The Neuroscience of Mindfulness:
Clinical / Neurological Applications

Sarah Mulukutla, MD MPH FAAN

Mindful Neurology, PLLC

January 19, 2025

Mindful Neurology

Learning Objectives:

- Review the neural, physiologic basis of meditation
- Understand therapeutic potential of meditation
- Experience a 15 minute breathing & meditation exercise

Disclosures

- Consulting/speaking honorariums for meditation instruction
- Course income
- No financial conflicts

Academic partners:

Weill Cornell Medicine

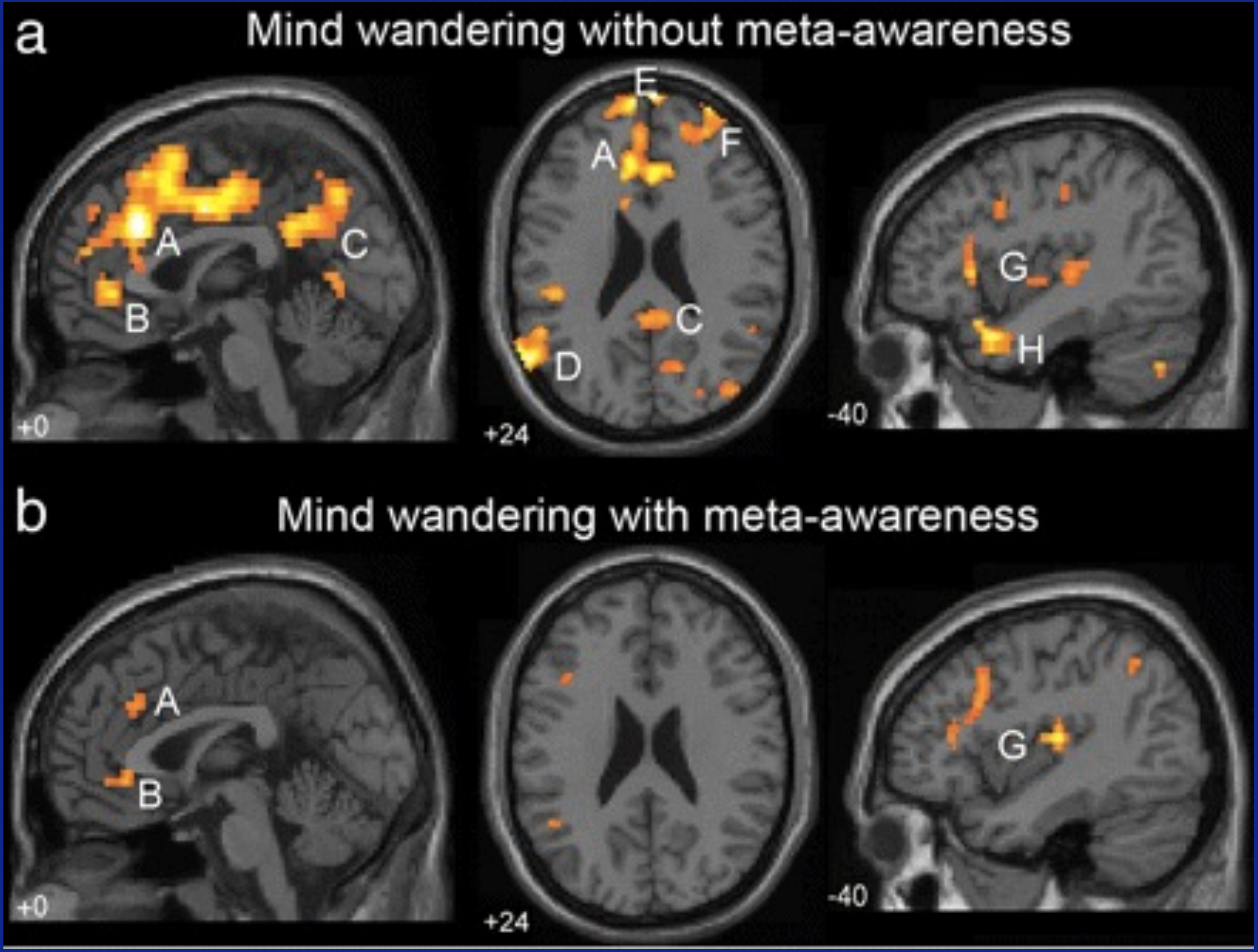
Yale

Video: Bradykinesia improves after meditation:

Link: https://youtu.be/E65NlksgRa0

The Steps of Meditation

1. Choose an object to focus on
2. Sustain attention
3. Disengage from spontaneous thoughts when they arise



Christoff K et al. PNAS 2009.

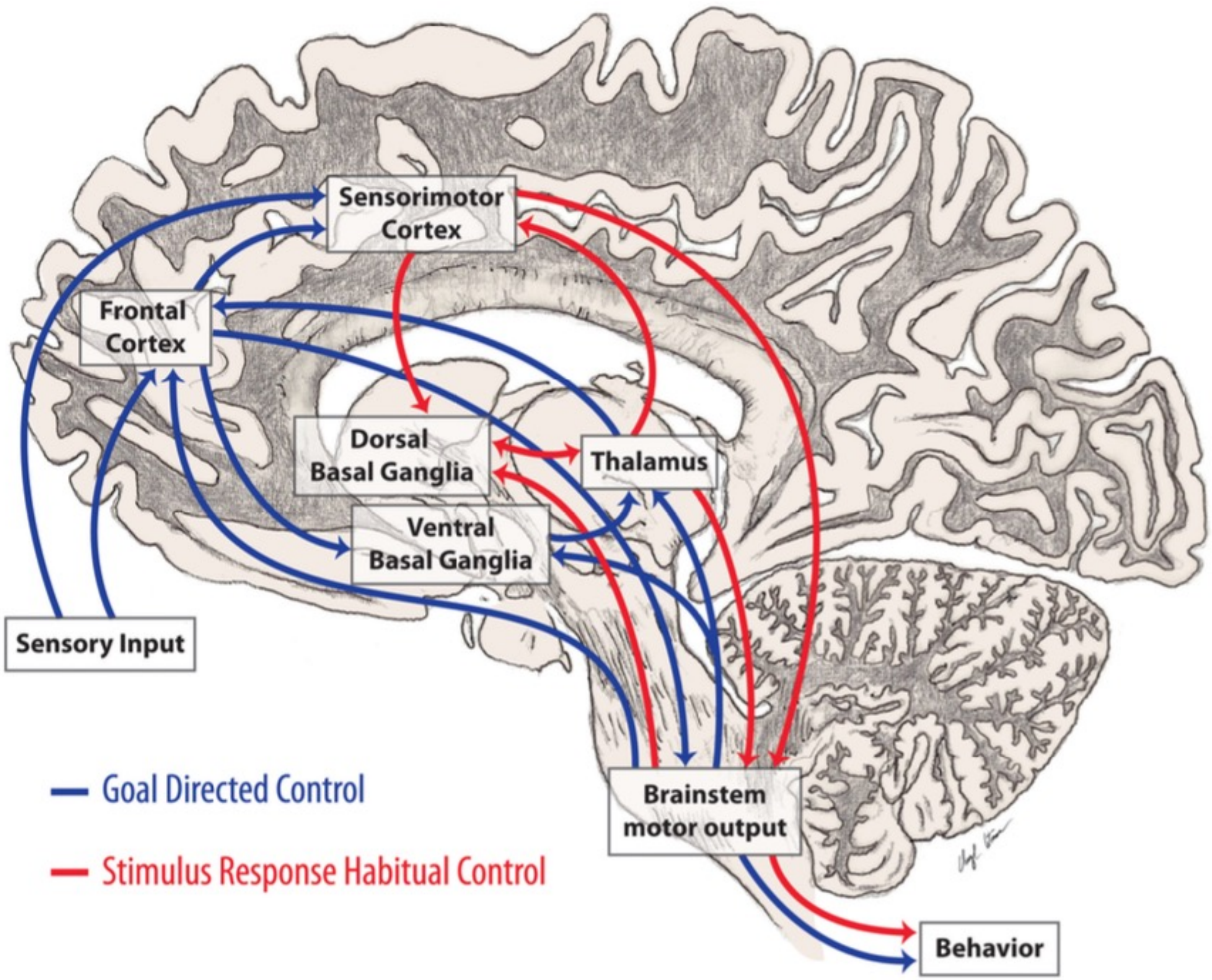


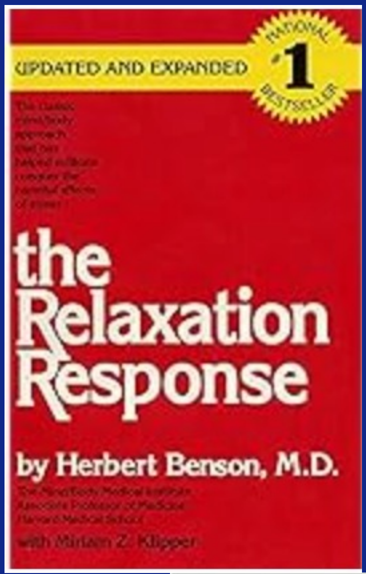
Figure 1. Cognitive and Automatic Motor Control

Motor control incorporates multiple cortical and subcortical structures. Most important are the connections between the basal ganglia and cortex that are involved in cognitive and automatic aspects of motor control. In PD, loss of DA in the caudal basal ganglia leads to impaired automatic movements involving circuits important in stimulus based habitual learning (red arrows) and over-reliance on cognitive components of motor control and circuits involved in reward based learning (blue arrows).

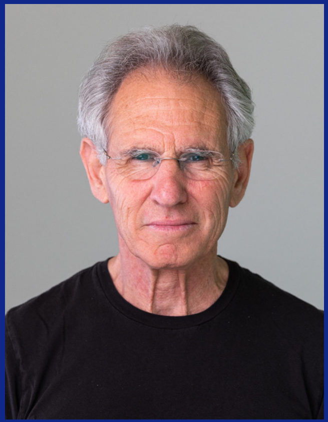
Interplay between Automatic and Cognitive Motor Control

Petzinger G et al
Lancet Neurology 2013
12(7):716-726
Doi:10.1016/S1474-4422(13)70123-6

