



Neural mechanisms supporting mindfulness-based pain relief as compared to placebo analgesia

Fadel Zeidan, PhD

Wake Forest School of Medicine

Department of Neurobiology and Anatomy

9th Annual NIH Pain Consortium Symposium

May 28, 2014



Chronic pain: A silent epidemic

- Over 100 million Americans and 1.5 billion people worldwide are affected by chronic pain (Institute of Medicine)
- With 42% of people reporting daily pain
- Costs the U.S ~ \$635 billion a year (Gaskin & Richard, 2012)
- Alternative approaches to treating pain are cost-effective without causing side effects

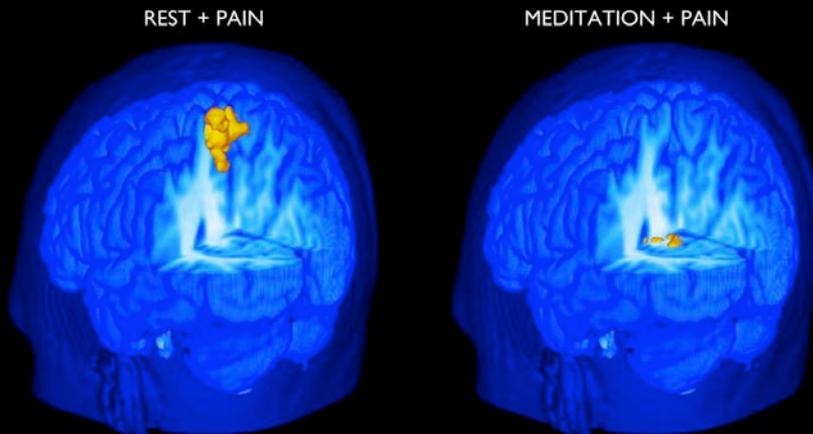
Why mindfulness meditation and pain?

Mindfulness meditation is associated with multiple pain relieving mechanisms:

- Coping strategies (e.g. acceptance) (Grossman, 2004)
- Positive mood (Zeidan et al., 2010)
- Reappraisal (Farb et al., 2009)
- Emotional and cognitive control (Zeidan et al., 2012)

Brief mindfulness-based mental training

- Meditation naïve participants
- Taught basic mindfulness skills (Shamatha/Vipassana)
- Four days of mental training (20m/d)
- Improves anxiety, depression, mood, pain and other health outcomes (Zeidan et al., 2010a, 2010b, 2010c, 2011, 2012; 2013)



Ongoing Project

Methods and Procedures

- Thermal heat (49° C) was used to evoke pain



- Pain intensity/unpleasantness ratings assessed with VAS



- Brain activation was assessed by examining cerebral blood flow with arterial spin labeled (ASL) MRI



Identifying the analgesic mechanisms of mindfulness

Meditation-related pain relief may be related to:

- Relaxation (Kabat-Zinn, 1982)
- Divided attention (Zeidan et al., 2010)
- Placebo analgesia (Kuyuci et al., 2011; Zeidan et al., 2013)
- Established beliefs associated with meditation's health promoting reputation (Zeidan et al., 2010)



Ongoing Project

Mindfulness meditation training (n=17)

Placebo-conditioning (n=19)

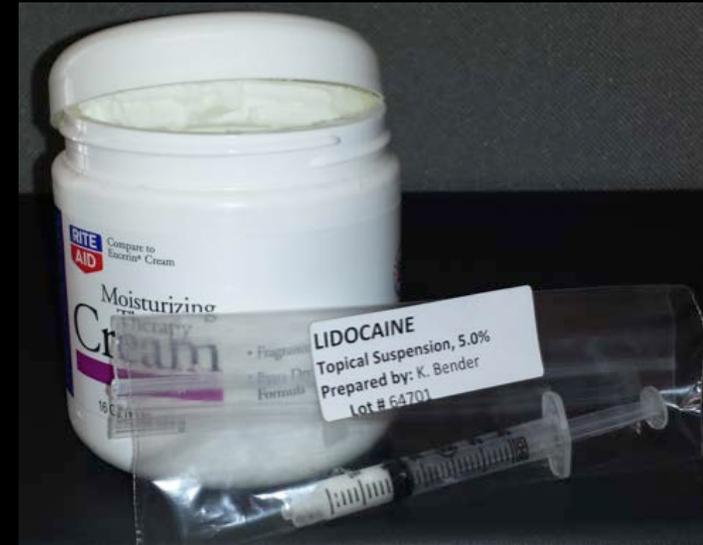
Sham mindfulness meditation (n=20)

Book listening (n=19)

Over 600 individually, tailored experimental sessions

Placebo group

- 4 placebo conditioning sessions (Price et al., 1999; Colloca et al., 2010)
- Baseline stimulation (49° C)
- Applied placebo cream on the calf
- Covertly reduced stimulation levels in each session
 - Session 1 = 48° C
 - Session 2 and 3 = 47° C
 - Session 4 = 46.5° C
 - Post-Intervention MRI session = 49° C



