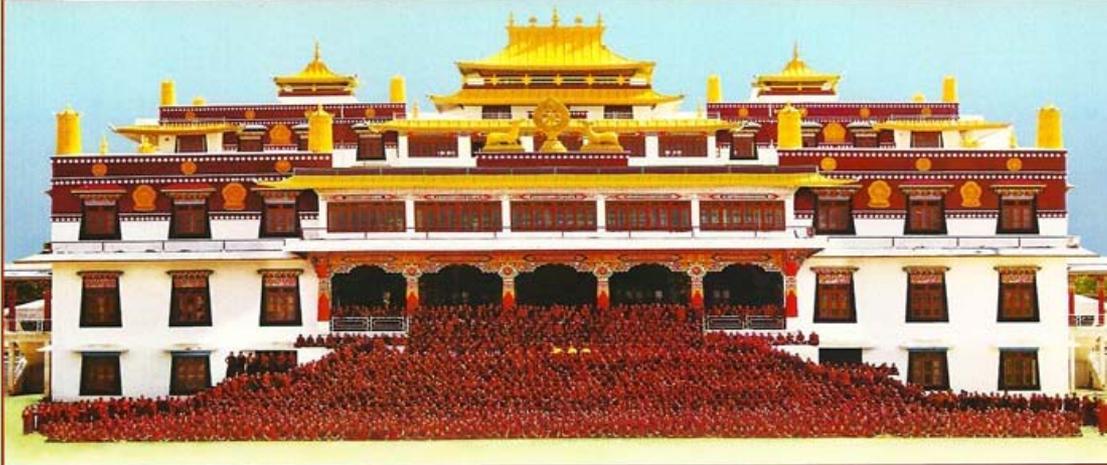
Feb 12, 2011

Scientific study of meditation: Exchanges between scientists and contemplatives



A New Chapter in the History of Education

On January 7, 2008, His Holiness the Dalai Lama officially introduced the Emory-Tibet Science Initiative to an assembly of over 15,000 Tibetan monastics at Drepung Loseling Monastery in India. The launching of this visionary and far-reaching program marks a new chapter in the history of the Tibetan monastic academic system, which traces back over a millennium, and a new frontier for science education.



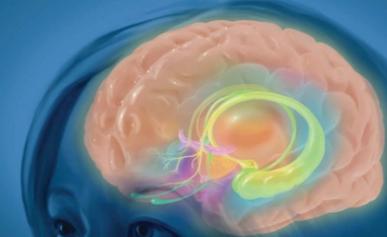
"The more modern science and the ancient science of mind come together and work together, the more our knowledge will be expanded. Then eventually we can educate humanity on the importance of our inner world, our mind, in order to promote peaceful families, a peaceful society, and a peaceful world."

- H.H. the Dalai Lama



མྱེད་པའི་གནས་ལུགས།

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EMORY
TIBET
SCIENCE
INITIATIVE

A quick history of the scientific study of meditation: the early stages

- Transcendental Meditation (TM)
- Herbert Benson (1975): Meditation (and other contemplative practices) induce a “Relaxation Response”, which is the opposite to the “stress response”

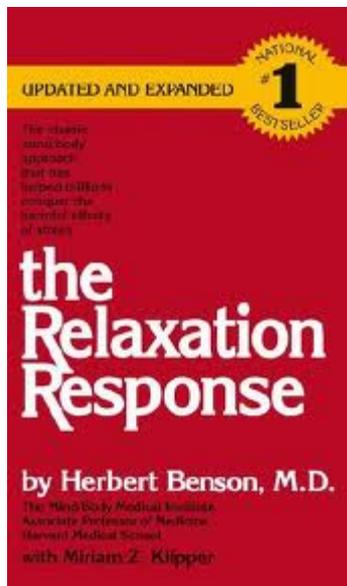
Body changes during stress



Image source:

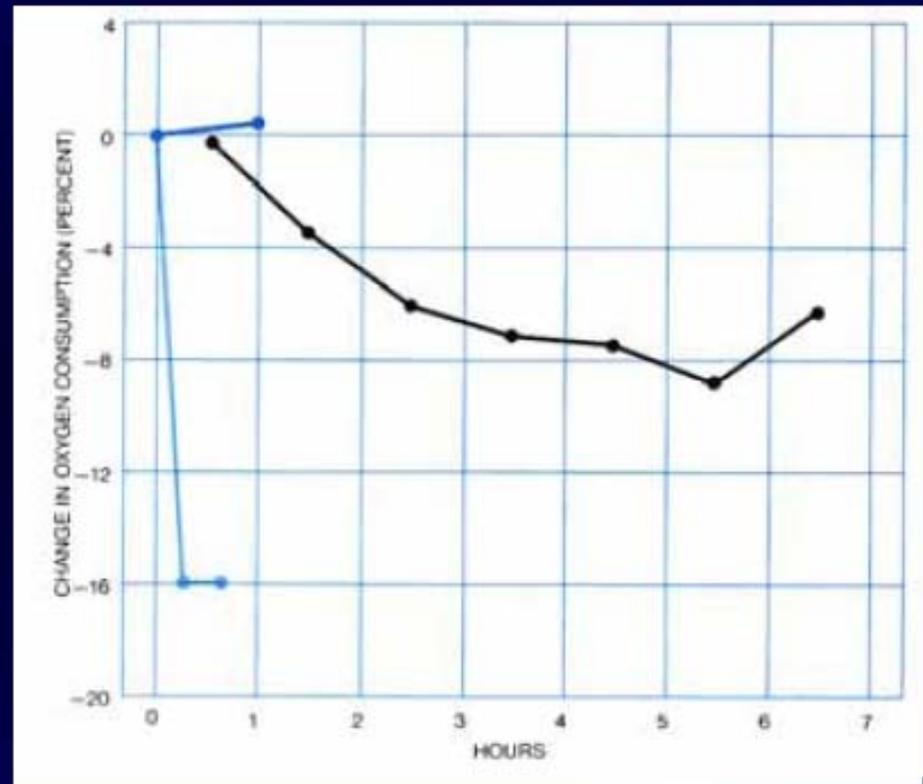
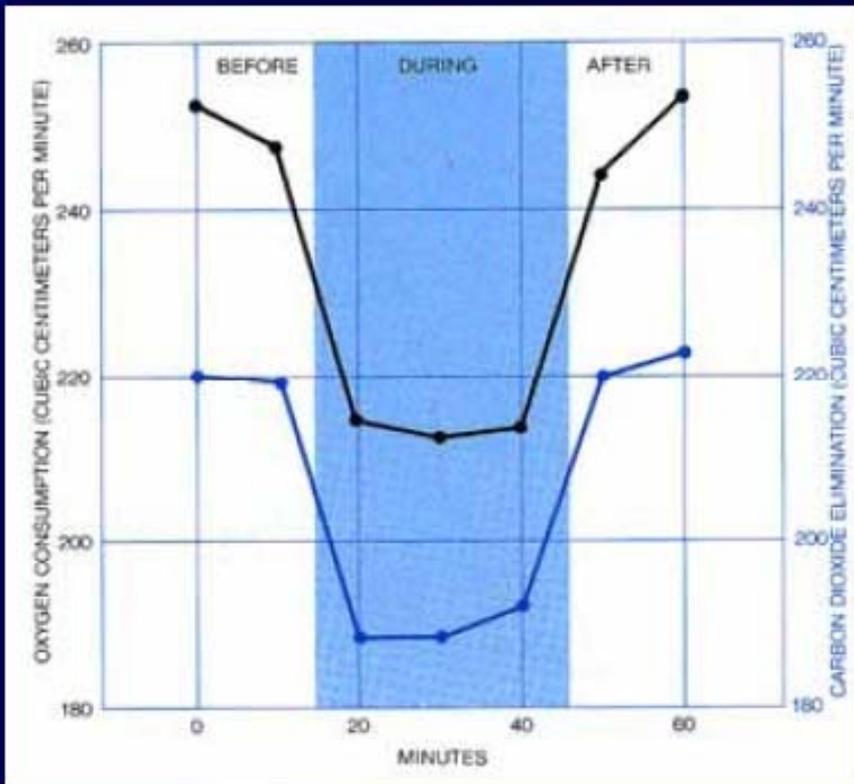
http://www.atomicmeme.com/_imgs/learninghub/stressbiol/body_fight_flight2.png

