Imaging Horizons: Functional Brain Dynamics in Health and Disease

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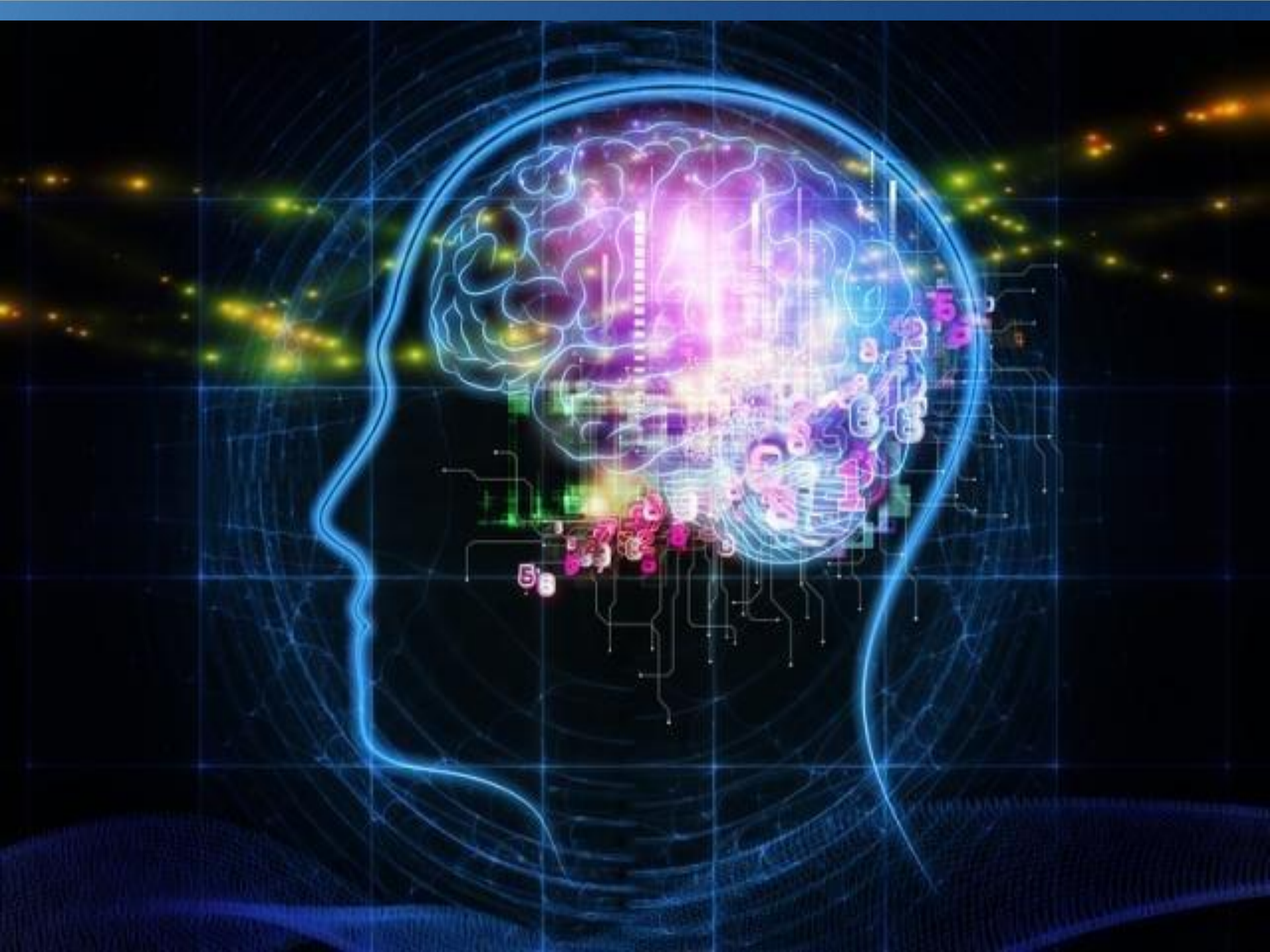
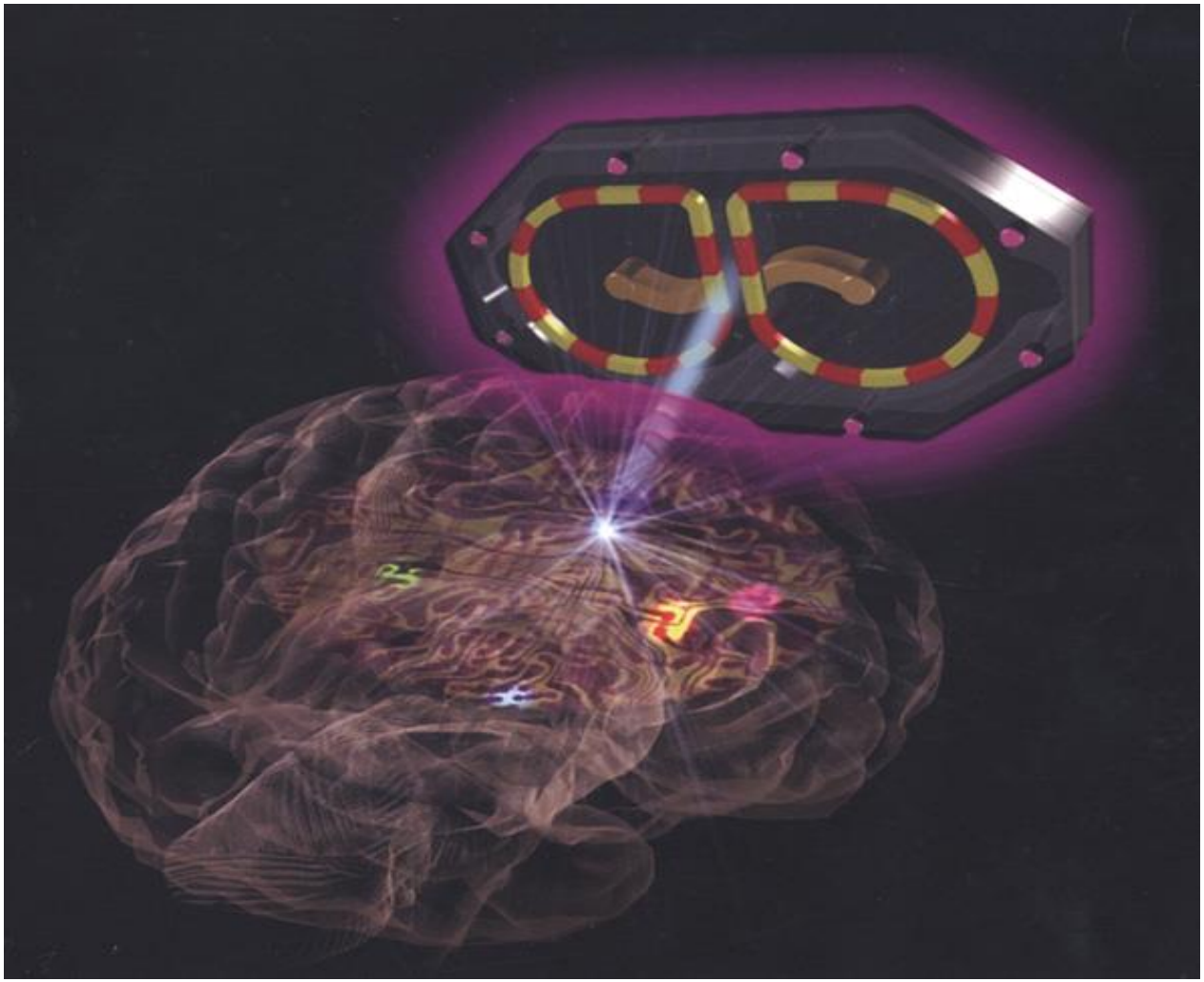
Lecture Objectives