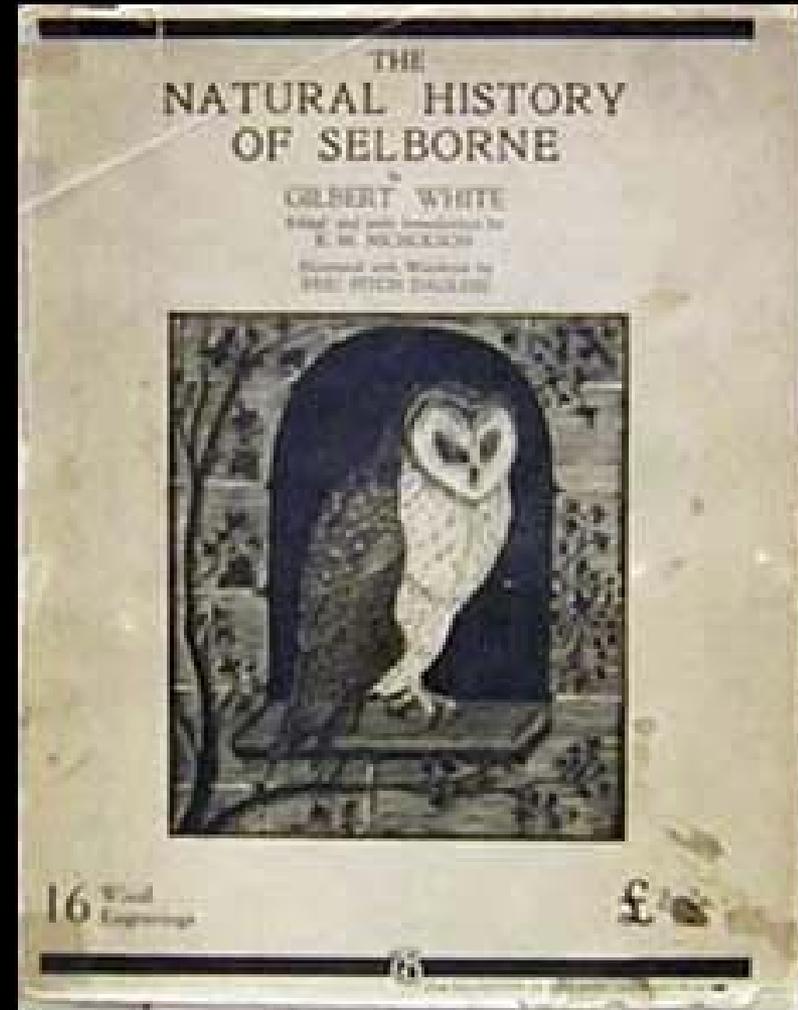
Sham mindfulness meditation group

- Aim was to lead participants to *believe* they were practicing *mindfulness* meditation (Zeidan et al., 2010)
- Taught to sit with straight posture and eyes closed
- Instructed to “take a deep breath” every 2-3 minutes “as we sit here in mindfulness meditation”
- Matched time spent giving instructions to the mindfulness meditation group



Control group

- Four sessions of listening to the *Natural History of Selborne*
- Employed to control for facilitator attention and time elapsed in the other group's interventions