H. Benson (1975): *the Relaxation Response* [is what meditation does]



 Relaxation Response	 Stress Response
<ul style="list-style-type: none"> ↓ Heartrate slows ↓ Blood Pressure lowers ↓ Blood Lactate Levels reduce ↑ Immune System improves ↑ Sense of Well-being increases ↑ Sleep improves ↑ Normal Libido ↓ Brain Wave Patterns slow ↑ Digestion improves 	<ul style="list-style-type: none"> ↑ Heartrate increases ↑ Blood Pressure rises ↑ Cholesterol Levels go up ↓ Immune System is less effective ↑ Anxiety increases ↑ Depression more prevalent ↑ Sleep Disorders increase ↓ Libido decreases ↑ Irritability increases ↓ Digestion works less effectively

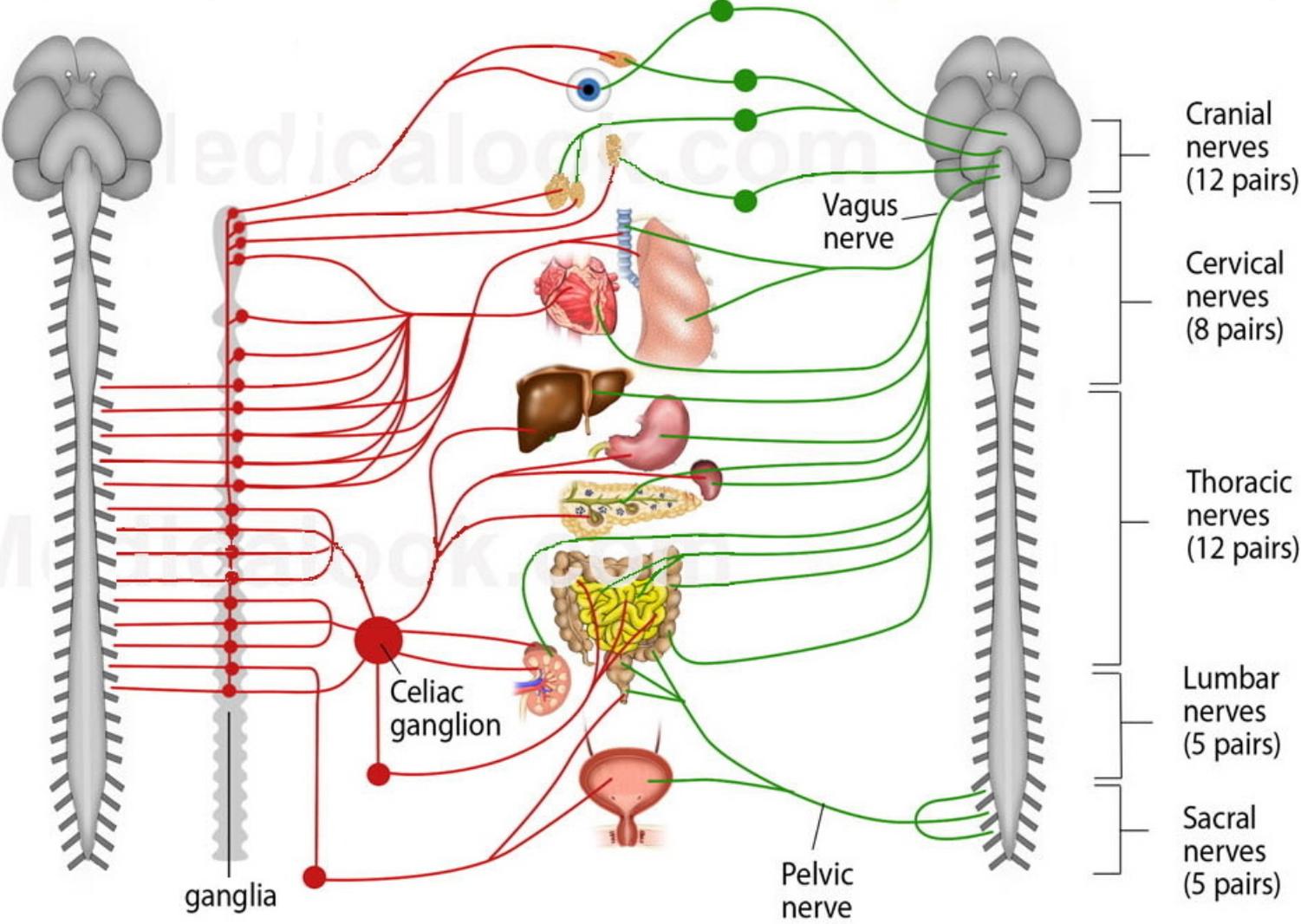
Physiology of Meditation



From: *The physiology of meditation*,
Wallace RK & Benson H, *Scientific American* 226:85, 1972.