Mind-Body Medicine Origin

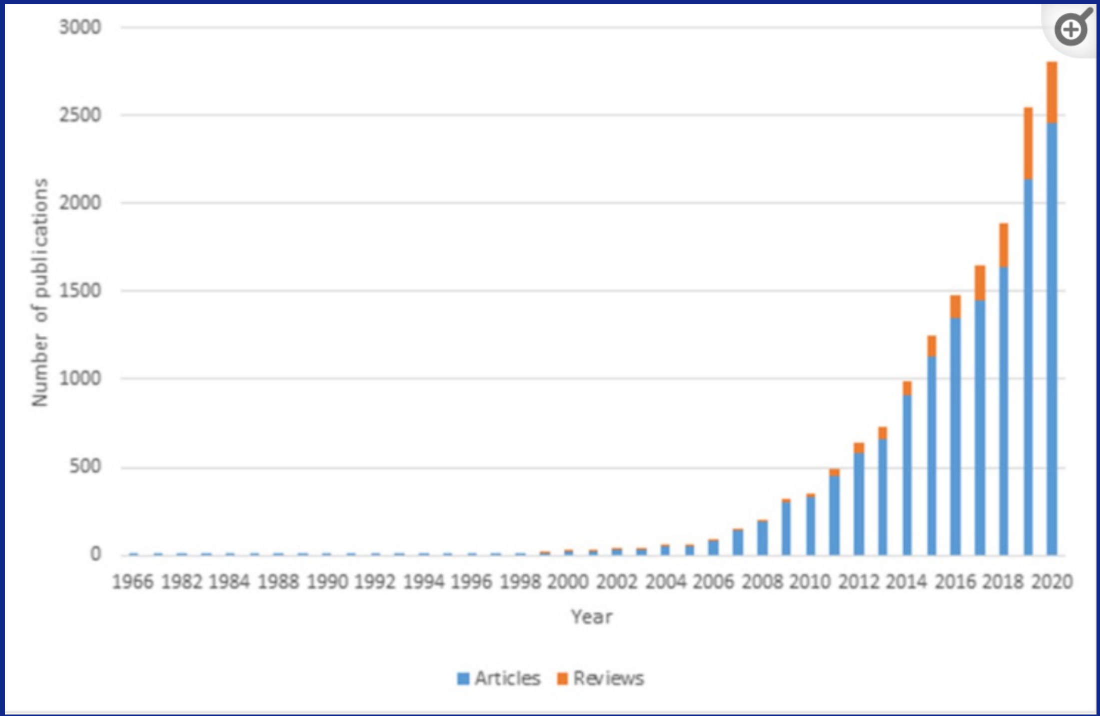


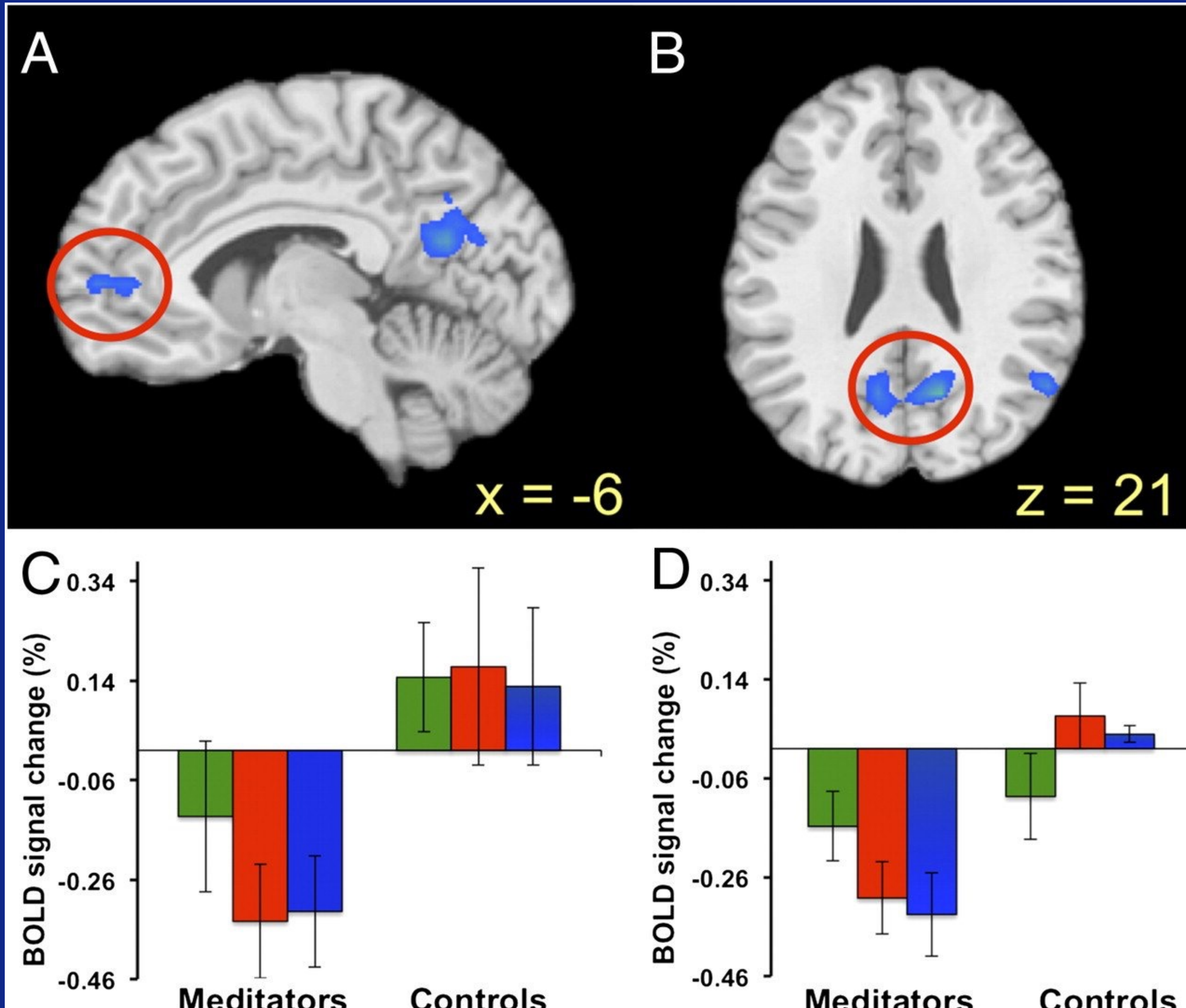
1975



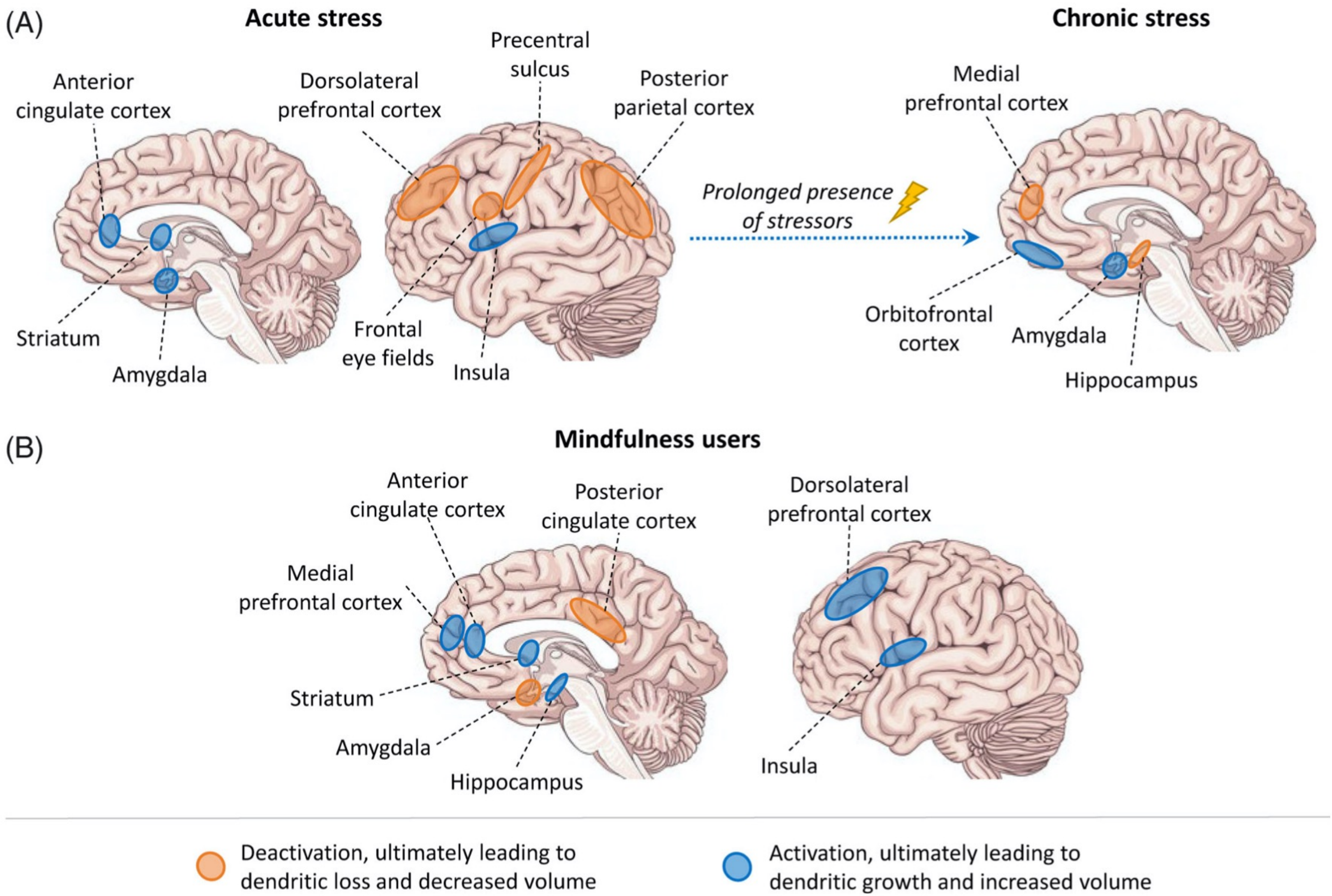
1979 – J Kabat-Zinn, MBSR

Academic mindfulness publications, by year.





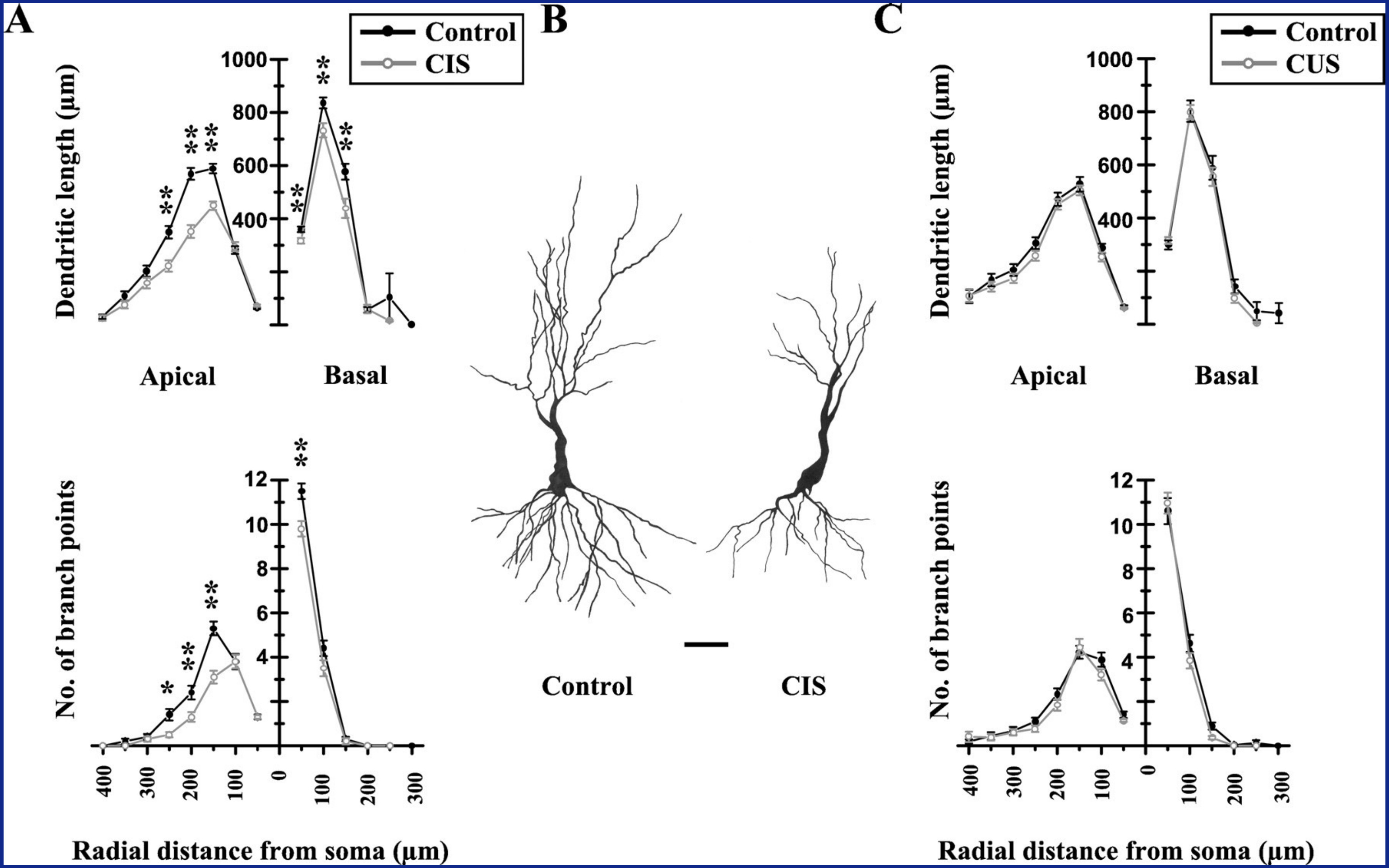
Brewer et al, PNAS 2011



Van der Heide et al. Mov Dis. 2021

Detrimental effects of Chronic Stress:

dendritic atrophy in the hippocampi, dendritic growth in the amygdala



Vyas A et al.Neurons. J Neurosci 2002

PNAS

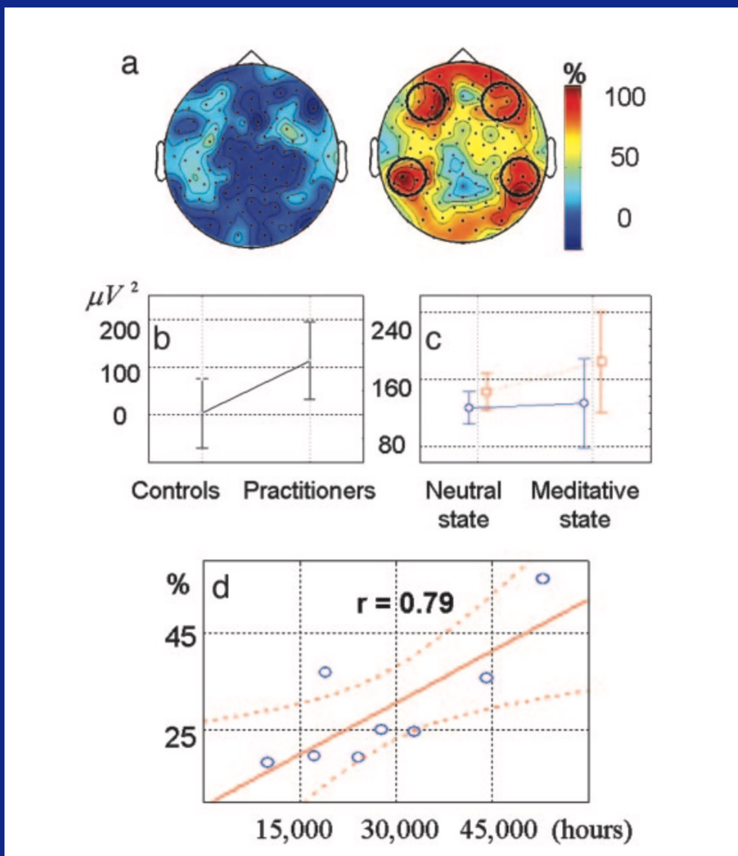
Long-term meditators self-induce high-amplitude gamma synchrony during mental practice

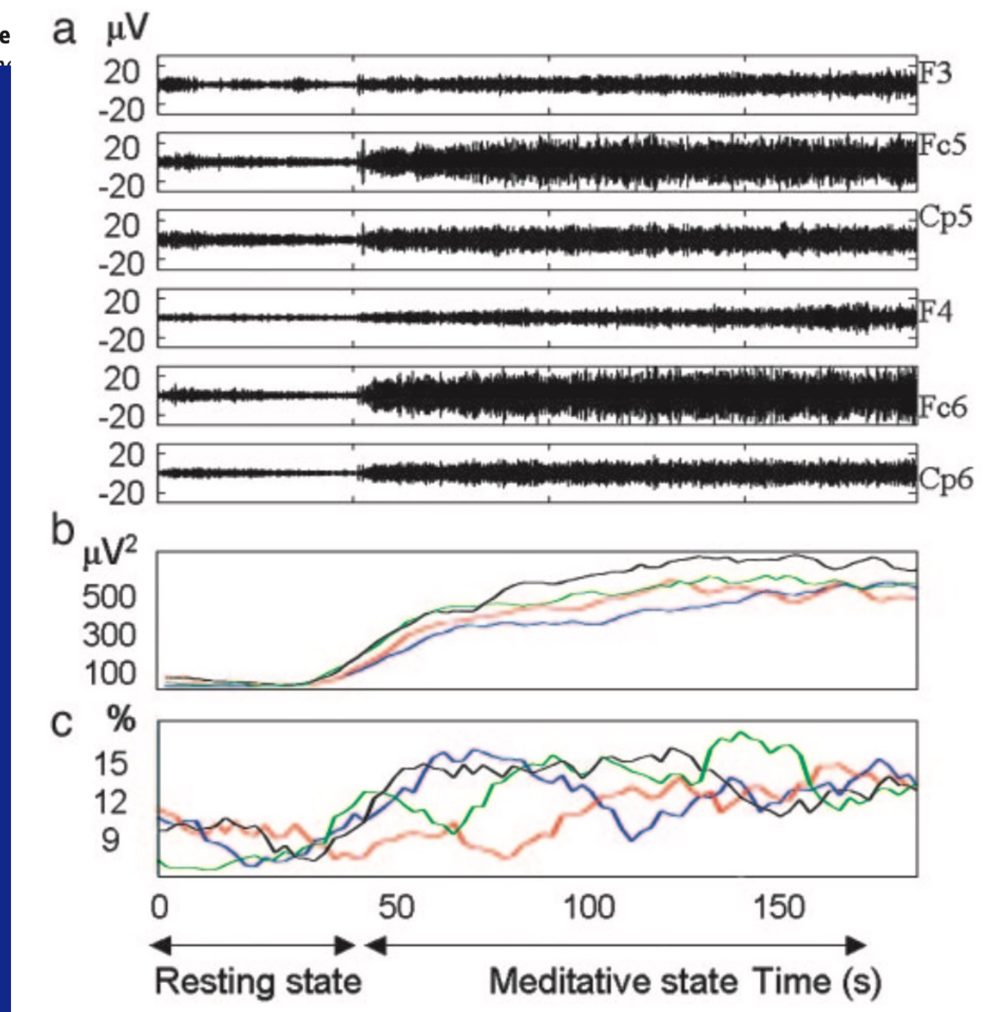
Antoine Lutz*†, Lawrence L. Greischar*, Nancy B. Rawlings*, Matthieu Ricard‡, and Richard J. Davidson*†

*W. M. Keck Laboratory for Functional Brain Imaging and Behavior, Waisman Center, and Laboratory for Affective Neuroscience, Department of Psychology, University of Wisconsin, 1500 Highland Avenue, Madison, WI 53705; and ‡Shechen Monastery, P.O. Box 136, Kathmandu, Nepal

Communicated by Burton H. Singer, Princeton University, Princeton, NJ, October 6, 2

Practitioners understand "meditation," or mental training, to be a **Me**



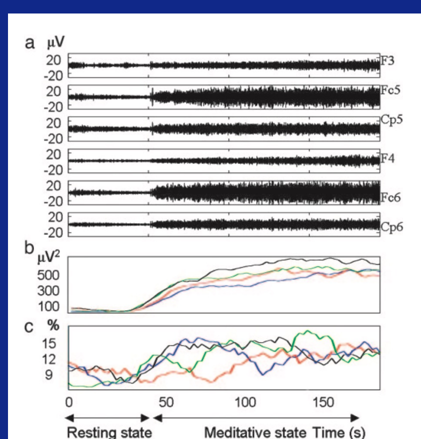


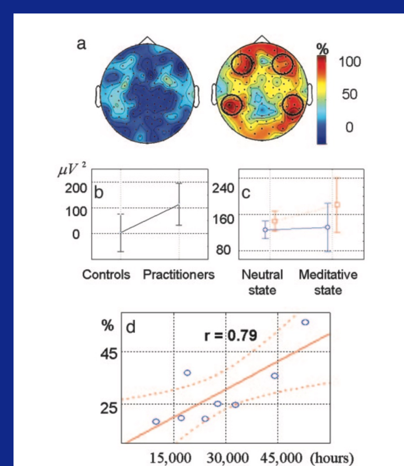
Supplemental Material: Annu. Rev. Neurosci. 2012. 35:203-25
doi: 10.1146/annurev-neuro-062111-150444
Mechanisms of Gamma Oscillations
Buzsáki and Wang

Supplemental Text

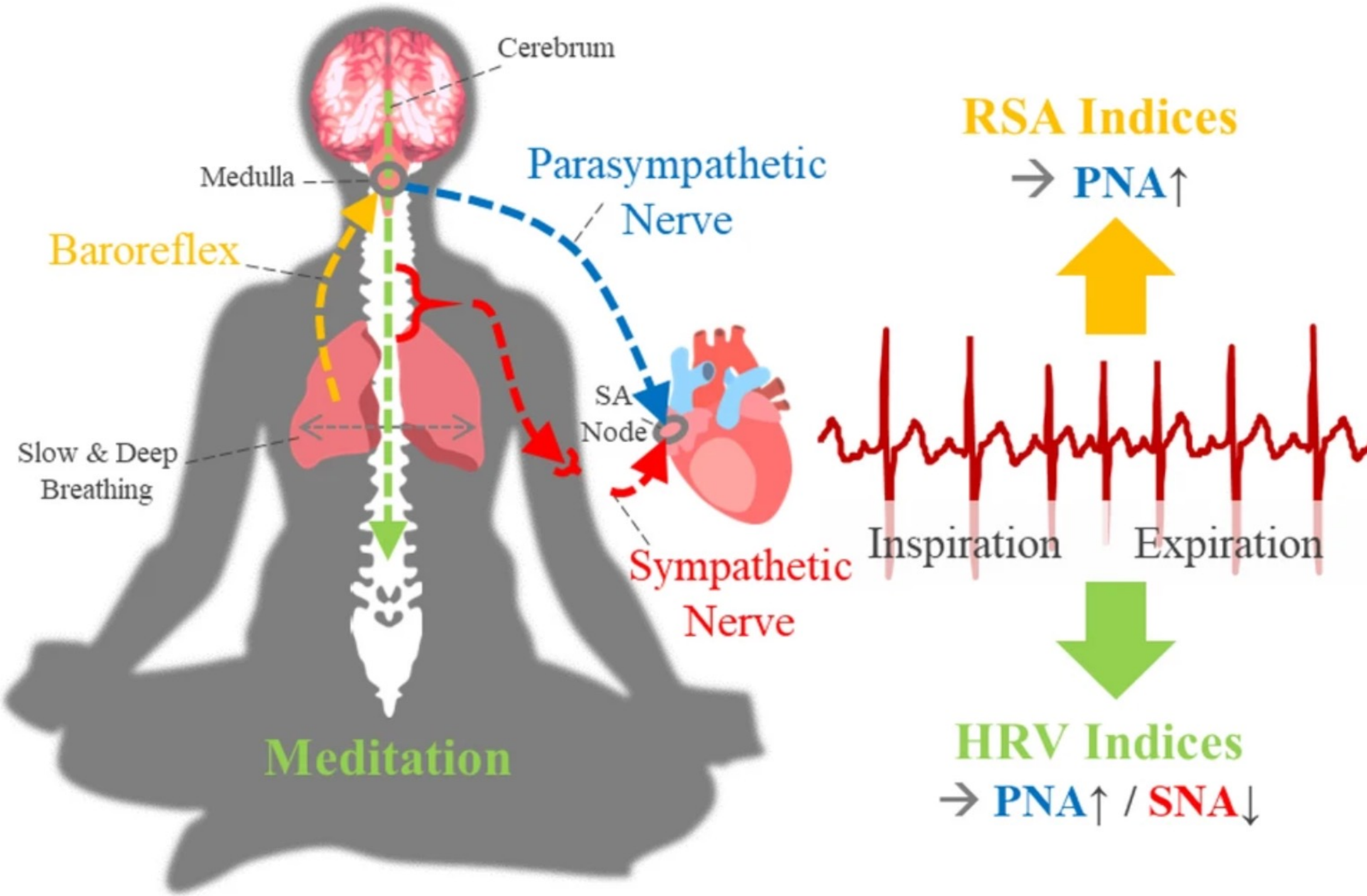
What's in a name? A short history of gamma oscillations