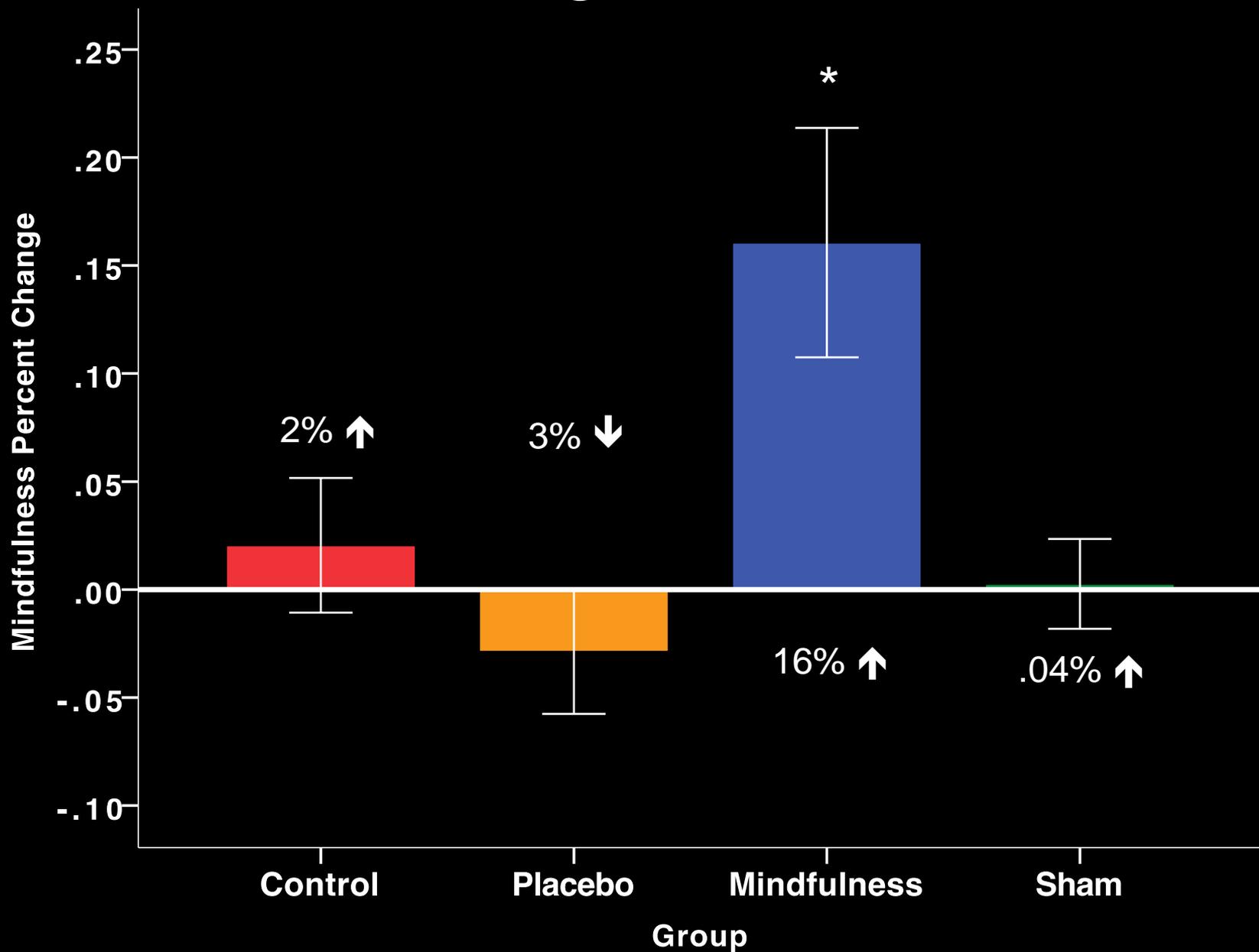




Outcome Measures

- Pain intensity and unpleasantness ratings
- Freiburg Mindfulness Inventory (FMI) scores
- Regional brain signals (CBF)