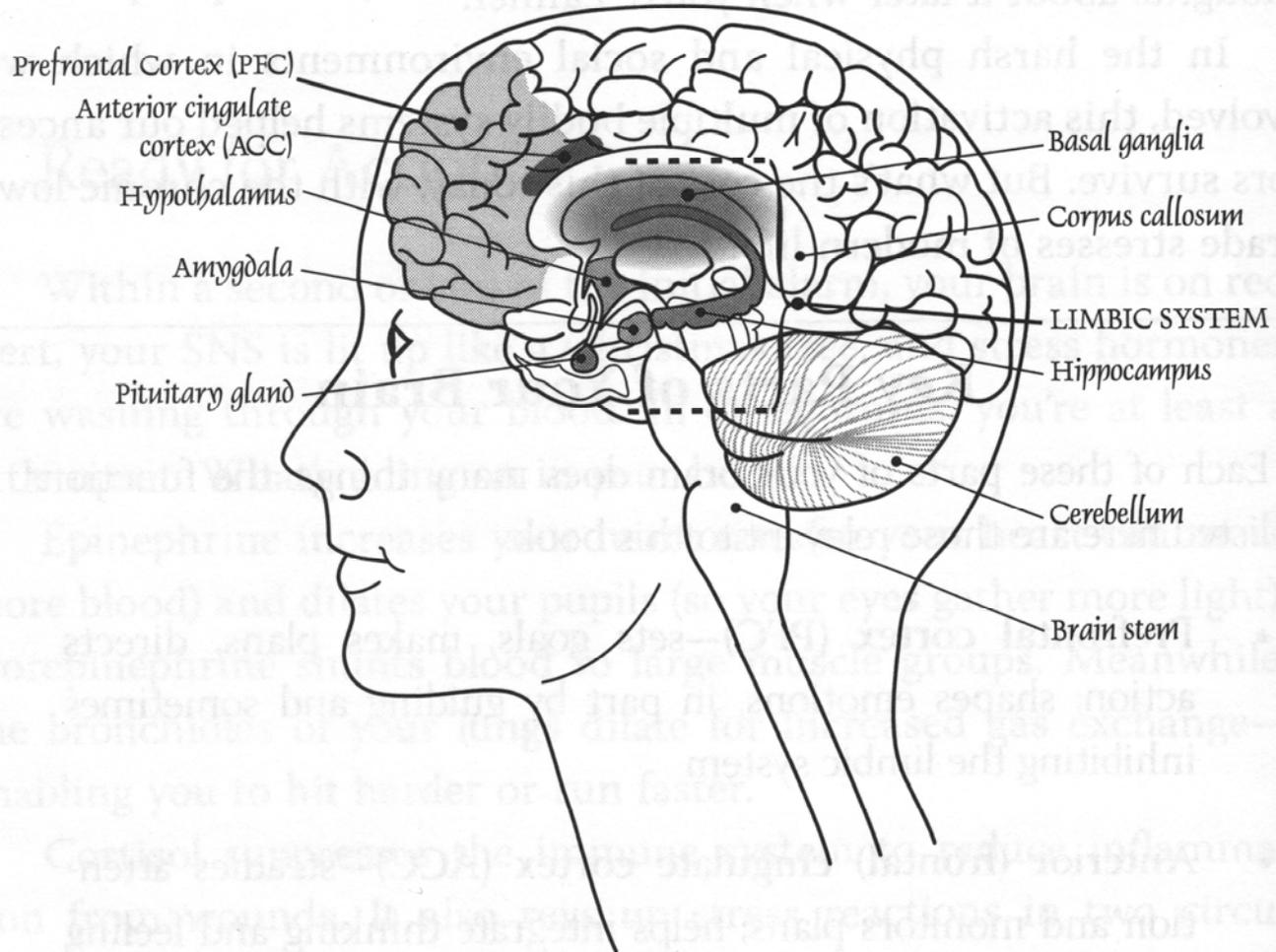
Sympathetic Nervous System : Fight-or-flight

Parasympathetic Nervous System: Rest-and-digest



... but recent research suggests that there is more to meditation than the relaxation response.

A quick tour of the brain



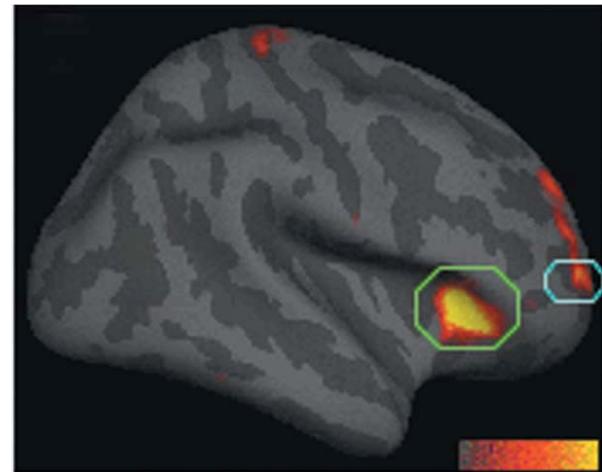
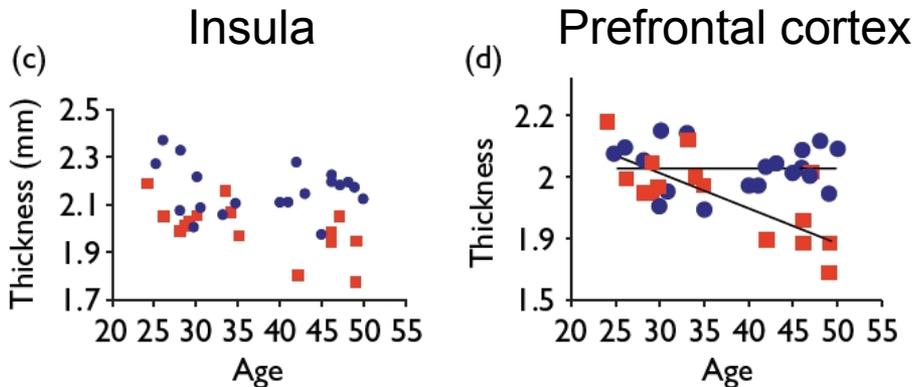
- Prefrontal cortex (PFC): sets goals, makes plans, directs action; shapes emotions, in part by guiding and sometimes inhibiting the limbic system
- Anterior cingulate cortex (ACC): steadies attention and monitors plans; helps integrate thinking and feeling
- Insula: interoception (senses the internal state of the body), including “gut feelings”; linked to empathy
- Thalamus: major relay station for sensory information
- Corpus callosum: bundle of fibers passing information between the two brain hemispheres
- Limbic system: includes the basal ganglia, hippocampus, amygdala, hypothalamus, and pituitary gland; central to emotion and regulation
- Basal ganglia: involved with rewards, stimulation seeking, and movement
- Hippocampus: forms memories, detects threats, ...
- Amygdala: responds very quickly to emotionally charged stimuli (especially negative ones); acts like an “alarm bell” to detect danger in the environment
- Hypothalamus: regulates primal drives such as hunger and sex; produces oxytocin; activates pituitary gland
- Pituitary gland: makes endorphins (i.e. internal “opiate”); triggers sex hormones; stores and releases oxytocin.