- Describe working models of functional brain dynamics
- Review the dynamics of nociceptive and anti-nociceptive peripheral and central networks
- Overview techniques of functional neuroimaging
- Demonstrate modulation of brain networks in clinical pain by non-pharmacologic interventions

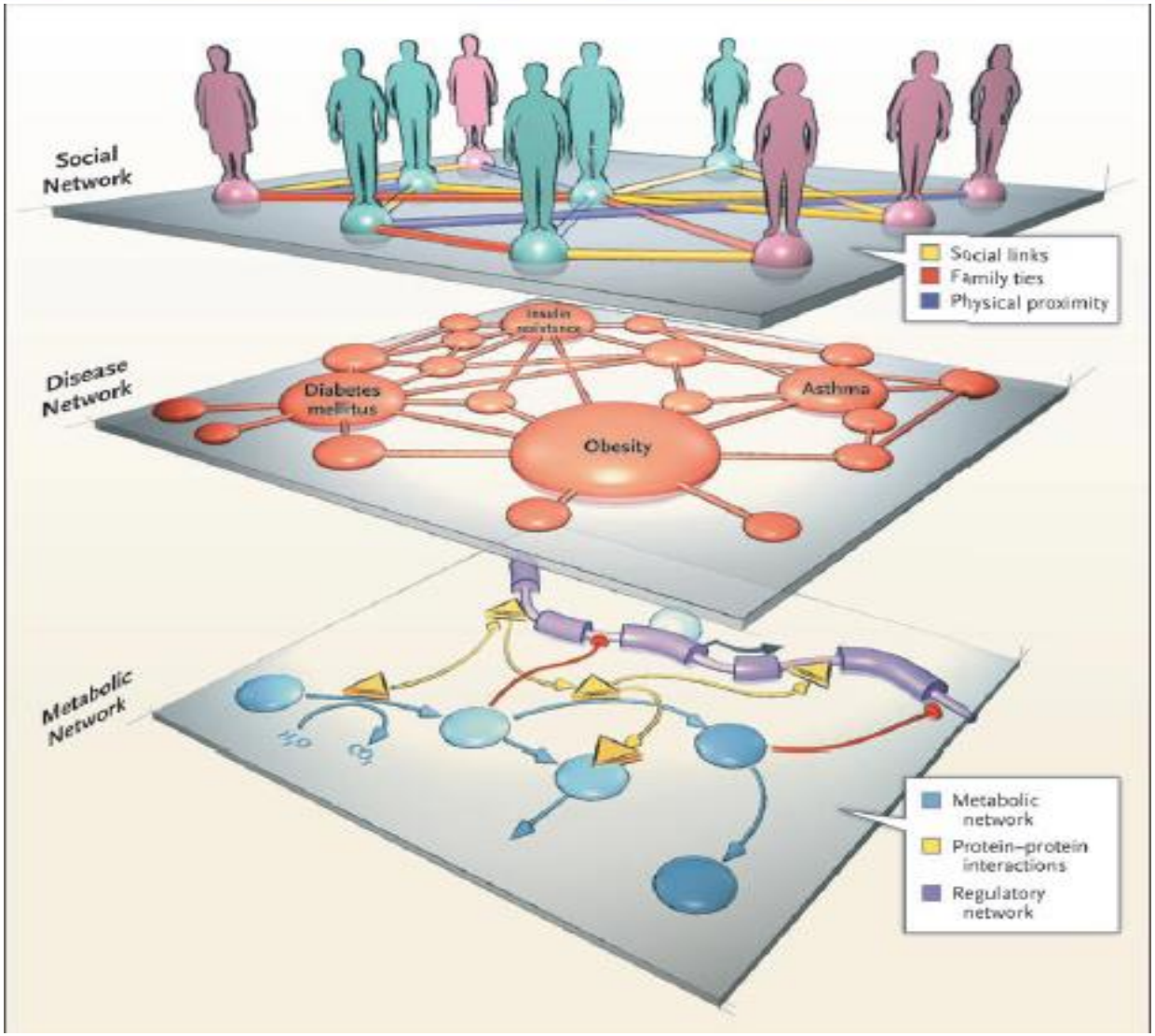


Transcranial Magnetic Stimulation



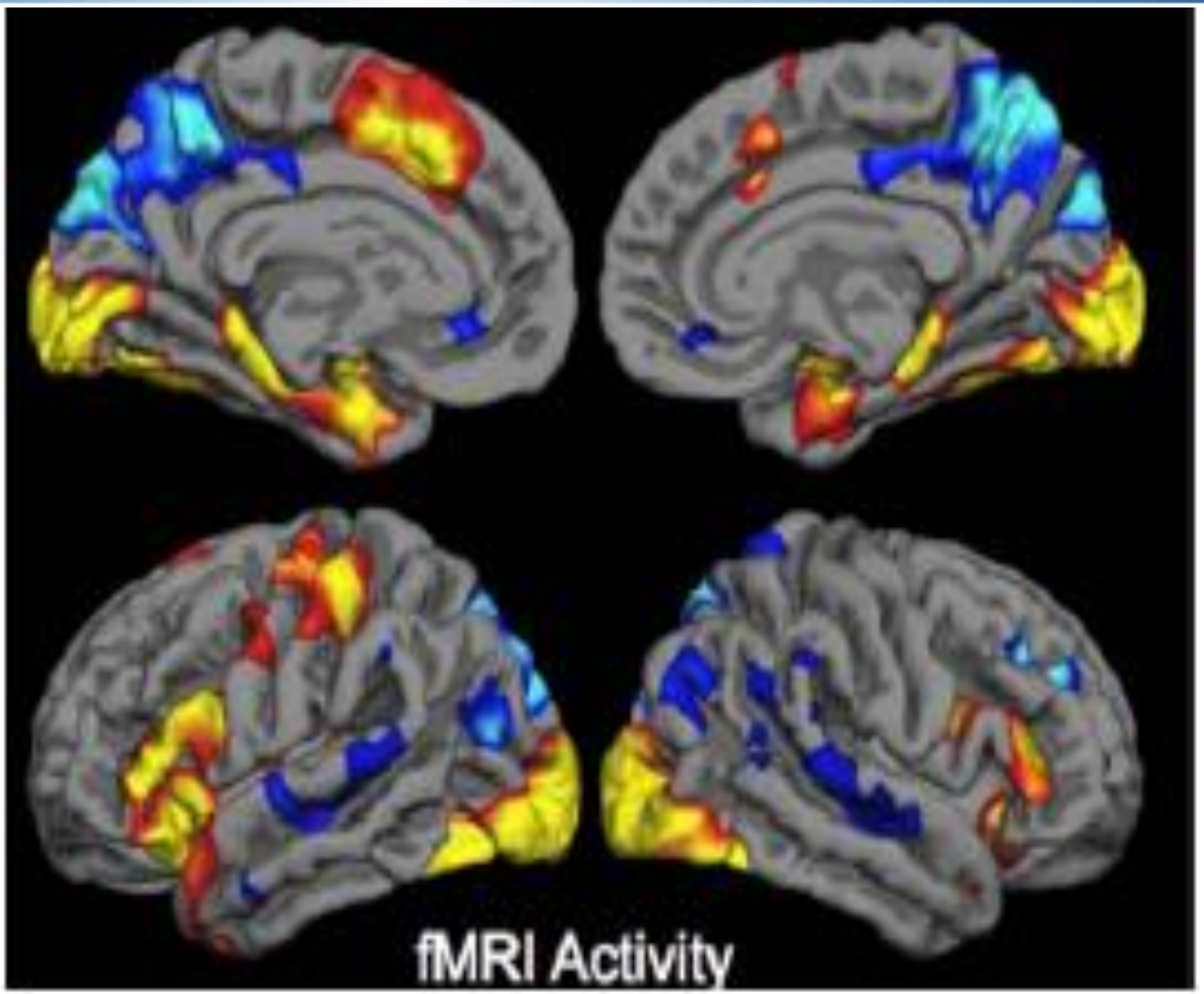
Human Brain Mapping, May 2004