Mindfulness training increased FMI ratings

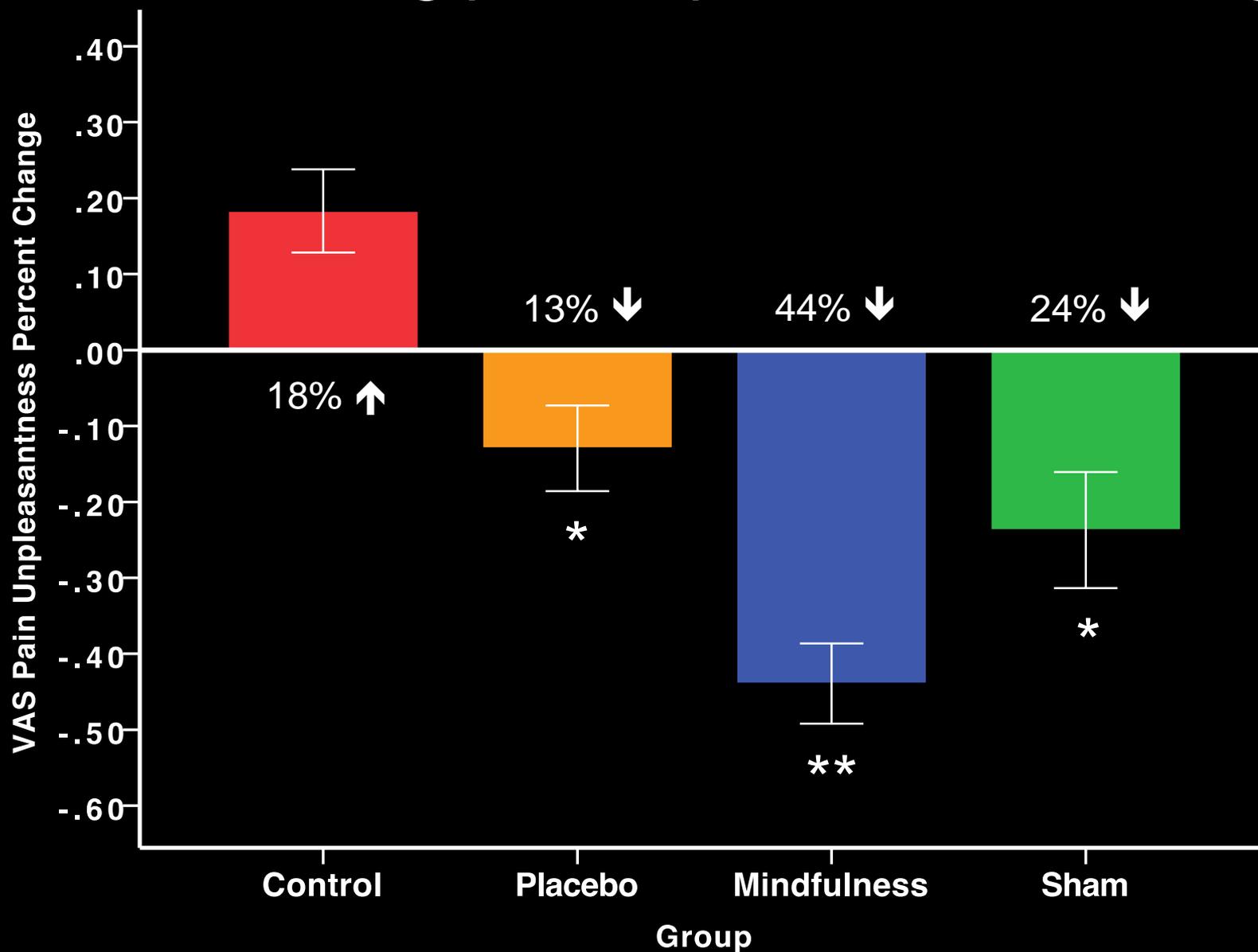


Mindfulness meditation was more effective at reducing pain intensity

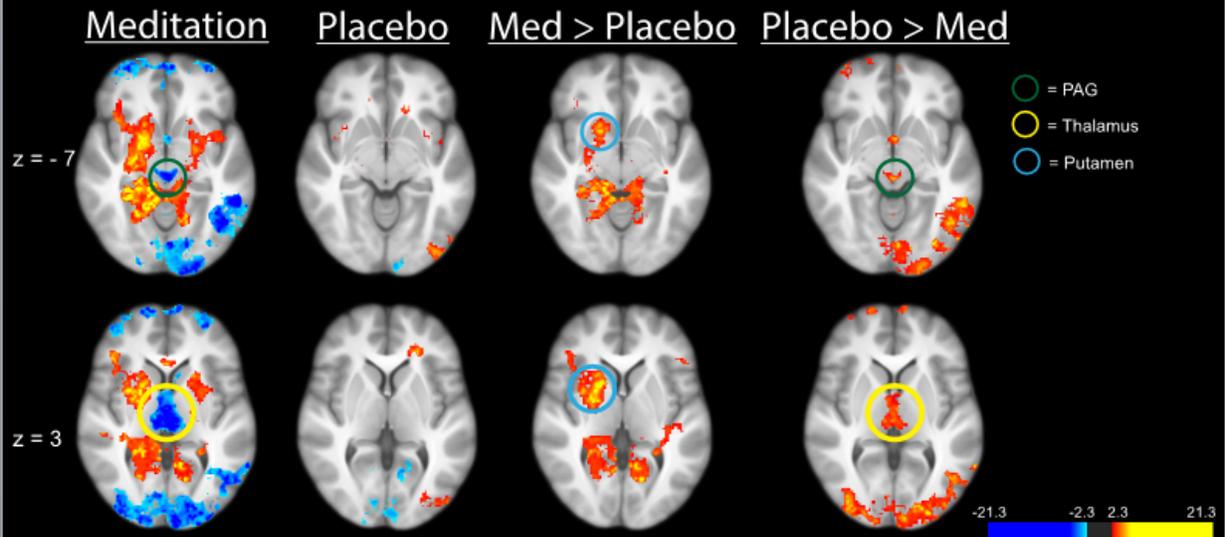




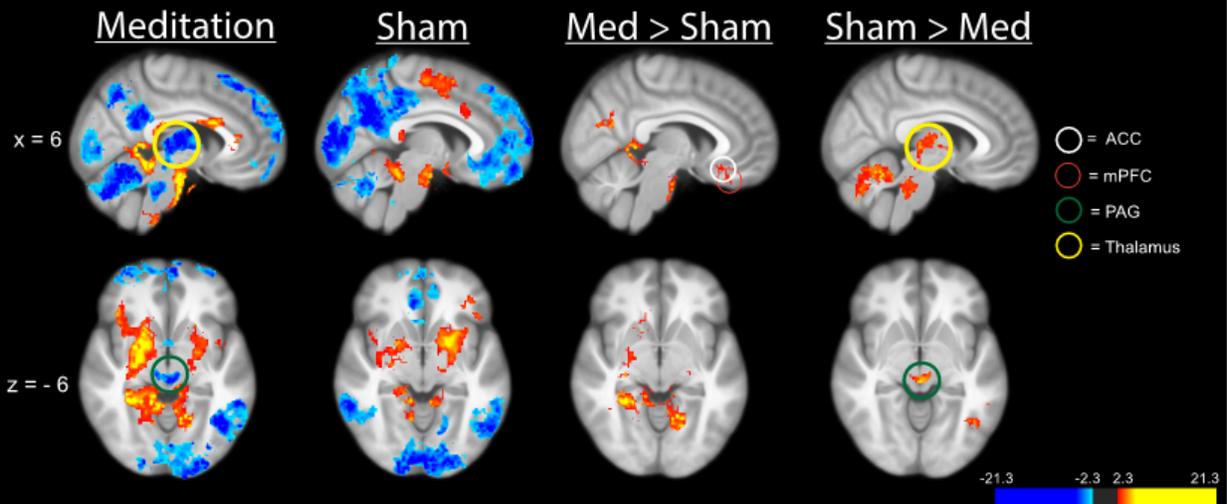
Mindfulness meditation was more effective at reducing pain unpleasantness ratings