Please note: the above list is an oversimplification! Each of these brain areas is involved in many other functions as well. Neuroscience is still a very young science, and we are only beginning to understand how the brain works.

Recent findings in neuroscience about meditation

Long-term changes in brain anatomy :

Meditation practitioners may have thicker cortex in brain regions associated with attention, interoception and sensory processing, including the prefrontal cortex and right anterior insula. Meditation might offset age-related cortical thinning.



From Lazar et al., 2005, *Neuroreport*

Recent findings in neuroscience about meditation: MBSR

- The eight-week Mindfulness-Based Stress Reduction (MBSR) Program has many beneficial effects on mental health, demonstrated in randomized controlled studies
- For example, it helps with chronic pain, autoimmune diseases (psoriasis), anxiety, depression...
- [See upcoming lecture on Mindfulness and Depression]
- However, the *mechanisms* by which MBSR works are still largely unknown and under investigation.
- For example, a recent study found small changes in the brain after 8 weeks of MBSR (see next slide)

Hölzel et al., 2011: Mindfulness practice leads to increases in regional brain gray matter density

Well



Tara Parker-Pope on Health

January 28, 2011, 10:29 AM

How Meditation May Change the Brain

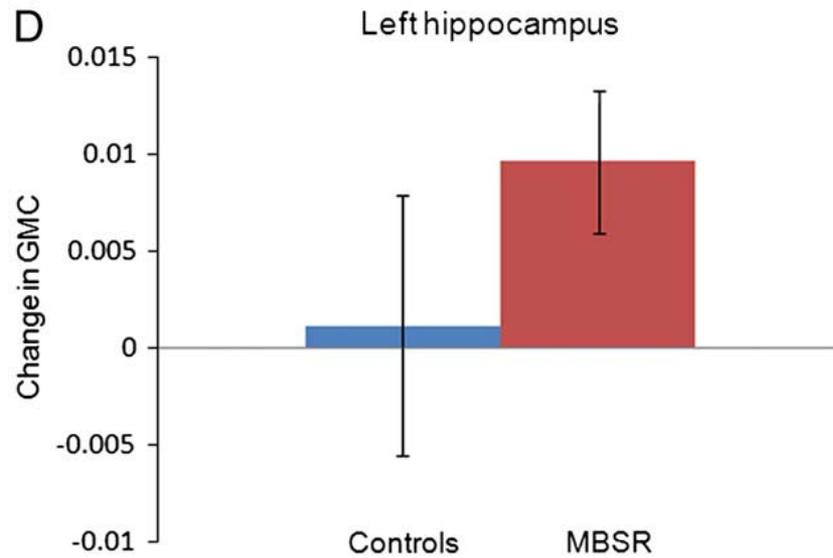
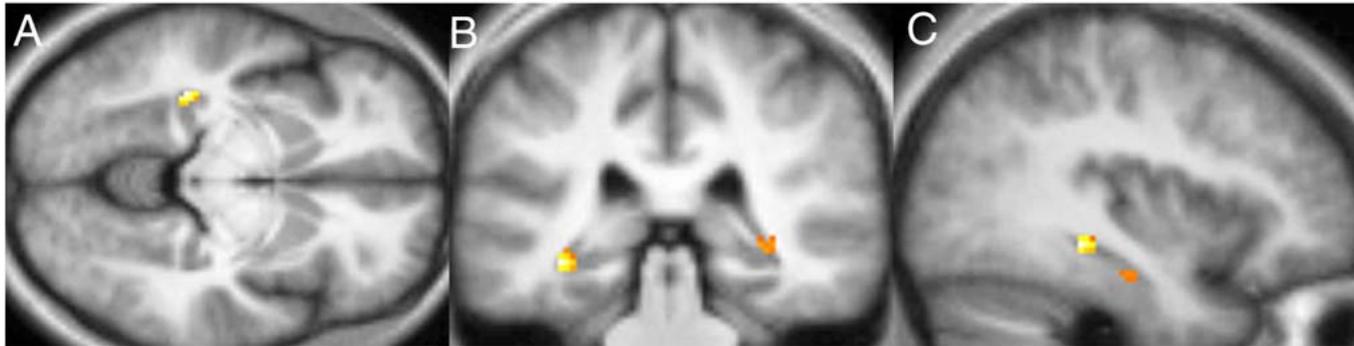
By SINDYA N. BHANOO



“Participants who meditated for about 30 minutes a day for eight weeks had measurable changes in gray-matter density in parts of the brain associated with **memory, sense of self, empathy and stress.**

M.R.I. brain scans taken before and after the participants’ meditation regimen found increased gray matter in the **hippocampus**, an area important for learning and memory. The images also showed a reduction of gray matter in the **amygdala**, a region connected to anxiety and stress. A control group that did not practice meditation showed no such changes.”