Integrative Biopsychosocial Physiology



Christakis and Fowler, 2007

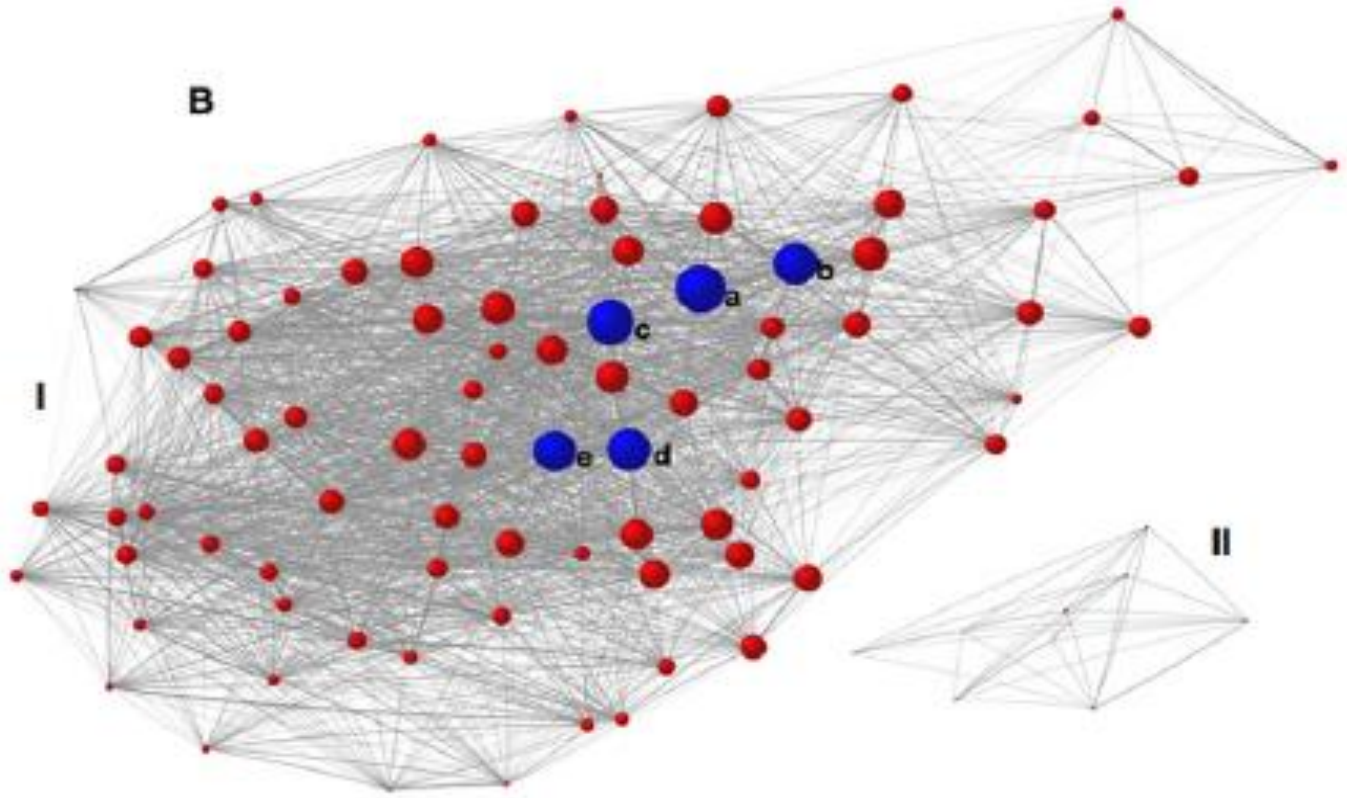
Memory Encoding Network



Sperling et al, 2009

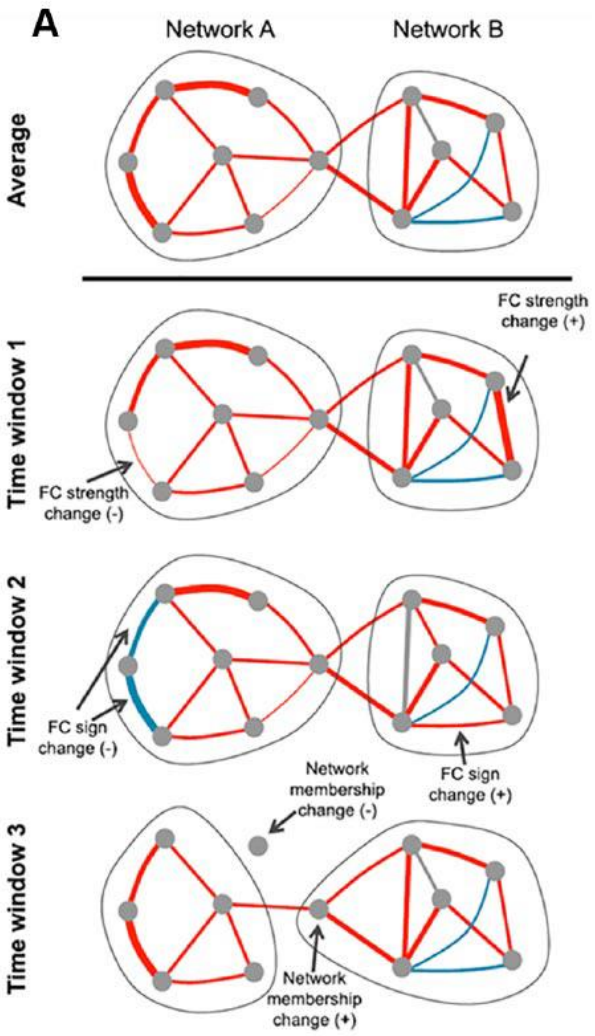
Brain Networks Nodes, Links and Hubs