Meditation significantly reduces thalamic and PAG activation when compared to placebo



Mindfulness reduces PAG and thalamic activity when compared to sham meditation





Final Considerations

- Brief Mindfulness-based mental training is more effective at reducing pain than placebo and sham meditation
- Meditation attenuates pain through multiple mechanisms
- Placebo likely engages descending control processes
- Sham meditation-related pain relief likely engages placebo and relaxation-related mechanisms
- Clinical efficacy

Acknowledgements

- Dr. Robert Coghill
- Dr. John McHaffie
- Dr. Robert Kraft
- Dr. Youngkyoo Jung
- Dr. Katherine Martucci
- Nicole Emerson
- Suzan Farris
- Jenna Ray
- Study Participants

This work was supported by NIH NCCAM (F32, R21), The Mind and Life Institute, The Wake Forest Center for Integrative Medicine and Wake Forest Center for Biomolecular Imaging.

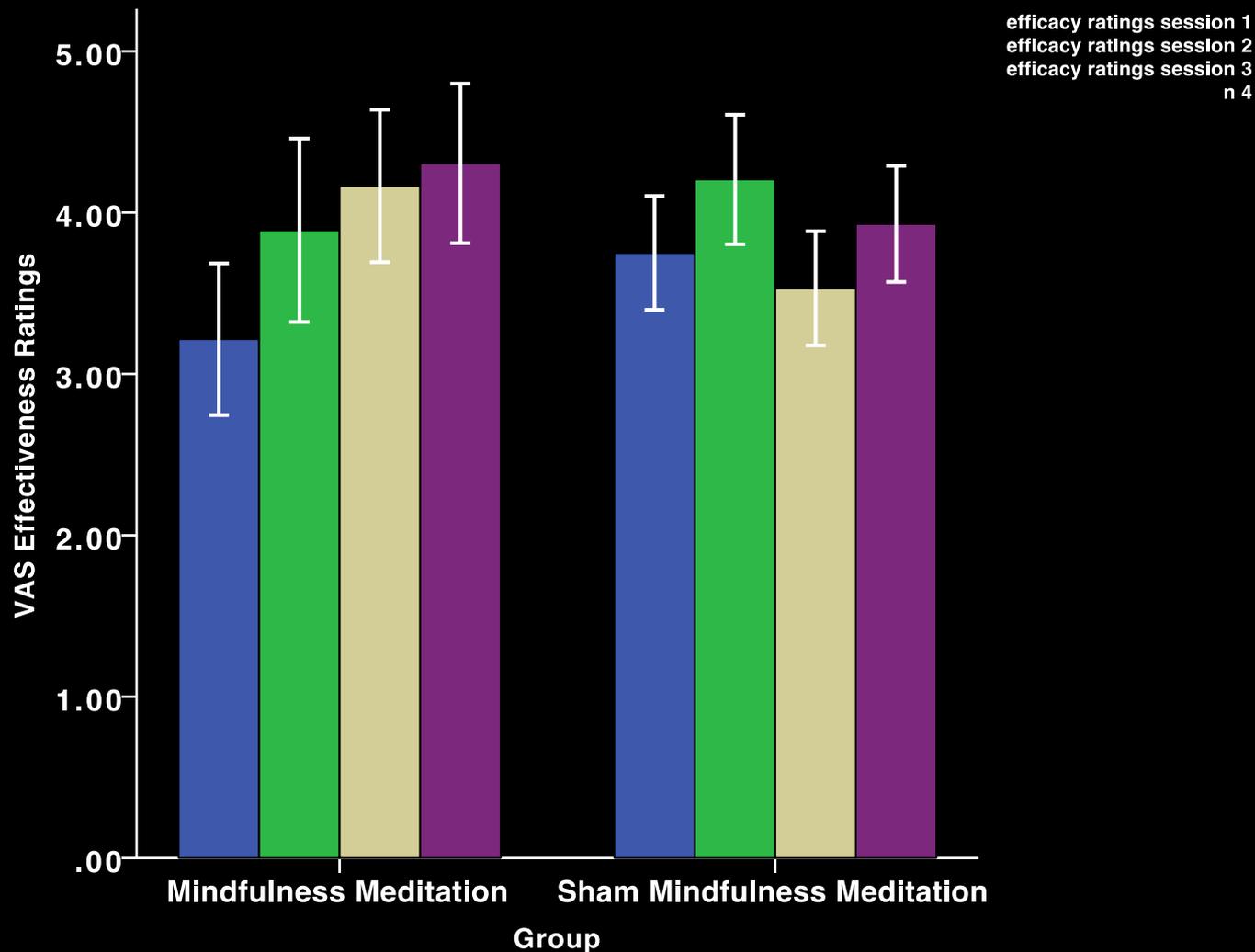


Thank you for your time and
attention

Questions?