Reconstruction of pieces of neuroscience history is not an easy act, and the origin of the "gamma oscillations" term is no exception. Alpha and beta waves have been introduced by Berger (1929), referring to the larger amplitude rhythmic 8-12 Hz and the lower amplitude faster than 12 Hz patterns, respectively (Niedermeyer and Lopes da Silva, 1993). Perhaps recognizing the different behavioral correlations of different faster rhythms, Jasper and Andrews (1938) used the term "gamma waves" for frequencies between 35 or 45 Hz. The idea that this "40-Hz" oscillation is a "cognitive" rhythm perhaps originates from Henri Gastaut (Das and Gastaut, 1955). The French investigators described high amplitude, 40 Hz rhythmic trains in the scalp EEG of trained yogis during the samadhi state. Banquet (1973) also observed 40-Hz bouts during the third deep stage of transcendental meditation. (For a modern day replication of these observations, see Lutz et al., 2004). In normal subjects, Giannitrapani (1966) found increases in 35-45 Hz



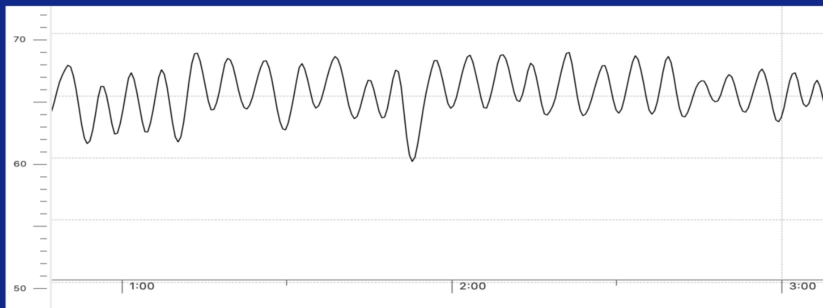


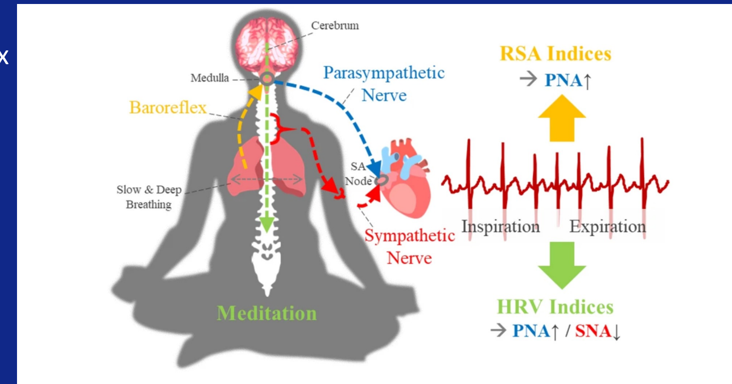
Lutz et al.
PNAS
2004.



Meditation and single-lead ECG.

Park, C., Youn, I. & Han, S. Single-lead ECG based autonomic nervous system assessment for meditation monitoring. *Sci Rep* **12**, 22513 (2022). https://doi.org/10.1038/s41598-022-27121-x

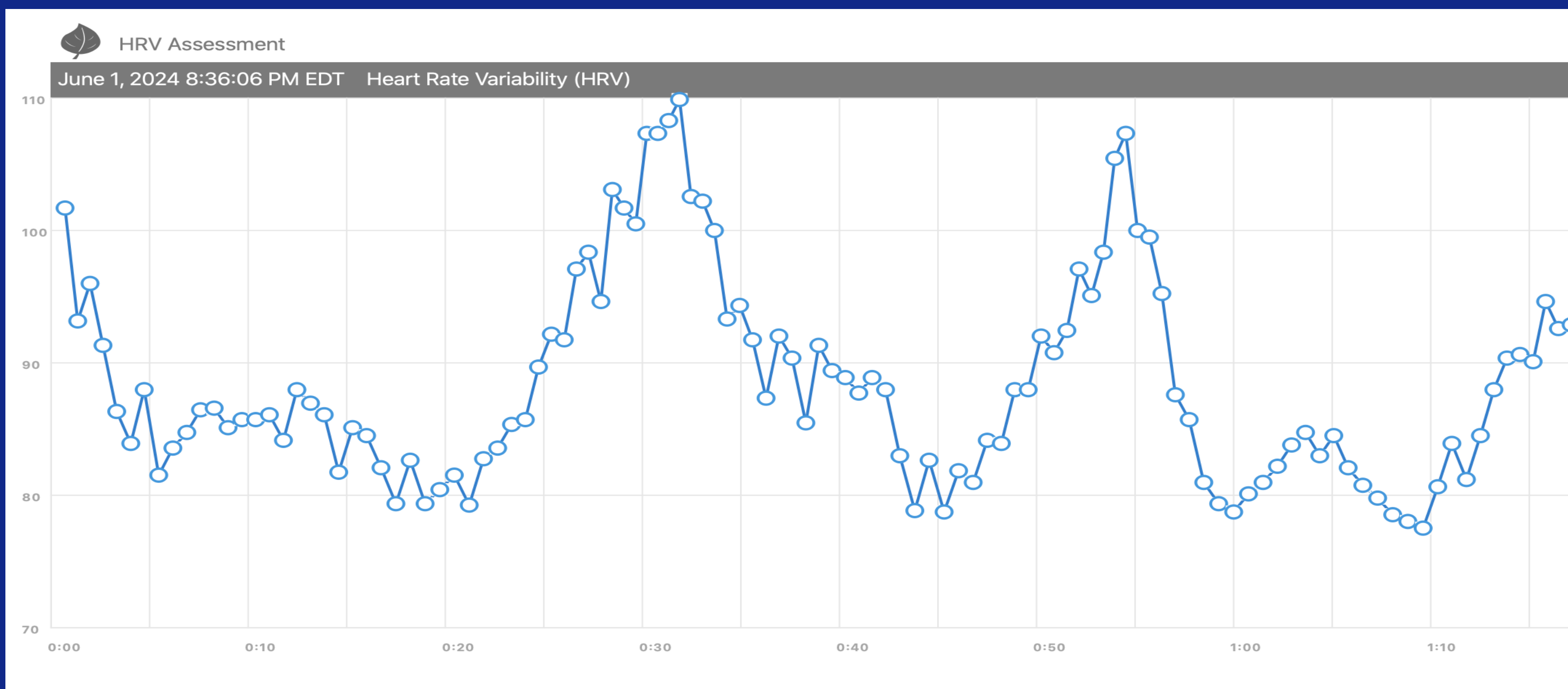




Meditation and single-lead ECG.

Heart Rate

110
100
90
80
70



Time
20 sec
45s
70s

Letter | Published: 21 January 1982

Body temperature changes during the practice of g Tum-mo yoga

Herbert Benson, John W. Lehmann, M. S. Malhotra, Ralph F. Goldman, Jeffrey Hopkins & Mark D. Epstein

Nature **295**, 234–236 (1982) | Cite this article

2438 Accesses | **74** Altmetric | Metrics

Kjaer T et al. **Increased dopamine tone during meditation-induced change of consciousness**. 2002. Cog Brain Research 13:255-259.

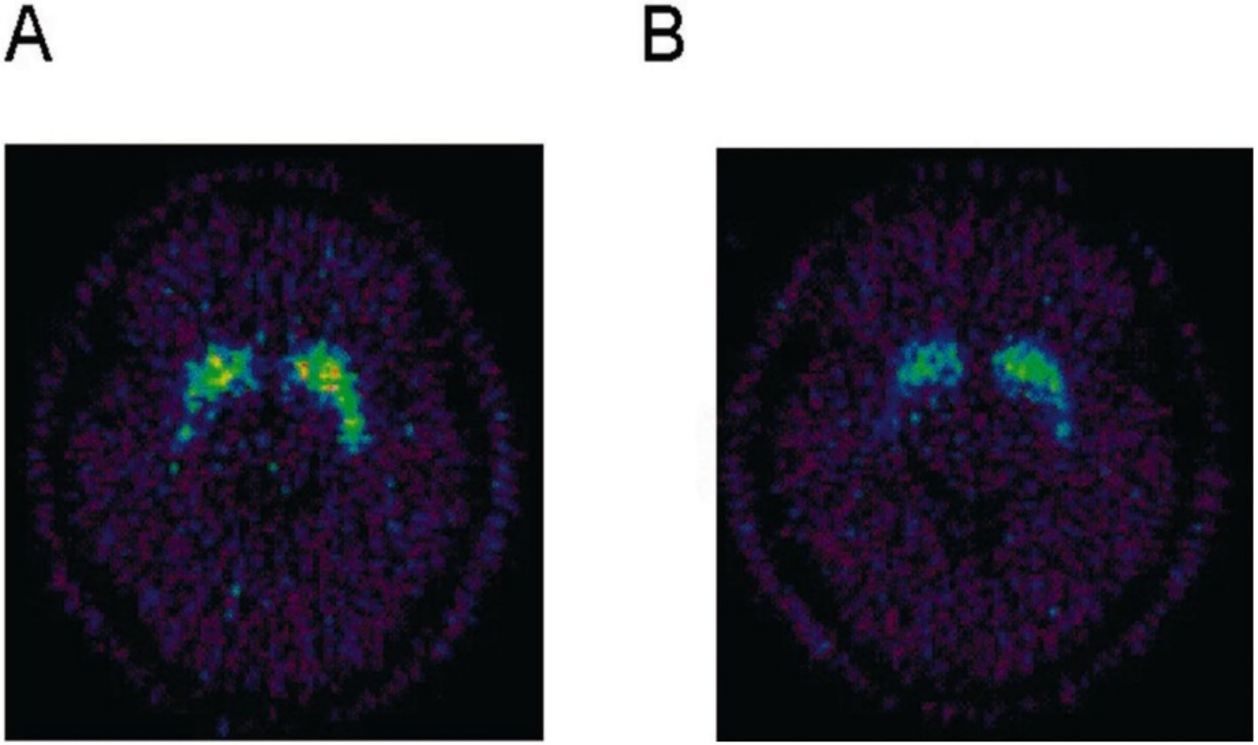


Fig. 1. The ^{11}C-raclopride binding potential images at the level of the striatum for one participant (No. 8) during attention to speech (A) and meditation (B). The reduced ^{11}C-raclopride binding potential in ventral striatum is evidence of increased endogenous dopamine release during meditation.

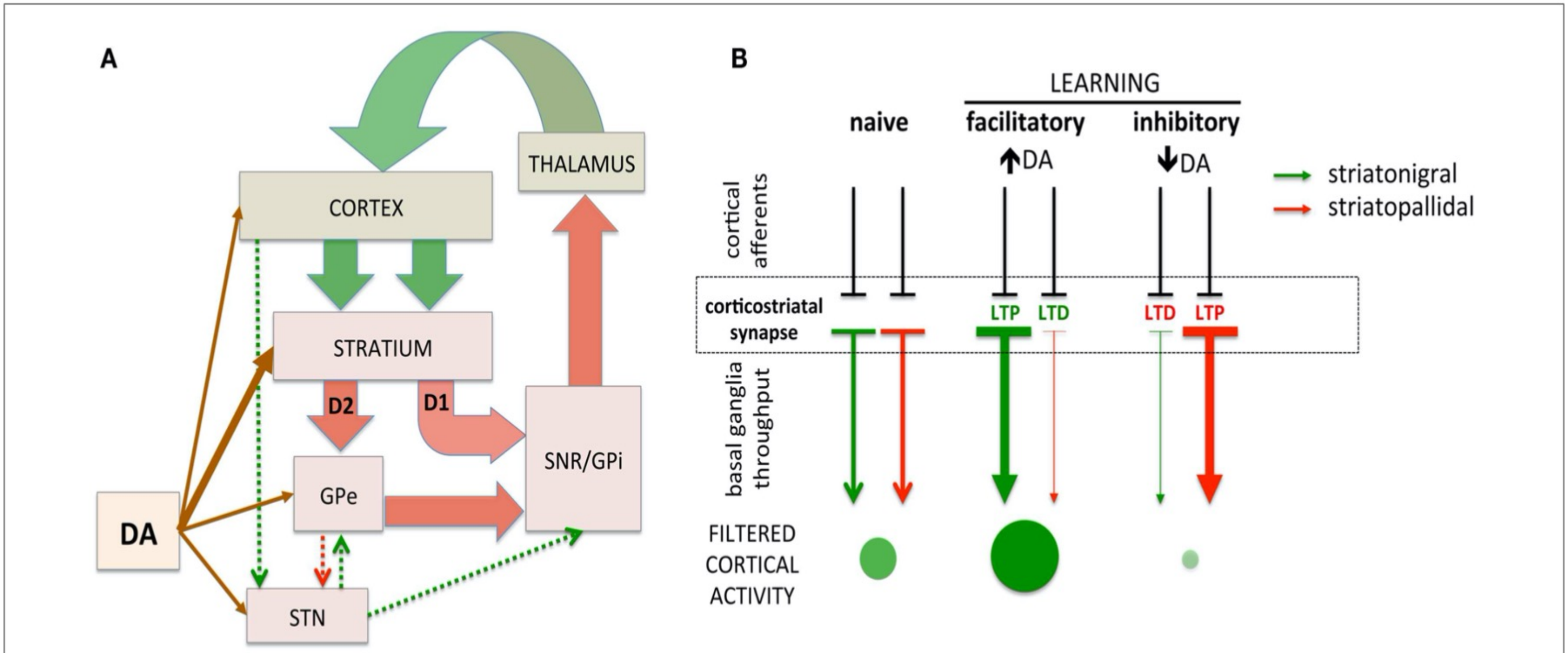
Fuente-Fernández R, Stoessl A. 2002. **The placebo effect in Parkinson's disease.** Trends Neurosci 25(2): 203-306. https://doi.org/10.1016/S0166-2236(02)02181-1.