From: <http://well.blogs.nytimes.com/2011/01/28/how-meditation-may-change-the-brain/>



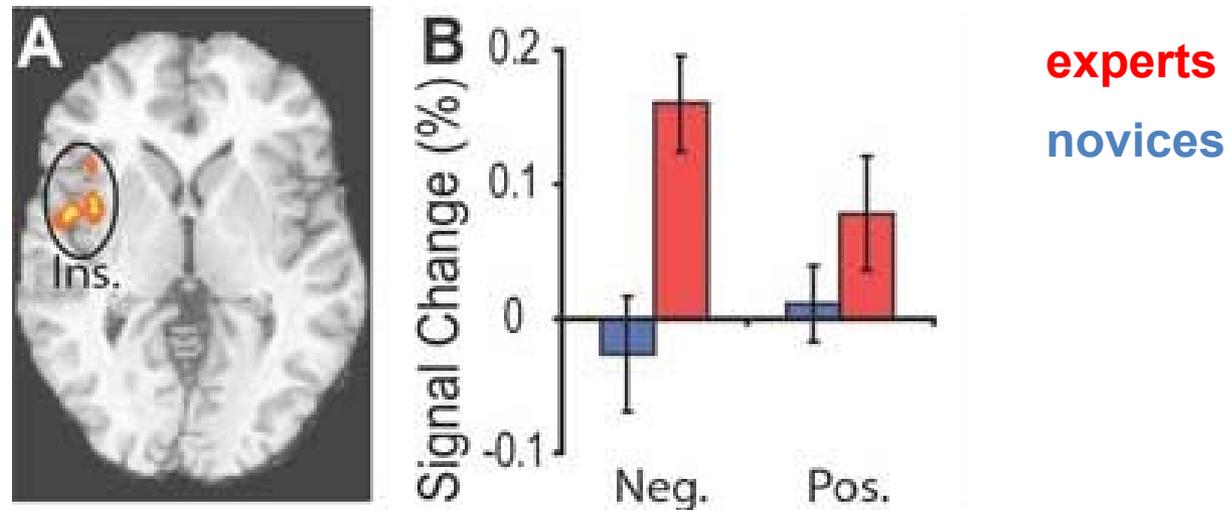
From Hölzel et al., 2011, *Psychiatry Research: Neuroimaging*

Recent findings in neuroscience: loving-kindness and compassion meditation

Most meditation research has focused on practices that emphasize calming the mind (e.g. TM), improving focused attention, or developing mindfulness (e.g. MBSR).

More recently, neuroscience research has turned to compassion and loving-kindness meditation.

In lovingkindness-compassion meditation, **expert practitioners** (compared to **novices**) show more, not less, emotional reactivity to sounds of people in distress: faster heart beat, and stronger response in the insula (linked to interoception and empathy), which cannot be explained by the relaxation response hypothesis.



From Lutz et al., 2008, *PLoS ONE*, Regulation of the Neural Circuitry of Emotion by Compassion Meditation: Effects of Meditative Expertise

“Pure Compassion” meditation can induce strong EEG patterns previously associated with positive emotionality and enhanced adaptive immune functioning:

(Lutz et al., 2004, *Proceedings of the National Academy of Sciences*, Long-term meditators self-induce high-amplitude gamma synchrony during mental practice)

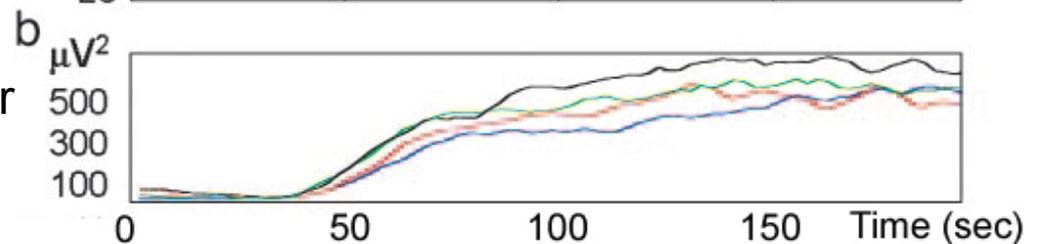
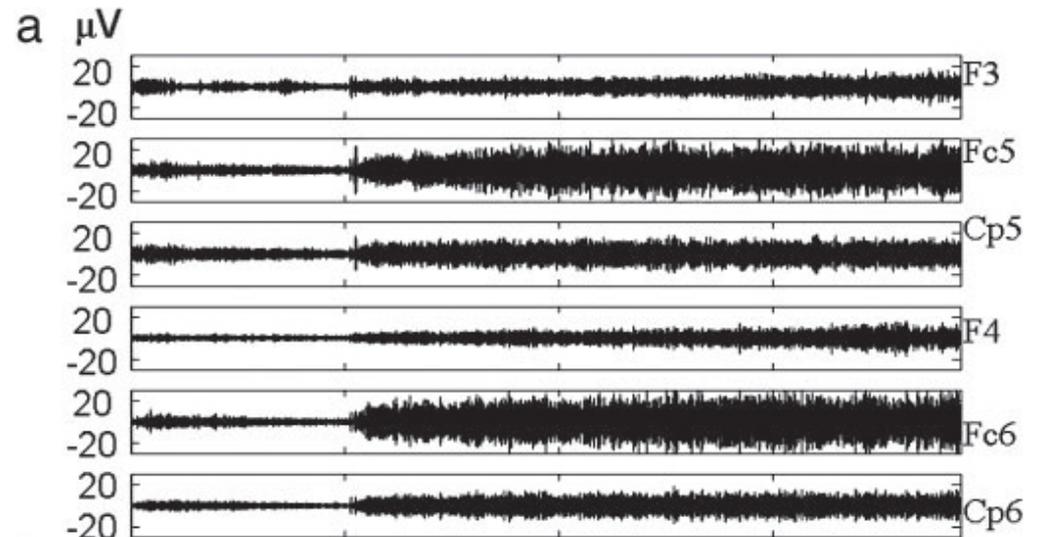
EEG brain waves during compassion meditation



EEG Gamma power

These high-amplitude gamma-band oscillations and phase-synchrony are “off-the-chart” from the normal range.

Lutz et al., 2004 *PNAS*



Start Compassion meditation

Phenomenology vs. hypothesis-driven research

At this point in time, meditation neuroscience is still at the stage of observing and describing what happens phenomenologically. There is no scientific theory quite yet, but this is the topic of active research.