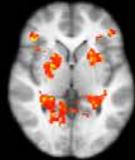
See more details at poster #32

No differences in perceived “meditative” effectiveness ratings between mindfulness and sham meditation groups ($p>.25$)

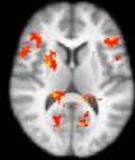


Neural correlates of mindfulness-based pain relief

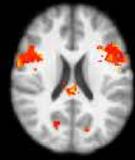
Med > Rest



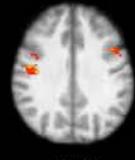
z = 1



z = 10



z = 21

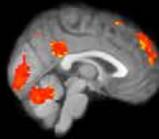


z = 32

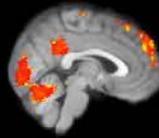


z = 38

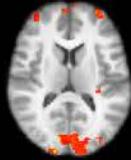
Rest > Med



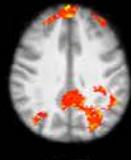
x = -1



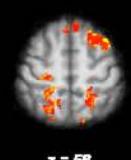
x = 3



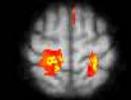
z = 12



z = 35

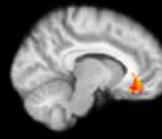


z = 58

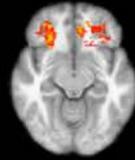


z = 64

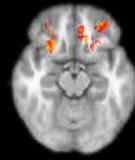
Pain Intensity



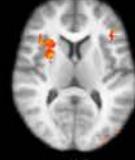
x = -9



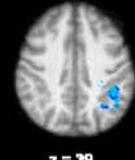
z = -11



z = -15

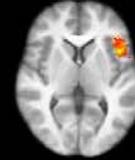


z = 8

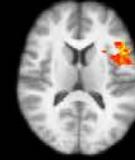


z = 38

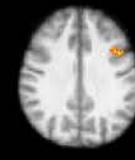
Pain unpleasantness



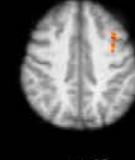
z = 4



z = 13



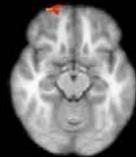
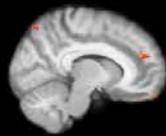
z = 32