PET study: dopamine release in response to placebo treatment in Parkinson's disease

Using PET with [^{11}C]raclopride (RAC), we found that patients with Parkinson's disease release substantial amounts of dopamine in the dorsal striatum (i.e. caudate and putamen) in response to subcutaneous injection of saline (Fig. 1) [50]. In this paradigm, changes in RAC binding between baseline and post-activation states (in this case, in response to placebo injection) represent a change in synaptic dopamine levels, reflecting the release of endogenous dopamine. Placebo-induced changes in

The Enemy Within: Propagation of Aberrant Corticostriatal Learning to Cortical Function in Parkinson's disease

Beele J, Petzinger G and Jakowec M. Frontiers Neurol 2013. 4:134. Doi:10.3389/fneur.2013.00134



Contents lists available at SciVerse ScienceDirect

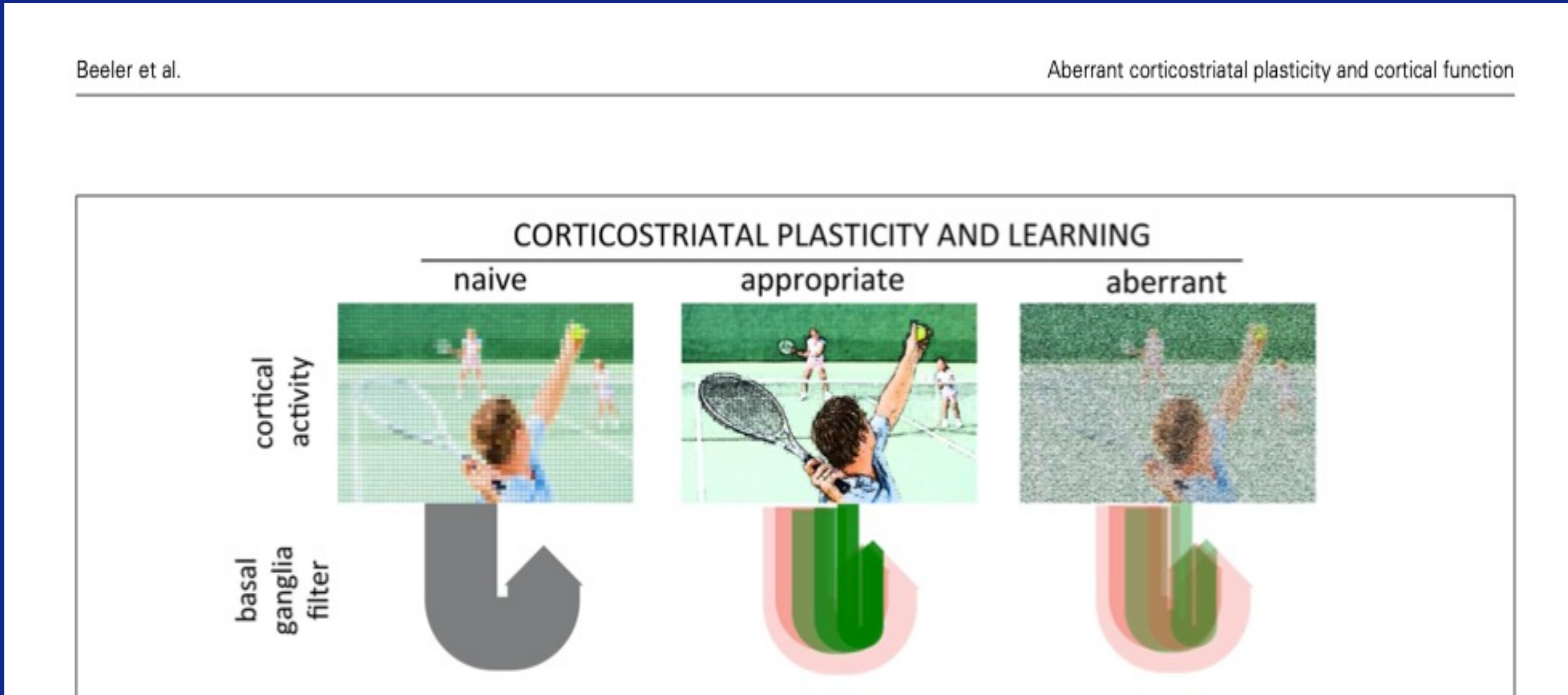
Brain Stimulation

journal homepage: www.brainstimjrnl.com

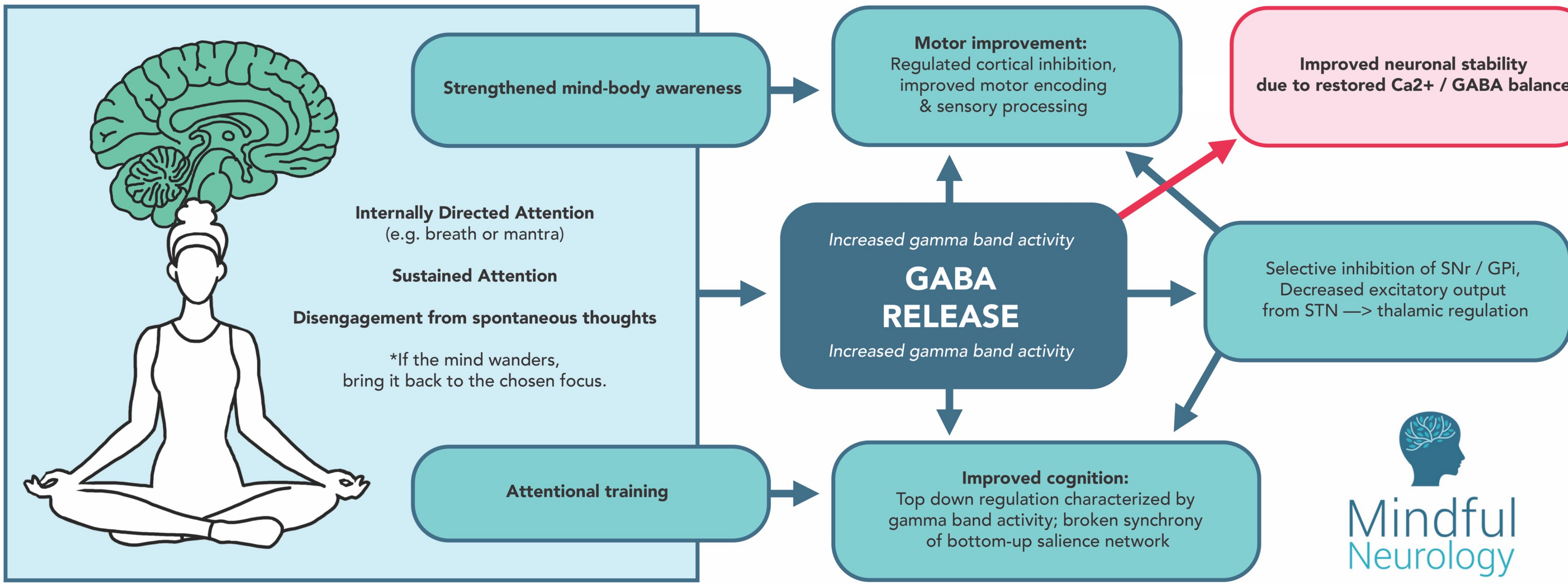
Meditation-Related Increases in $GABA_B$ Modulated Cortical Inhibition

Crissa L. Guglietti [a], Zafiris J. Daskalakis [b], Natasha Radhu [b], Paul B. Fitzgerald [c], Paul Ritvo [a,d,*]

[a] York University, Department of Kinesiology and Health Science, Toronto, Ontario, Canada
[b] Centre for Addiction and Mental Health, University of Toronto, Toronto, Ontario, Canada
[c] Monash Alfred Psychiatry Research Centre, The Alfred and Monash University Central Clinical School, Commercial Rd. Melbourne, Victoria, Australia
[d] Cancer Care Ontario, Toronto, Ontario, Canada

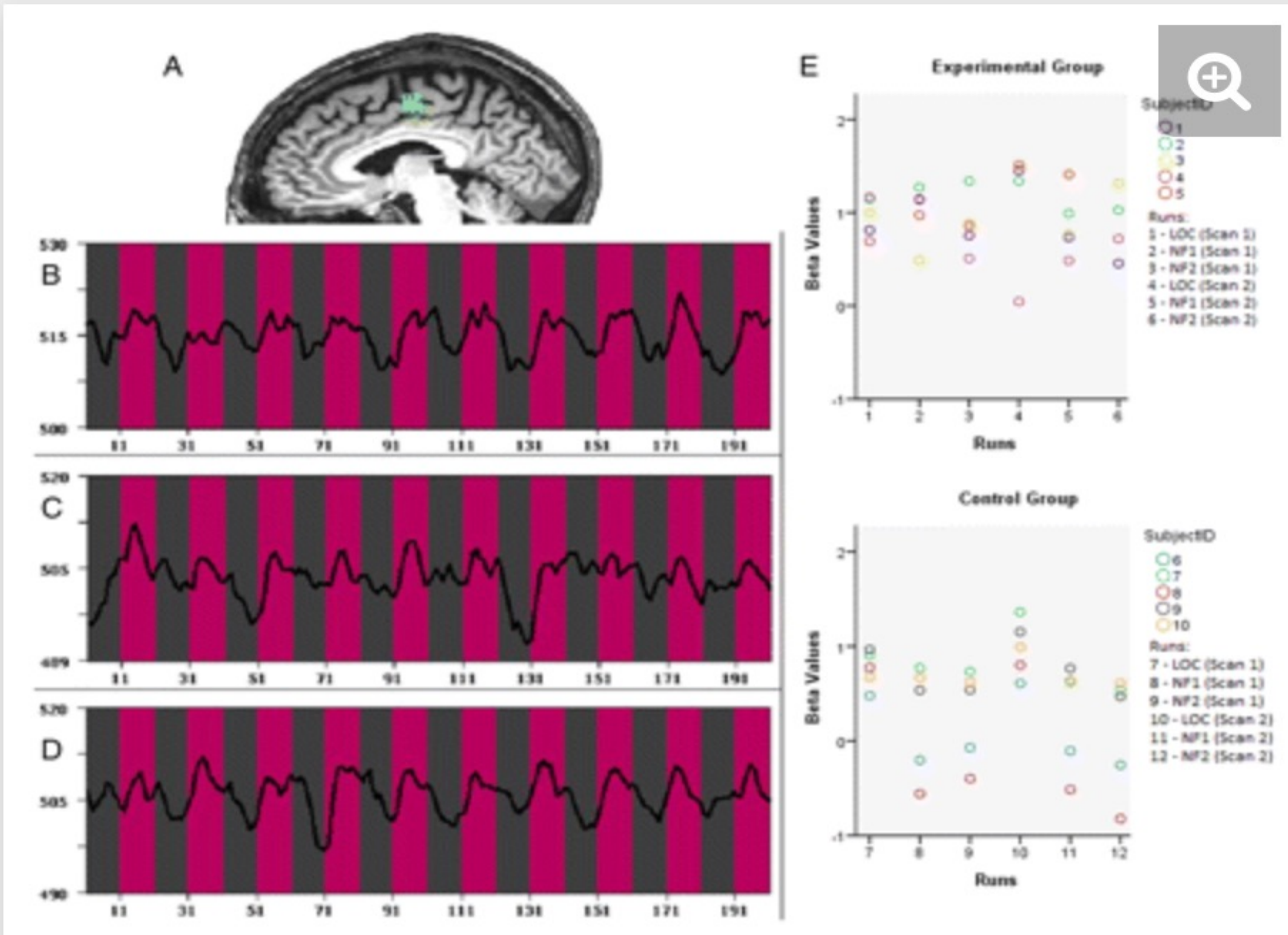


The Enemy Within: Propagation of Aberrant Corticostriatal Learning to Cortical Function in Parkinson's disease. Beele J, Petzinger G and Jakowec M. Frontiers Neurol 2013. 4:134. Doi:10.3389/fneur.2013.00134