Ongoing research at Emory University

Physiological mechanisms linked with **meditation:**

Meditation may improve emotional and physical health by **reducing inflammatory reactivity to stress and illness**

Depression itself is characterized by **increased inflammation** (Raison et al., *Trends in Immunology*, 2006)

Also inflammatory: fibromyalgia, neuropathic pain, heart disease, stroke, Alzheimer's disease, etc.



Dr. Chuck Raison, MD,
Department of Psychiatry
and Behavioral Sciences



Geshe Lobsang Tenzin Negi, PhD,
Department of Religious Studies

Benefits of compassion meditation: pilot study on college students

Compassion meditation effects on reductions in inflammation and emotional distress in response to psychological stress



Pace et al., Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress, *Psychoneuroendocrinology*, 2009

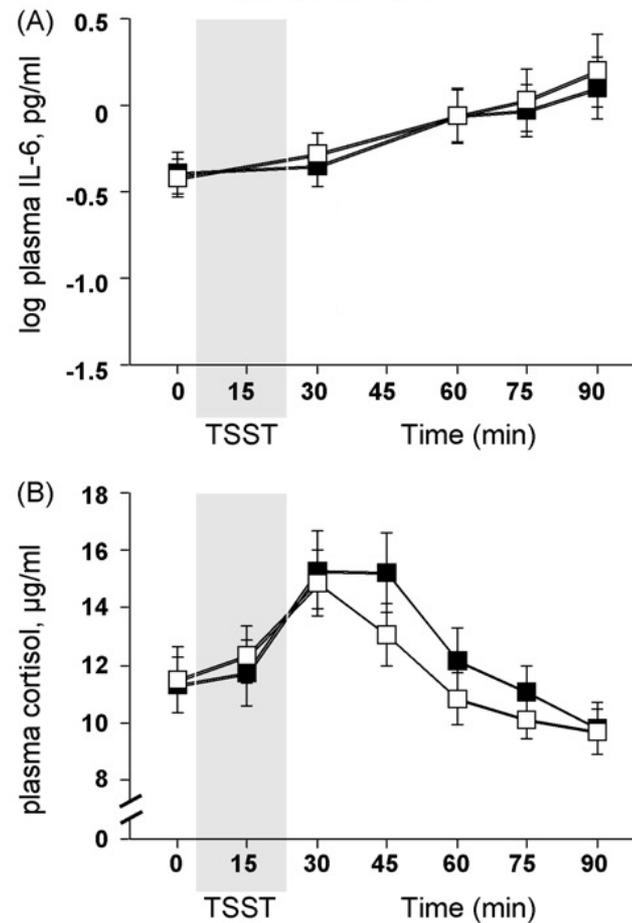
Pace et al., Innate immune, neuroendocrine and behavioral responses to psychosocial stress do not predict subsequent compassion meditation practice time, *Psychoneuroendocrinology*, 2010

Trier Social Stress Test (TSST)

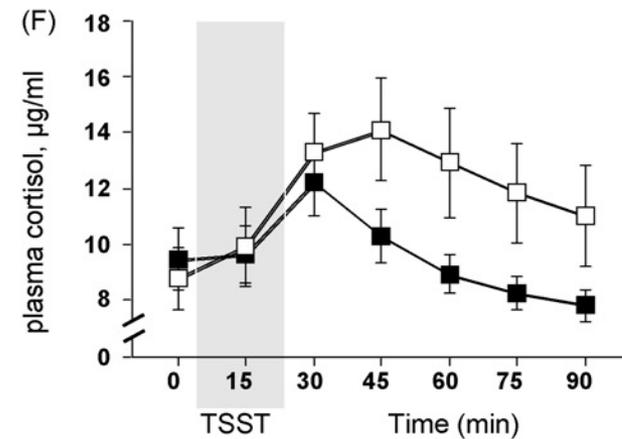
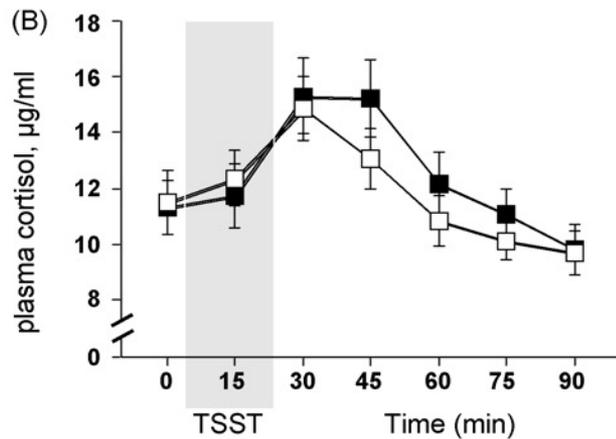
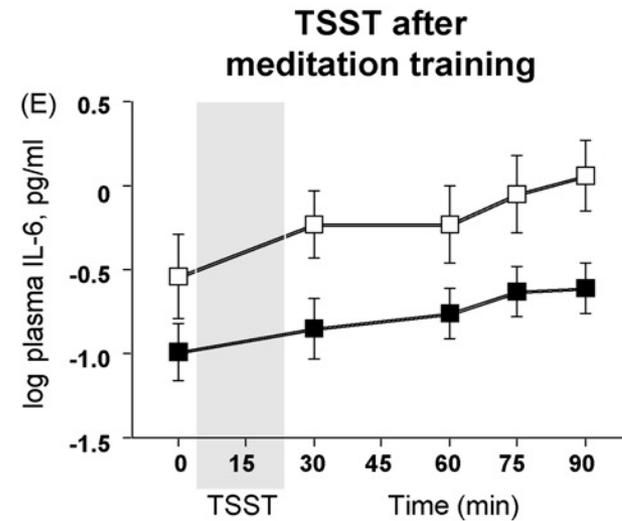
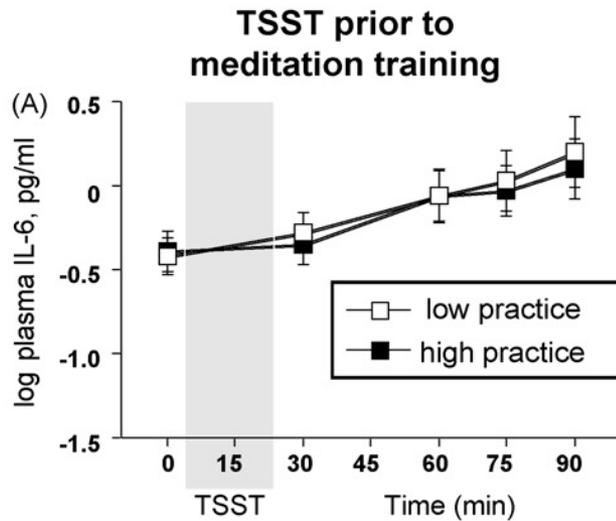