z = 43

Neural correlates of placebo analgesia

Placebo > Rest



$z = -14$

Rest > Placebo

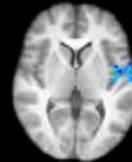
$x = 2$

$z = -1$

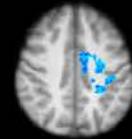
$z = 4$

4

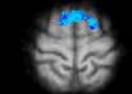
Pain Intensity



$z = 4$

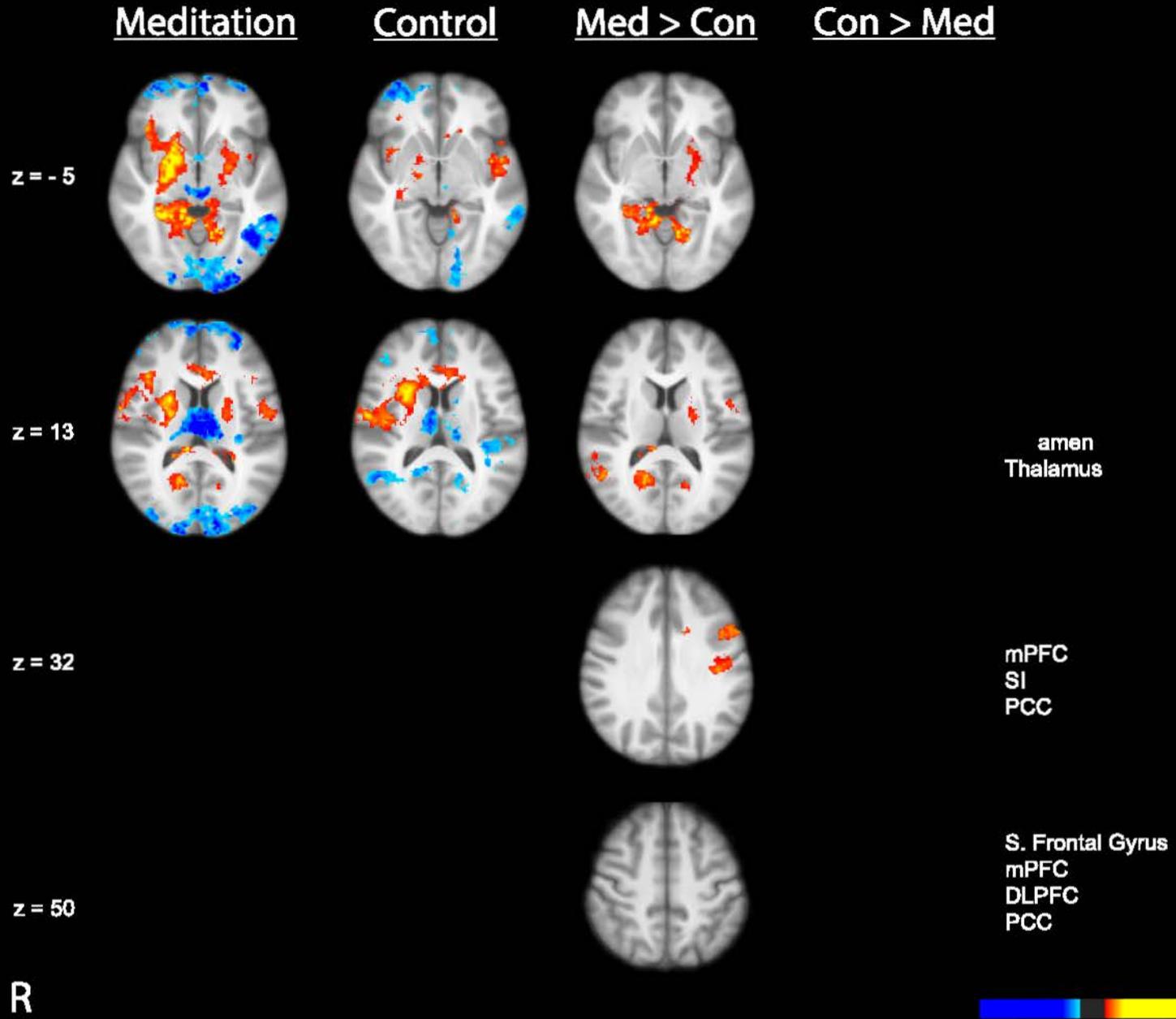


$z = 41$



$z = 67$

Main effect of meditation and control comparison



Control group pain correlations

Pre > Post

Post > Pre

↑ Pain Int

↑ Pain Unp



Pain sensitivity decreased after meditation training

Table 1. Mean (SD) Stimulus Intensity (mA) Values for High and Low Pain for Each Experiment

		<i>SESSION 1</i>		<i>SESSION 2</i>	
		<i>HIGH PAIN</i>	<i>LOW PAIN</i>	<i>HIGH PAIN</i>	<i>LOW PAIN</i>
Experiment 1	(Meditation)	279.0 (154.9)	167.5 (100.7)	353.4 (219.3)	240.0 (168.2)
Experiment 2	(Control)	252.0 (130.6)	149.8 (73.0)	278.1 (94.3)	176.2 (74.31)
Experiment 3	(Meditation)	354.0 (232.06)	215.8 (151.42)	409.7 (220.8)	260 (232.06)

Pre vs Post Training

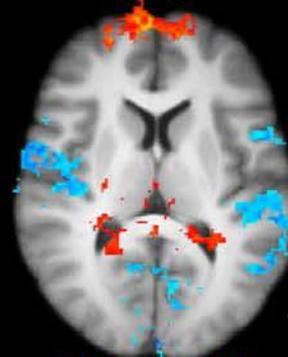
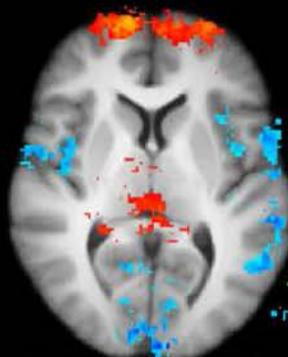
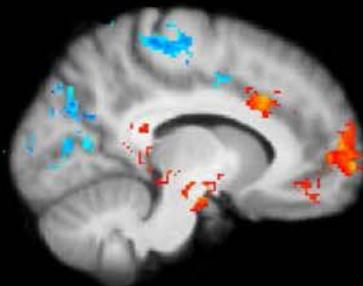
Pain