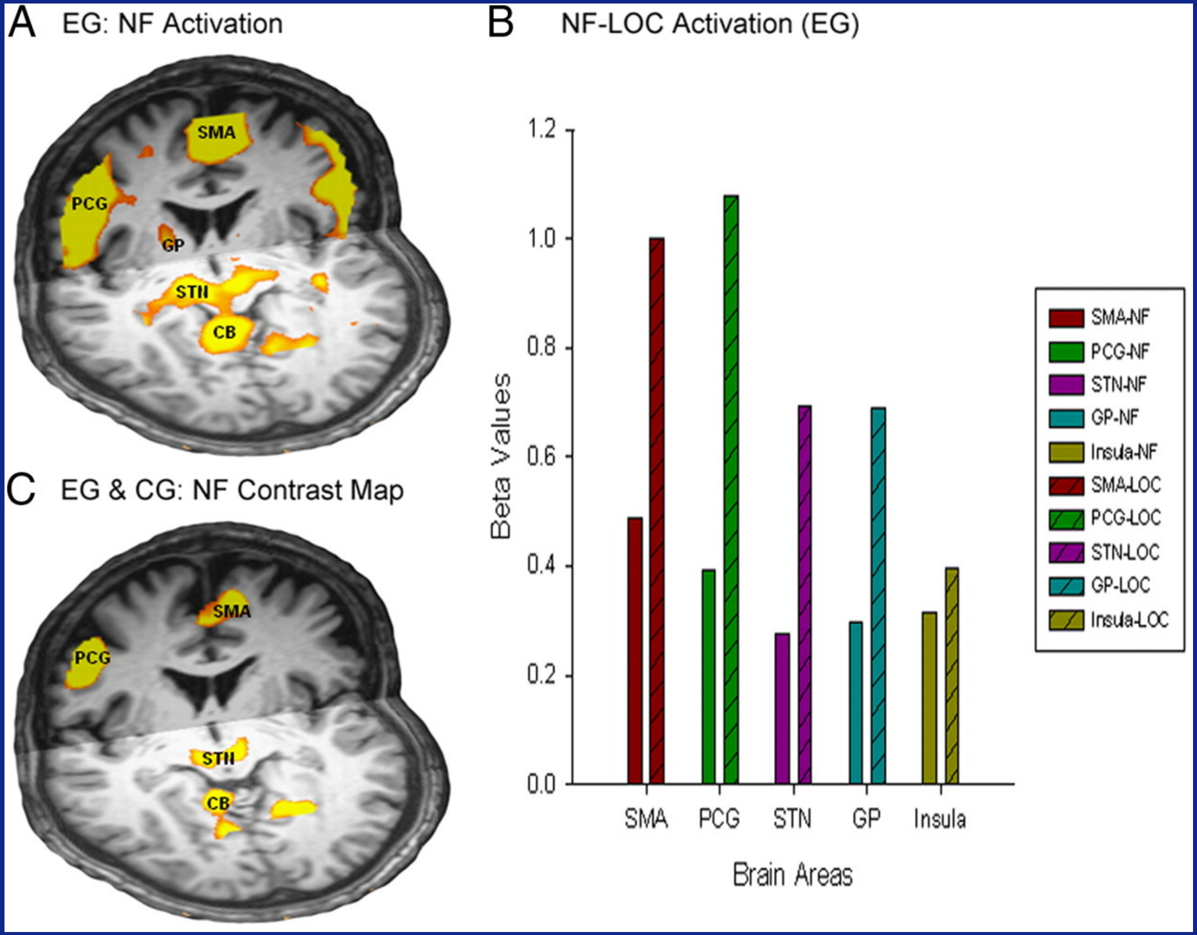
Mulukutla S et al. 2023. Parkinson's Study Group poster presentation.

Kinesthetic Motor Imagery: Neurofeedback for PD



Leena Subramanian et al. J. Neurosci. 2011;31:16309-16317

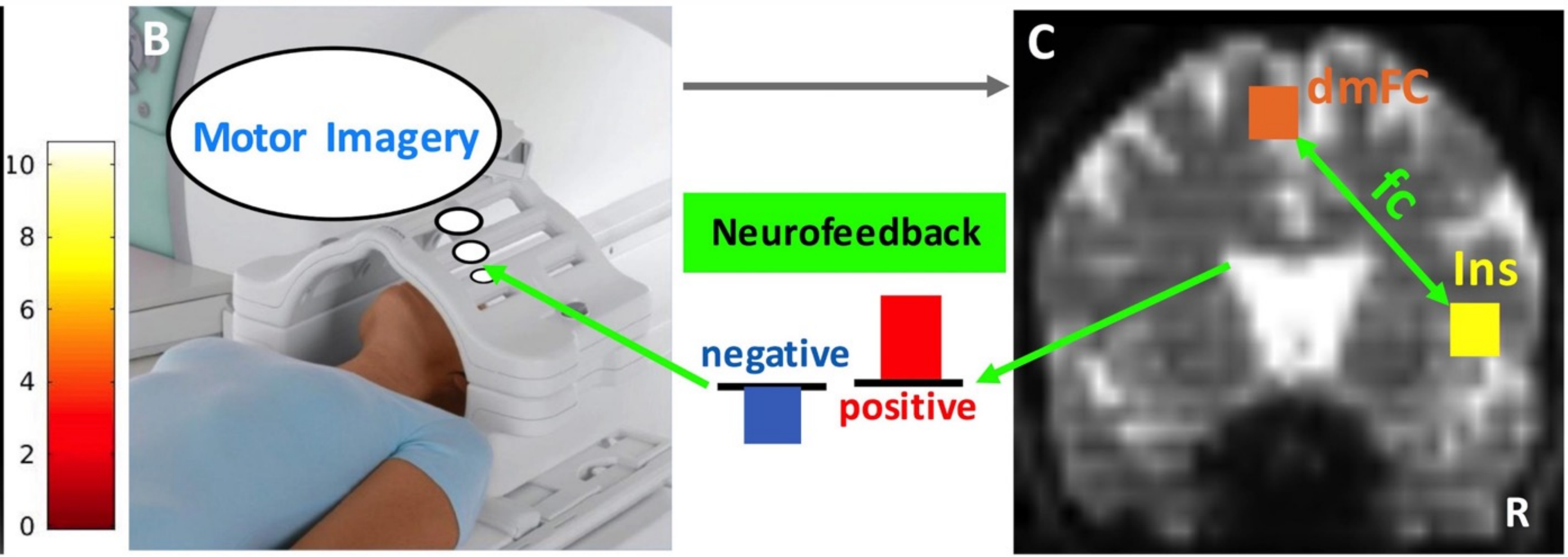
Kinesthetic Motor Imagery for PD:



Leena Subramanian et al. J. Neurosci. 2011;31:16309-16317

HYPOTHESIS AND THEORY article
Front. Hum. Neurosci., 07 December 2018
Sec. Motor Neuroscience
Volume 12 - 2018 | https://doi.org/10.3389/fnhum.2018.00496

Insula as the Interface Between Body Awareness and Movement: A Neurofeedback-Guided Kinesthetic Motor Imagery Study in Parkinson's Disease



Mindfulness = paying attention on purpose

The Steps of Meditation

1. Choose an object to focus on
2. Sustain attention
3. Disengage from spontaneous thoughts when they arise

6 – week Virtual Training program for PwP and their Care Partners

Technique	Why?
Body Scan	Strengthen sensory processing
Focused concentration	Parasympathetic activation, attentional training, mindfulness
Paced Breathing	Relaxation, ↓ rigidity,
Kinesthetic Motor Imagery	Aid for freezing of gait / off med, upregulate motor networks
Mindful Walking, Mindful Eating	Mindfulness on the go
Attitudes of mindfulness	Stress Management, reduction of rumination/anxiety/depression