- public speaking in a mock “job interview” format in front of a panel of “experts in behavioral analysis” and video camera
- mental arithmetic
- anticipatory stress/anxiety
- Heart Rate Variability and Skin Conductance Level
- Intravenous line to test several blood markers (IL-6, cortisol, NE, E, NPY, VIP, NF- κ B, PBMC...) at 15 min intervals, before, during and after the stressor

Trier Social Stress Test effects on immune and inflammatory markers



Inflammation markers (the lower, the better) before and after compassion meditation training



Dose-response relationship for immune response after stressor

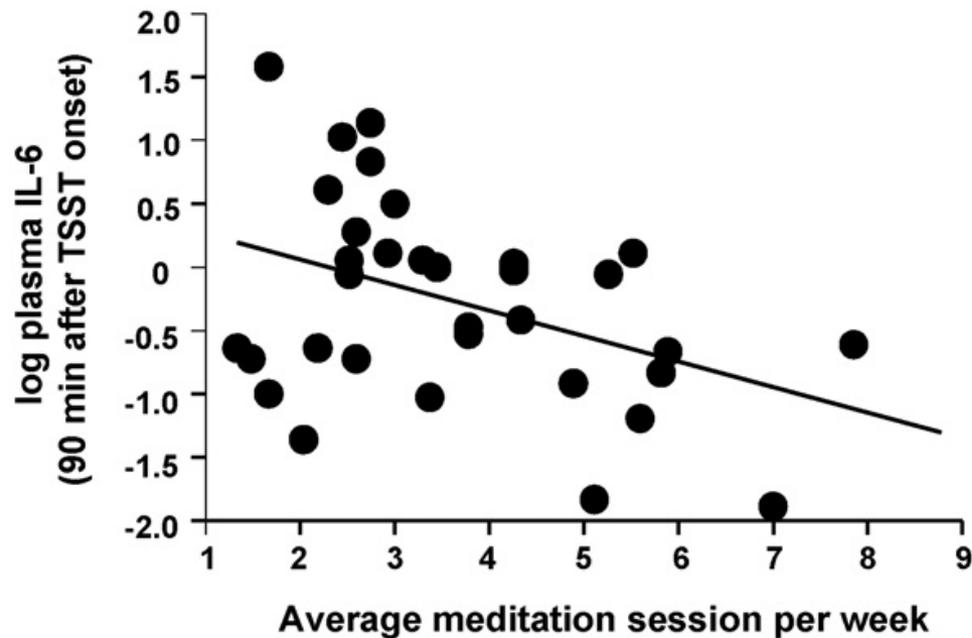


Figure 4 In participants randomized to compassion meditation training ($n = 33$), the mean number of meditation practice sessions engaged in per week (in class + at-home) during the study was inversely correlated with maximal interleukin (IL)-6 responses to the Trier social stress test (TSST) ($r_p = -0.46$, $p = 0.008$; $r_p = -0.51$, $p = 0.004$ when adjusted for baseline IL-6).

Dose-response relationship for emotional distress after stressor

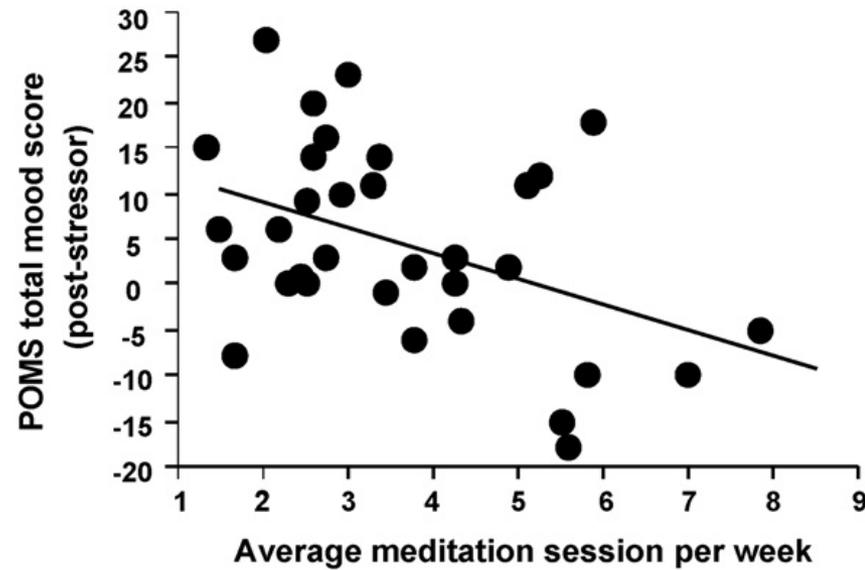


Figure 5 In participants randomized to compassion meditation training ($n = 33$), the mean number of meditation practice sessions engaged in per week (in class + at-home) during the study was inversely correlated with Profile of Mood States (POMS) emotional distress scores immediately after completion of the Trier social stress test (TSST) public speaking/mental arithmetic stressor ($r_p = -.42, p = 0.014$). A trend for an inverse correlation between post-stressor POMS distress scores and amount of meditation practice was observed when baseline POMS scores were included as a covariate ($r_p = -0.3-1, p = 0.09$).

Based on the above pilot studies, a large-scale randomized clinical trial to test the physiological effects of meditation is currently underway at Emory University and Boston University (in collaboration with Harvard and the Massachusetts General Hospital):

The Compassion and Attention Longitudinal Meditation study

The Compassion Attention Longitudinal Meditation (CALM) study

- Compassion meditation and its effect on inflammatory responses to acute and chronic stress
- NIH (R01) funded study at Emory University, Atlanta, GA
- Principal Investigator: Dr. Charles Raison
- Compassion vs. Mindfulness-Attention vs. Controls
- Targeted enrollment: $N=360$ adults over 5 years

Study participants

- Healthy, age 25-55
- Targeted enrollment: $N=360$ people over 5 years:
 - 120 Mindfulness-Attention
 - 120 Compassion
 - 120 controls
- Racial/ethnic diversity representative of the larger population

What does the study consist of?