Pre-training > post-training
Post-training > pre-training

x=-10

z=6

z=10



SI

Bilateral insula

Bilateral SII

M PFC
ACC

SII
Frontal Pole
Bilateral Thalamus

9.2
2.3

-2.3
-9.2

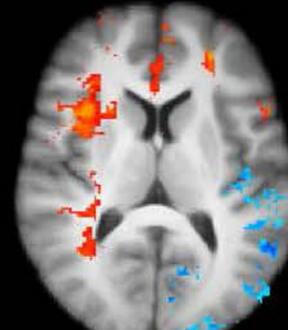
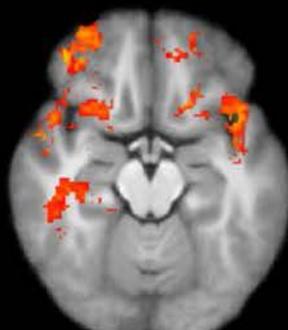
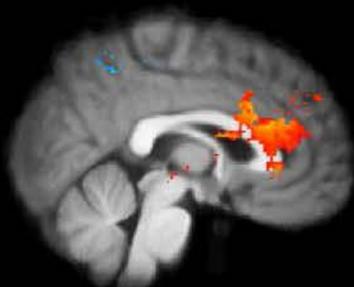
Meditation

ATB greater than meditation
Meditation greater than ATB

x=2

z=-16

z=10



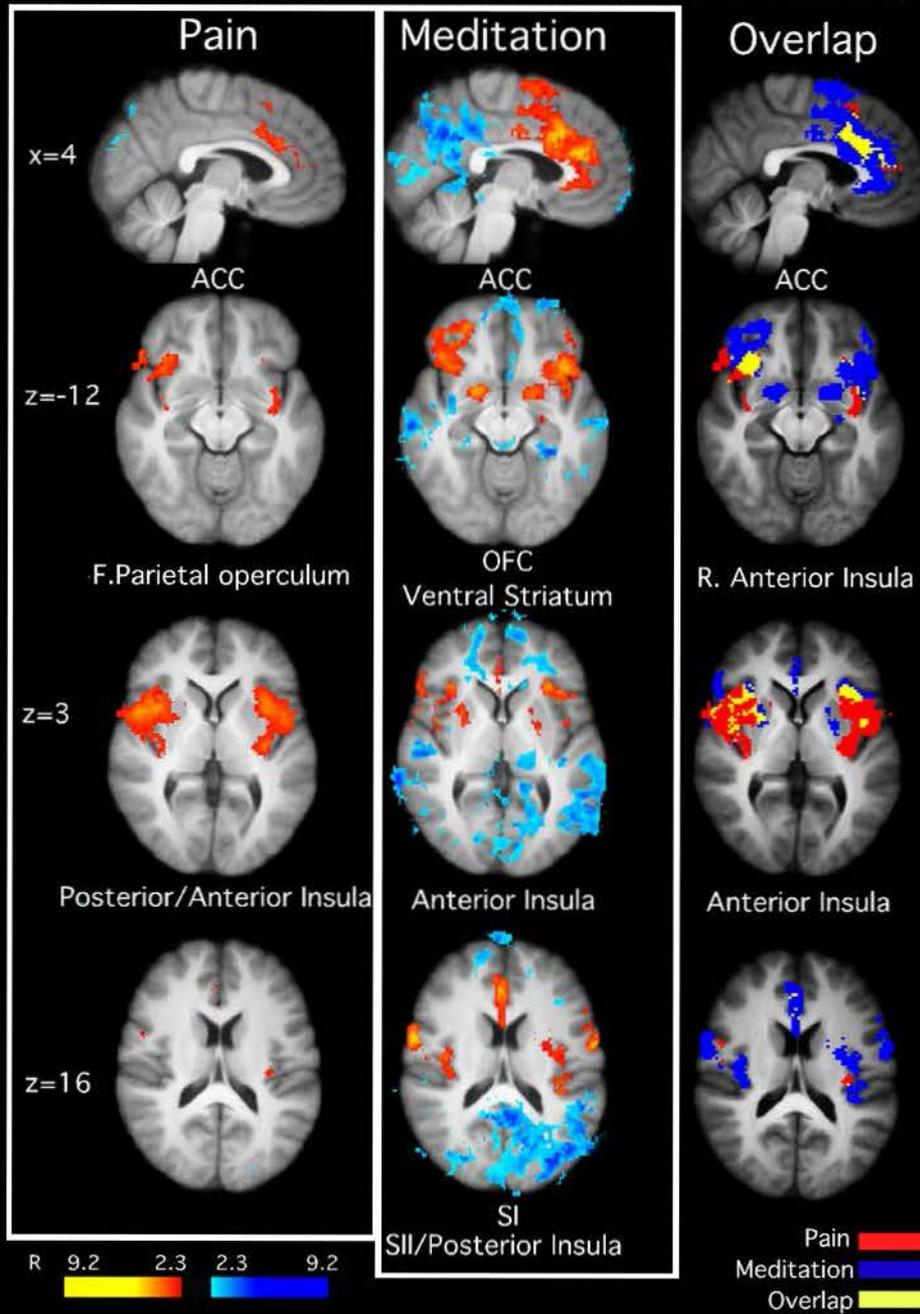
ACC

Bilateral OFC

R. Anterior Insula

R

Post-Meditation Training





MINDFULNESS RESEARCH PUBLICATIONS BY YEAR, 1980 - 2013