Psychological Benefits

Trait mindfulness

Body-sensory awareness

Stress awareness

Attentional training

Emotional regulation

The Steps of Meditation

1. Choose an object to focus on
2. Sustain attention
3. Disengage from spontaneous thoughts when they arise

Parasympathetic activation

Gamma wave neural activity

Sympathetic deactivation

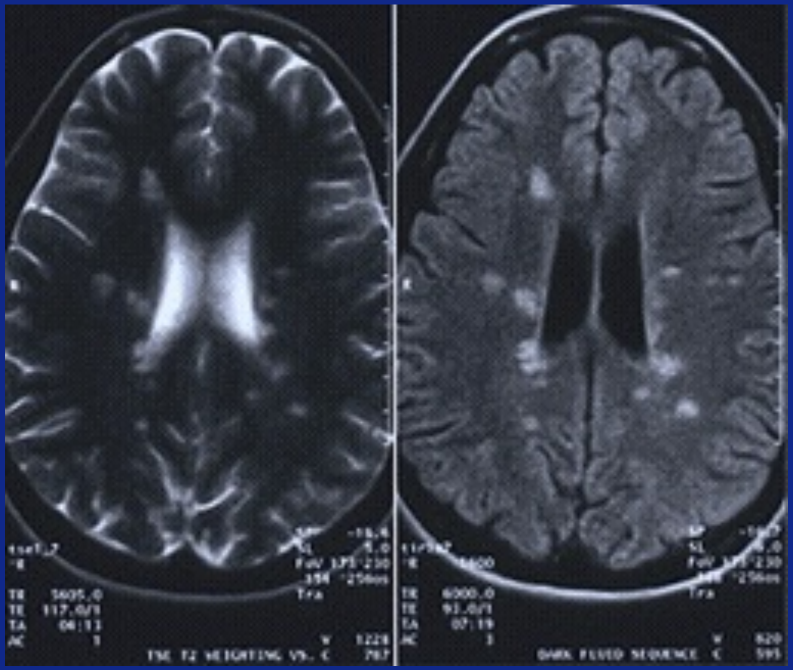
Cortical inhibition

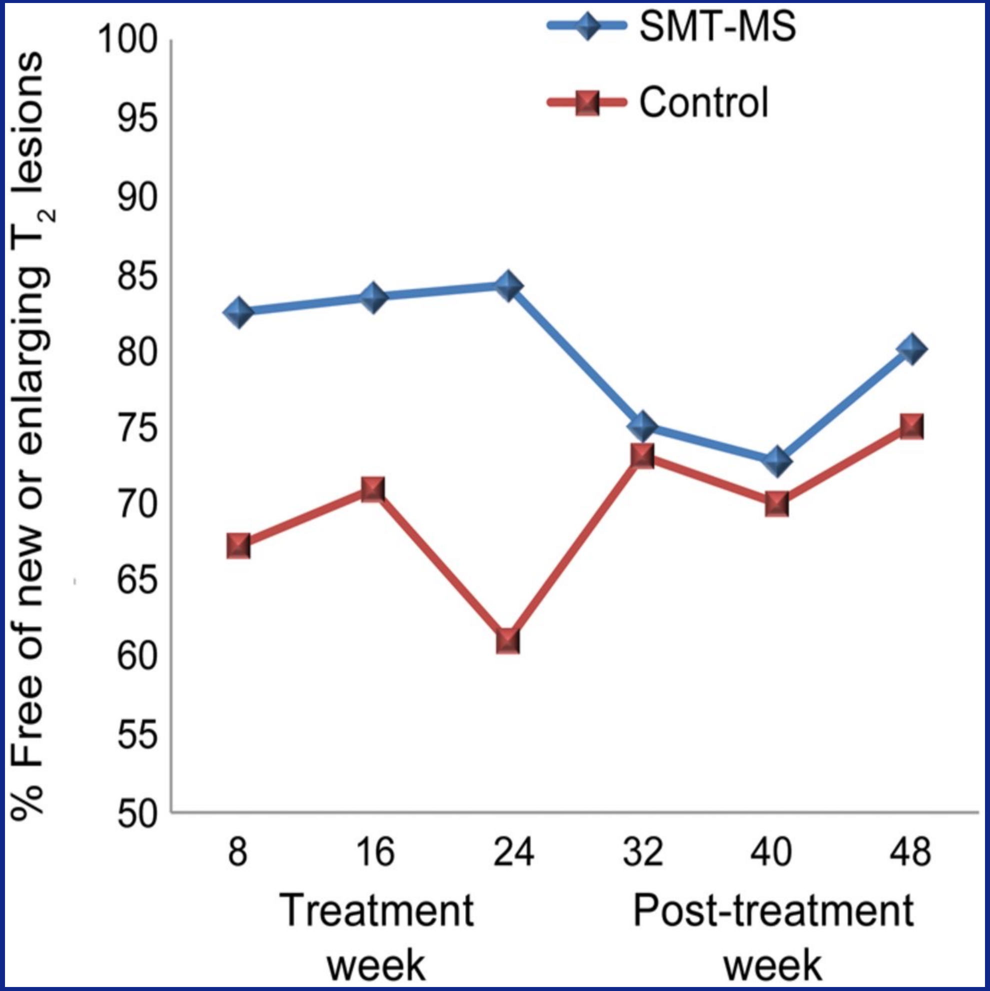
GABA/Dopamine release

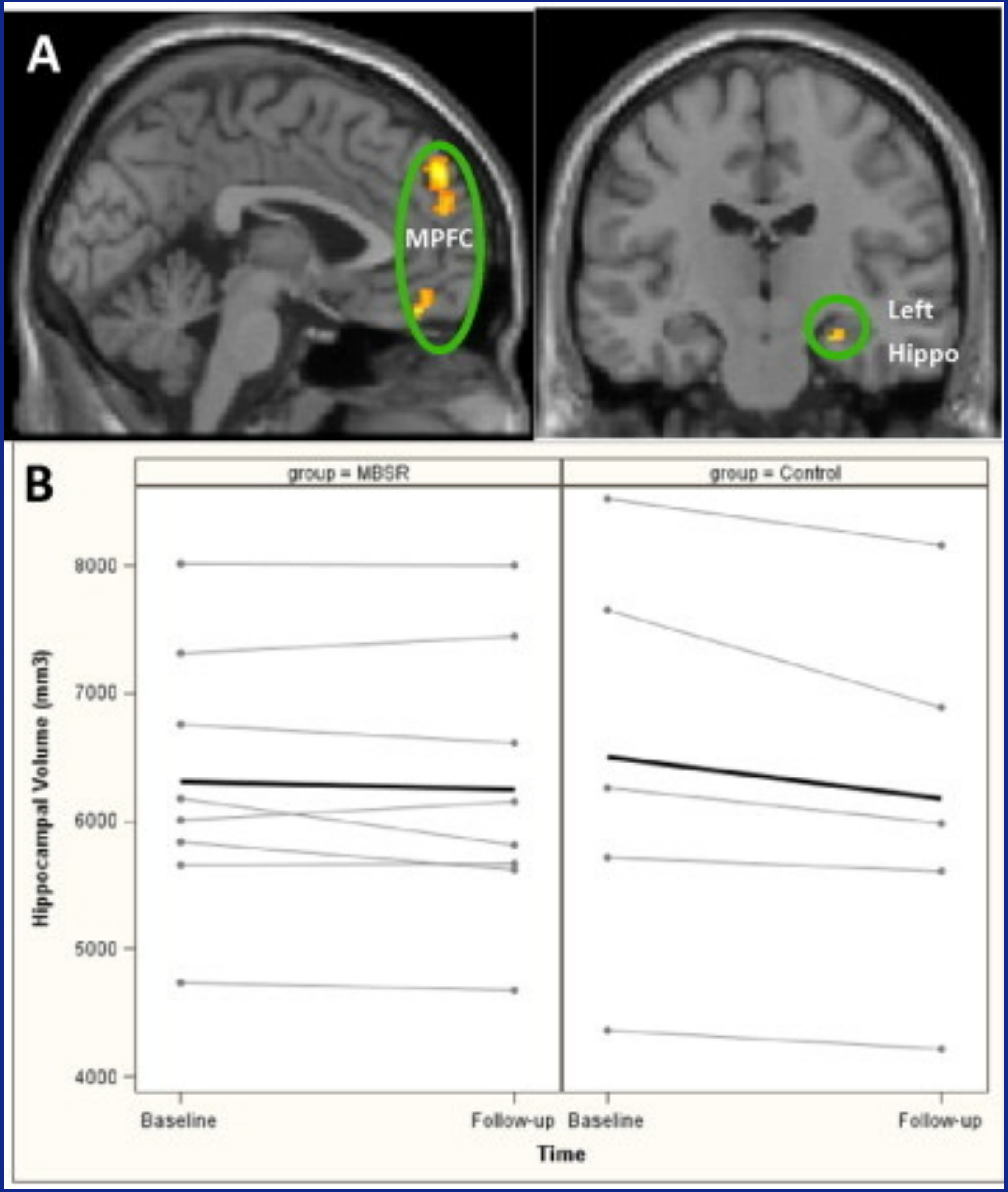
Physiological Benefits

Stress Management Counseling for people with MS:
Decreased Plaque Development while undergoing counseling

Class I Evidence:
Mohr et al Neurology 2012







MBSR for MCI

Wells RE
Neurosci Let
2013

BREVIA

A Wandering Mind Is an Unhappy Mind

Matthew A. Killingsworth* and Daniel T. Gilbert

Science

AAAS

Science 2010, 330:932

"Although negative moods are known to cause mind wandering, time-lag analyses strongly suggested that mind wandering in our sample was generally the cause, and not merely the consequence, of unhappiness"

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Lutz A et al. Long-term meditators self-induce high-amplitude gamma synchrony during mental practice, *Proc. Natl. Acad. Sci. U.S.A.*101 (46) 16369-16373, https://doi.org/10.1073/pnas.0407401101 (2004).

Park, C., Youn, I. & Han, S. Single-lead ECG based autonomic nervous system assessment for meditation monitoring. *Sci Rep* 12, 22513 (2022). https://doi.org/10.1038/s41598-022-27121-x

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Thank you!

Learn to Meditate: An innovative program teaching mind-body strategies to people with Parkinson's disease

Sarah Mulukutla, MD MPH[1]; Kristina Zawaly PhD[1]; Mark Reed BA[2]; Evelyn Ooi MD[3]; Deborah Zhang, BA;[3] Harini Sarva MD[3].

1.Mindful Neurology, PLLC. Monroe, NY. 2. California Northstate University College of Medicine, Elk Grove, CA. 3. Weill Cornell Parkinson's Disease & Movement Disorder Institute. New York, NY.

Objective

To test the efficacy of a virtual program delivering education on mind-body strategies

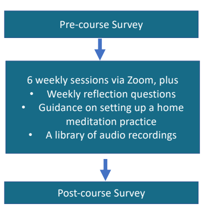
Rationale

Research suggest that mind-body approaches could be effective for PD-related motor and non-motor symptoms, but no authoritative training program currently exists.

The Intervention

A 6-week, virtual training in: Sitting Meditation; Neurologic Relaxation (Coherent Breathing); Visualization & Kinesthetic Motor Imagery; Mindful Walking; Progressive Muscle Relaxation; Compassion; and Foundations of Stress Management.

The program was developed as a partnership between Weill Cornell Parkinson's Disease & Movement Disorders Institute and Mindful Neurology, PLLC. A neurologist directed and executed the training. Participants paid $295 to join the program; enrollment fee waived for low income PwP.



Participants

37 PwP from 4 countries & 13 US States joined the course.

28 paid the enrollment fee; 9 were given gratis entry.

9 spouses / children enrolled to support their family member; no additional fee required for care partner registration.

41 participants completed the pre-course survey (34 PwP, 7 family members)

Mean age of participants: 65.7yrs; SD 9.3.

Program Evaluation & Statistical Evaluation

QI data was collected at conclusion of the program. 4 Rating scales were included in the pre- and post-course survey: Comprehensive Inventory of Mindfulness Experiences (CHIME); GAD-7; PDQ-8; Athens Insomnia Scale (AIS). Family members completed the Caregiver Self-Assessment Questionnaire instead of the PDQ-8.

We received 16 completed pre & post-course rating scales from PwP. Wilcoxan Signed Rank Test was used to evaluate for meaningful impact of the intervention.

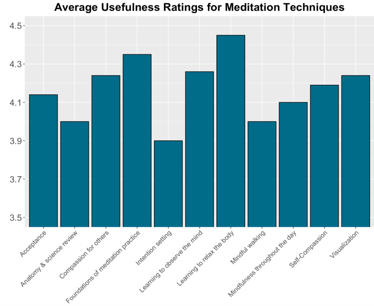
Video: Bradykinesia improves after a single relaxation/meditation session

Sample Exercise:

Course Website:

Key Findings

PwP ranked the following tools most useful:



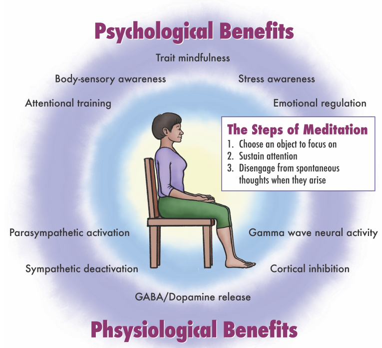
Likert Scale: 1 = Not at all useful, 2 = Slightly useful, …, 5 = Extremely useful.
Scores averaged for each technique. N = 21.

PDQ-8 and GAD-7 scores significantly decreased (n=16)

An exploratory investigation looked at individual questions, to seek clarity on which aspects of non-motor symptoms might be targeted with mind-body interventions.

Rating Scale	Pre-Course Average	Post-Course Average	Statistical Significance
PDQ-8	**18.63**	**16.13**	**p = 0.0043**
Q2. Had difficulty dressing yourself			p = 0.05
Q3. Felt depressed			p = 0.02
Q5. Had problems with your concentration e.g. when reading or watching TV			p = 0.03
GAD-7	**8.00**	**4.50**	**p = 0.0027**
Q3. Not being able to stop or control worrying			p = 0.02
Q4. Worrying too much about different things			p = 0.03
Q5. Trouble relaxing			p = 0.01
AIS	**6.06**	**5.25**	**p = 0.09**
Q1. Sleep induction: Time it takes you to fall asleep after turning off the lights			p = 0.05
CHIME	**108.4**	**116.9**	**p = 0.07**
It is easy for me to stay focused on what I am doing			0.033
When I talk to other people, I notice what feelings I am experiencing			0.029
Q9. I see my mistakes and difficulties without judging myself			0.013

Meditation: Mechanisms of Action



Meditation – the act of sitting quietly while practicing active concentration and disengagement from spontaneous thoughts – has been associated with numerous health benefits relevant for the PD population:

- Strengthened parasympathetic tone[1]
- Immune modulation[2]
- Improved ROS clearance and cellular metabolism[1,3]
- Epigenetic changes[4,5]
- Release of BDNF[6]
- Regulation of the HPA Axis[7]
- Cortical Inhibition [8,9]
- Release of dopamine and/or GABA[9,10]

Long-term benefits may include an upregulation of sensorimotor cortices (as seen in a recent Tai Chi study) and downregulation of the body's stress response and amygdala signaling.[7,11] Our research uses high-density EEG to evaluate cortical and subcortical coupling and coherence as biomarkers for the impact of meditation in PwP. We hypothesize that meditation training has the potential to physiologically modulate aberrant neural network connectivity, which is featured in Parkinson's disease.