- Iterative training over 8 weeks
- Twice-a-week one-hour meetings/teachings
- Meditation subjects are asked to meditate 20-30 min every day (Practice time is tracked by a “portable meditation log” device)
- Control subjects are asked to keep a daily journal of health discussions
- There is NO physical exercise (e.g., yoga) or dietary change involved; people keep their habitual lifestyle.

Meditation training in the first group: Mindfulness-Attention Training (MAT)

Protocol outline over the course of 8 weeks:

- Settling the body and respiration in their natural state
- Mindfulness of breathing with relaxation and stability of attention
- Mindfulness of breathing with relaxation, stability and vividness
- Settling the mind in its natural state
- Awareness of awareness

The MAT protocol was designed by Alan Wallace (Santa Barbara Institute for Consciousness) and Geshe Lobsang Tenzin Negi (Emory University) based on Tibetan Buddhism, but completely secular in content

Meditation training in the second group: loving-kindness and compassion meditation

Protocol outline over the course of 8 weeks:

- Developing attention and stability of mind, as in MAT (included in all subsequent steps)
- Developing compassion for oneself through mindfulness of sensations, feelings and emotions
- Cultivating equanimity and appreciation for others
- Developing affection and empathy
- Wishing and aspirational compassion
- Active compassion for others

The Compassion meditation protocol was designed by Geshe Lobsang Tenzin Negi (Emory University)

based on traditional Tibetan “lo-jong” = “mind training” techniques, but completely secular in content

Control: Health discussion group

Protocol outline over the course of 8 weeks:

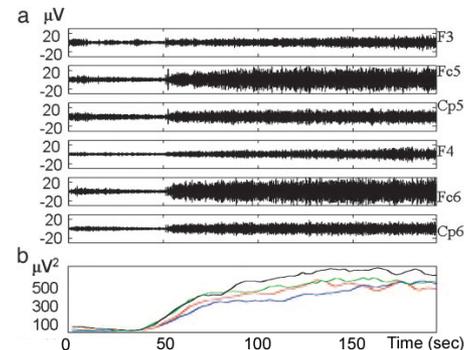
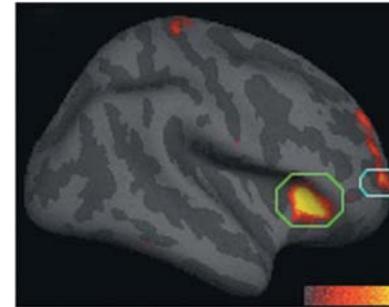
- One-hour talk on a health-related topic by a local expert
- One-hour active participation in small group discussions, role-playing, and friendly debates designed to make the health topics covered personally relevant
- As a substitute for daily meditation practice, these control subjects are keeping a daily log of their reflections on how to incorporate the current health topic into daily life
(Logs will not be collected, but average time spent on it per day will be recorded)

Pre- and post-intervention assessments

- Trier Social Stress Test (TSST):
 - public speaking in a mock “job interview” format in front of a panel of “experts in behavioral analysis” and video camera
 - mental arithmetic
 - anticipatory stress/anxiety
 - Heart Rate Variability and Skin Conductance Level
 - Intravenous line to test IL-6, cortisol, NE, E, NPY, VIP, NF- κ B, PBMC... at 15 min intervals, before, during, and after the stressor
- Neuropsychiatric, psychosocial and lifestyle assessments
 - 12 different self-report and clinician-based assessments
- Brain imaging (at MGH): structural, diffusion-based, and functional MRI
 - On a subset of the subjects (target $N=48$, or 16 per group)
 - Funded separately by an NIH Research Challenge grant (ARRA) to Professor Eric Schwartz at Boston University

Recap of previous neuroimaging studies

- Sara Lazar, MGH:
 - cortical thickness larger in meditators in regions associated with attention, interoception and sensory processing, including prefrontal cortex and right anterior insula
 - Longitudinal study: Stress reduction (following MBSR intervention) correlates with decrease in amygdala grey matter density
- Antoine Lutz, Richie Davidson (U. of Wisconsin-Madison): compassion meditation in experts
 - High-amplitude gamma synchrony (EEG)
 - enhanced activation of insula, cingulate cortices, amygdala, etc. (fMRI)
- and others...



Motivations for brain imaging

- Changes in stress response involve the brain, esp. limbic and subcortical structures (e.g. Hypothalamic–pituitary–adrenal (HPA) axis)
 - The “where” question: Which neural regions and circuits are involved?
- **Neuroplasticity**: “Use it or lose it”; can we train the brain to be more
 - Attentive? Mindful?
 - Compassionate?
- Different reactions to emotional stimuli, linked to better quality of life (change in **trait**)
- Neural correlates of meditative **states** as altered states of consciousness

Hypotheses on longitudinal effects of meditation training

- Structural changes: cortical thickness, grey matter density
- Changes in anatomical connectivity
- Changes in functional connectivity (in default mode network + other networks)
- Physiological “trait” changes in the resting state
 - longitudinal differences in baseline brain activation
 - Changes in autonomic physiology
- Changes in response to emotional stimuli
 - longitudinal differences in brain response to stimuli
 - Changes in autonomic physiology
- Neural correlates of meditation: mindfulness vs. compassion vs. rest probably activate different regions of the brain (“state” changes)

Brain imaging experimental design

- Siemens 3T with 32-channel head coil
- Simultaneous recordings of autonomic physiological data:
ECG, breathing belt, pulse-oxymeter, GSR
- Anatomical (structural and diffusion-based) scans:
cortical thickness, grey matter density, white-matter connectivity
- fMRI in resting state to measure functional connectivity
- fMRI task: passive viewing of emotional visual stimuli
 - Photographs of human beings in various situations (from IAPS database)
 - 3 emotional valences: positive, negative, neutral, presented in random order

Thanks to:

Boston University:

Eric Schwartz

Emory University:

Chuck Raison

Geshe Lobsang Tenzin Negi

Harvard/MGH:

Lama Willa Miller

Ted Kaptchuk

Bruce Fischl

Larry Wald

Vitaly Napadow

Sara Lazar

... and many others for inspiration and feedback!

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Mind and Life Institute Varela Award (G. Desbordes)

Thank you!

Please feel free to contact me if you have any questions: gdesbord@bu.edu