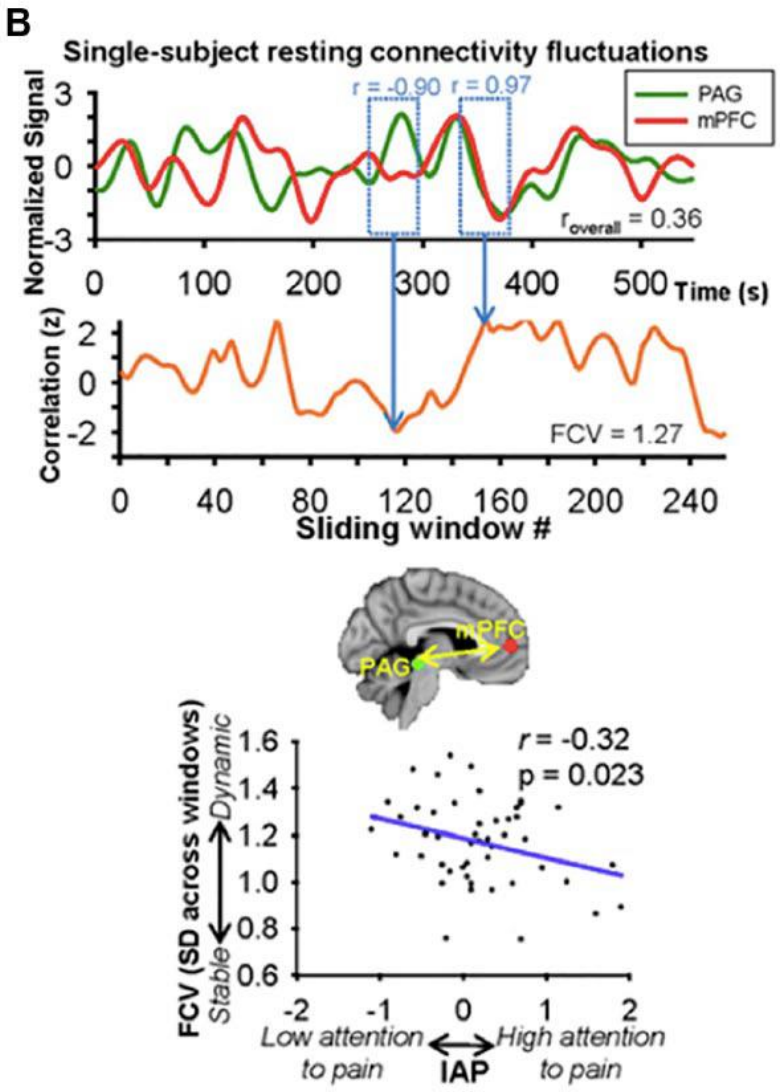
Large Scale Network



Buckner, et al, 2009

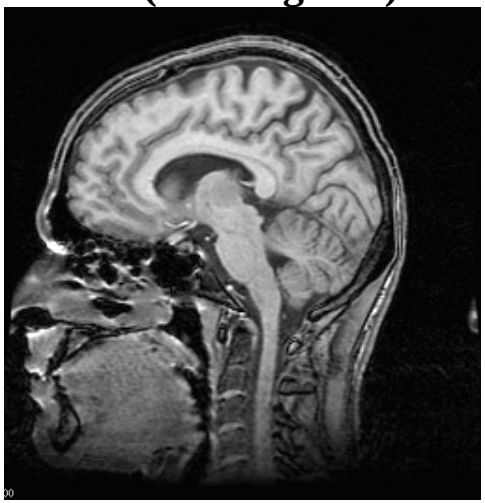
Network Dynamics





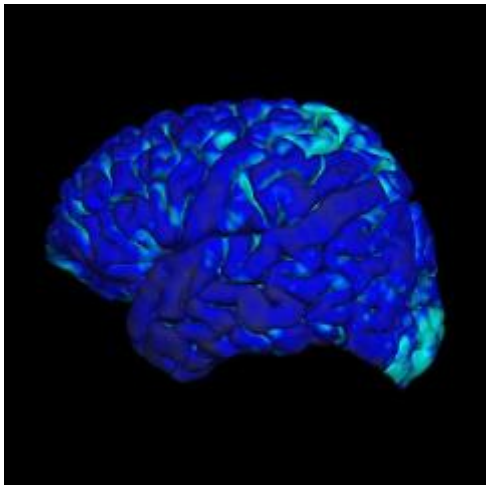
MRI Techniques

Anatomical MRI (T1-weighted)