Qualitative Feedback

"Rigidity is a major problem for me so learning to relax is very helpful."

"I am still using the visualization technique to help with my freezing. It happens less and less often!"

"If I apply the techniques consistently, they are surprisingly effective. This is development of a skill, not magic."

"If I am mindful when I am getting up out of the chair, instead of being angry that my feet are not moving, I seem to be more fluid."

General Feedback:

- Participants found scientific explanations helpful, especially when techniques were related to Parkinson's pathophysiology (i.e. Kinesthetic Motor Imagery was introduced by explaining sensory processing deficits in PD and showing MRI neurofeedback studies in which networks were upregulated via mental motor imagery.)
- Group discussions created motivation for participants to attend weekly sessions.
- Participants needed more time to learn how to apply the techniques more effectively.

Conclusions & Next Steps

Delivering mind-body strategies via virtual workshops is feasible and was well-received. Objective data about motor benefits is necessary to verify anecdotes shared by participants (e.g. via wearable symptom trackers).

We are pursuing the following research protocol:

Phase I – Pilot Data collection

Outcome Measures: High-density EEG evaluation of coherence, coupling and network connectivity; UPDRS-III; and visuo-spatial and executive function neuropsychological evaluation before and after a single session of focused concentration meditation.

Goals: Determine biomarker signatures of meditation in PwP.

Phase II – Multi-Site, longitudinal, single-arm cohort of PwP undergoing 10 weeks of meditation training

Outcome Measures: Pre- and Post-Intervention and 3-month follow-up: High-density EEG; functional MRI; UPDRS-III; digital symptom trackers; neuropsychological evaluation; anxiety/depression; and QOL rating scales.

References

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Protocol Design: Investigation into Meditation-Induced Neuromodulation for Parkinson's Disease (PD)

Sarah Mulukutla MD MPH[1], Evelyn Ooi MD[2]; Harini Sarva MD[2]; Deborah Zhang BA[2]; Kristina Zawaly, PhD[1]; Veronica Santini, MD[3]; Nabin Koirala, PhD[4]; Kenneth Pugh, PhD[4]; Adam Noah, PhD [5]; Mark Reed, BA[6]; Joy Hirsch PhD[5]

1. Mindful Neurology, PLLC. Monroe, NY. 2. Weill Cornell Medicine Parkinson's Disease & Movement Disorder Institute. New York, NY. 3. Dept of Neurology, Yale University. New Haven, CT. 4. School of Medicine, Yale University. New Haven, CT. 5. Brain Function Laboratory; Dept of Psychiatry, Yale University. New Haven, CT. 6. California Northstate University College of Medicine, Elk Grove CA

Meditation

The act of directing and sustaining attention on an internally-generated focus (e.g. breath or mantra).

- Down-regulates and changes connectivity of the default mode network[1,2]
- When combined with voluntary breath control, promotes heart rate variability and improved clearance of amyloid and tau proteins[3]

Has been associated with:

- Improved CV health[4]
- Regulation of HPA Axis[2]
- Immune modulation[5]
- Release of BDNF[6]
- Improved ROS clearance and cellular metabolism[7]
- Epigenetic changes[8,9]

Three features about meditation relevant for PD

I. Meditation releases GABA

Post-meditation cortical inhibition has been observed; studies on Yoga using spectroscopy have shown a GABA spike in the thalamus after a single session.[10-12] Mindfulness interventions for PD population have shown improvement in motor scores, even though mindfulness practice was the only intervention—without any motor component—suggesting a targeted mechanism directly from mental training.[2]

People with PD have increased cortical excitability and low GABA levels in motor cortex.[13,14] Zolpidem (GABA-A agonist) has been associated with rapid improvement in motor symptoms.[15,16] Administration of L-Dopa to PD subjects increases upper brainstem GABA.[17] GAD gene therapy is currently being trialed as a therapeutic intervention for PD, with the intention to increase GABA synthesis to regulate STN/GPi hyperexcitability.[18]

GABA deficiency is thought to contribute to alpha-synuclein aggregation and Lewy Body formation, as adequate Ca2+/GABA balance is required to maintain cellular stability.[19-21]

Could GABA-mediated mechanisms be responsible for some of the remarkable improvements we've seen following meditation? During trainings programs, we saw a significant reduction in anxiety (close to 50% decrease in GAD-7 scores) and at times a rapid correction of motor abnormalities.

II. Meditators exhibit high – amplitude gamma waves

Will people with PD generate gamma waves during meditation similar to healthy controls? If detected, will gamma band activity be associated with improved motor function?

High-Gamma oscillations (60-90Hz) were first detected during meditation in experienced meditators, are GABA-mediated, and play a role in attention and cognition.[22,23] Gamma waves are considered prokinetic in Parkinson's disease, but their relevance has not been clearly established. When co-occurring with decreased beta band activity, the emergence of high-gamma has been associated with improved motor scores.[24]

III. Trait mindfulness, body sensory awareness and enhanced attentional capacity are natural consequences of meditation practice

Meditation is essentially a training of attentional control, and one which emphasizes bodily sensations. People with PD are at risk for impaired attentional regulation, and demonstrate deficits in sensory processing and proprioception.[25-27] Additionally, mindfulness has been shown to mitigate stress and anxiety, which would be very helpful to the PD population regardless of physiological biomarker changes.[2] To the best of our knowledge, neuropsychological testing before and after meditation training to assess for improvement in attention and executive function in people with PD has not previously been published, despite known efficacy in healthy controls. People with MCI can learn to meditate and demonstrate trends toward improved memory scores.[28-30]

Will people with PD demonstrate improved neuropsychological performance after meditation training? If yes, can this serve as a long-term preventive strategy?

Proposed Research Design

Phase I: Exploratory Investigation into Physiologic Biomarkers of Focused Meditation in People with PD

Target Subjects: 3-4 PwP who have regular meditation practice

Data Collection: High Density 128-channel EEG recording before, during and after meditation.

Session 1: ≥ 12hrs since last dopamine augmentation

Session 2: Post-dopamine augmentation.

Outcome measures:

- EEG Spectral Analysis of sources (using electrical source imaging) in motor & sensorimotor cortices; basal ganglia; thalamus & STN; attentional networks
- EEG Frequency Coupling, Coherence, and Connectivity between the sources
- Neuropsychological tests before and after Session 1 / Session 2
- UPDRS before and after Session 1 / Session 2

Research Goal: Determine neuro-physiological biomarkers to be used in Phase II

Phase II: Longitudinal Changes in Biomarkers following Meditation Training

Target Subjects: 15 PwP – Novice to meditation, H-Y ≤ 4 (+/- MedTronic Percept DBS)

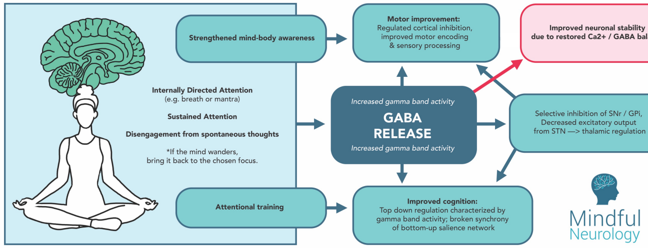
Intervention: Single arm investigation evaluating clinical and neuro-physiological biomarkers pre- and post- meditation training, using the Mindful Neurology Learn to Meditate™ program (6-week training on meditation techniques specific to PD symptoms)

Outcome Measures:

- Feasibility evaluation
- EEG spectral analysis and connectivity pre-/post training & 3 months later
- fNIRS network connectivity analysis pre/post training & 3 months later
- MedTronic Percept Brain Sense local field potential recordings
- Neuropsychological eval pre/post training and 3 months after training conclusion
- Symptom trackers: 1 month pre-training thru 3 months post training
- Stress, anxiety, depression and QOL rating scales

Research Goal: Preliminary investigation to prepare for randomized trial

GABA Hypothesis



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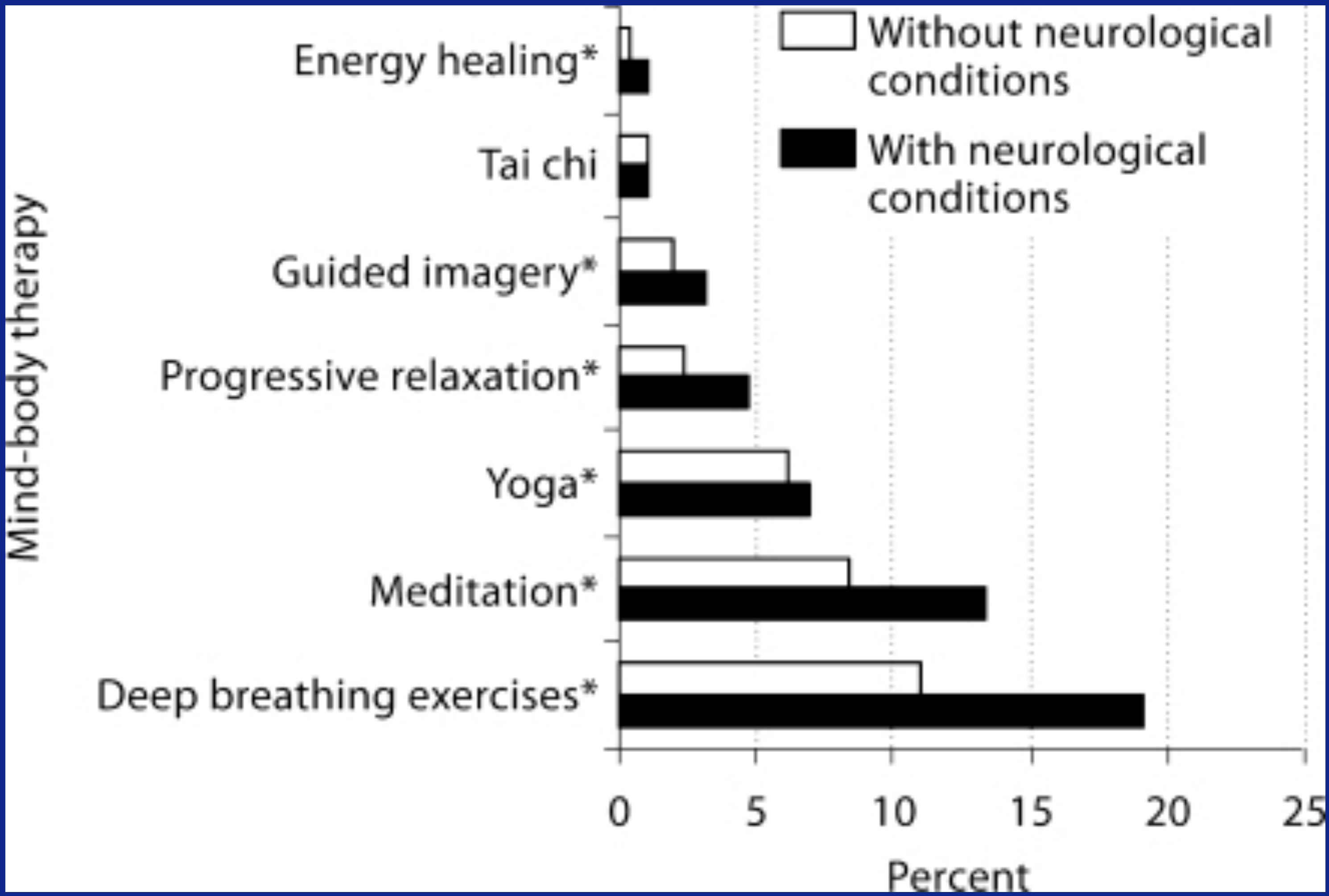
Utilization of Mind-Body Therapies by our patients



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