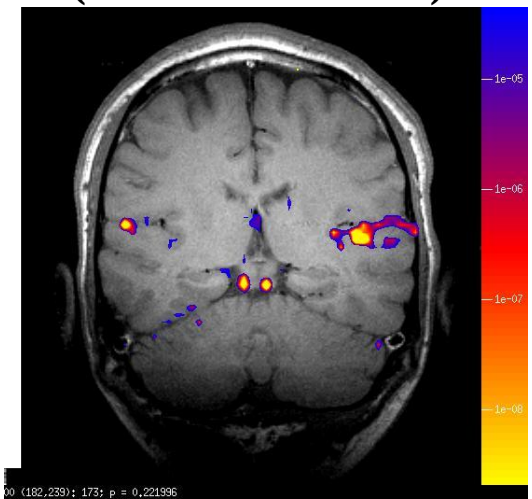
Angiogram (blood vessels map)

Structural MRI (gray matter thickness map)

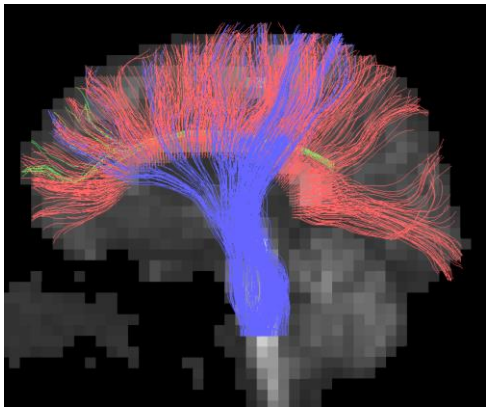


Anatomical MRI (T2-weighted)

Functional MRI (activation to music)

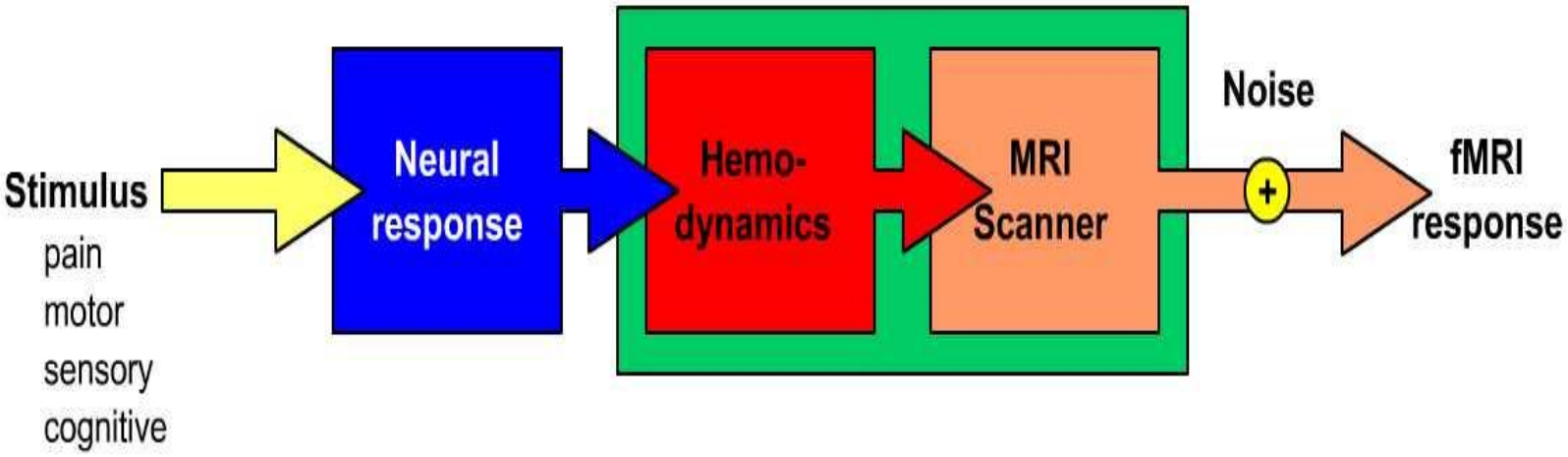


Diffusion Tensor MRI (white matter tracts)



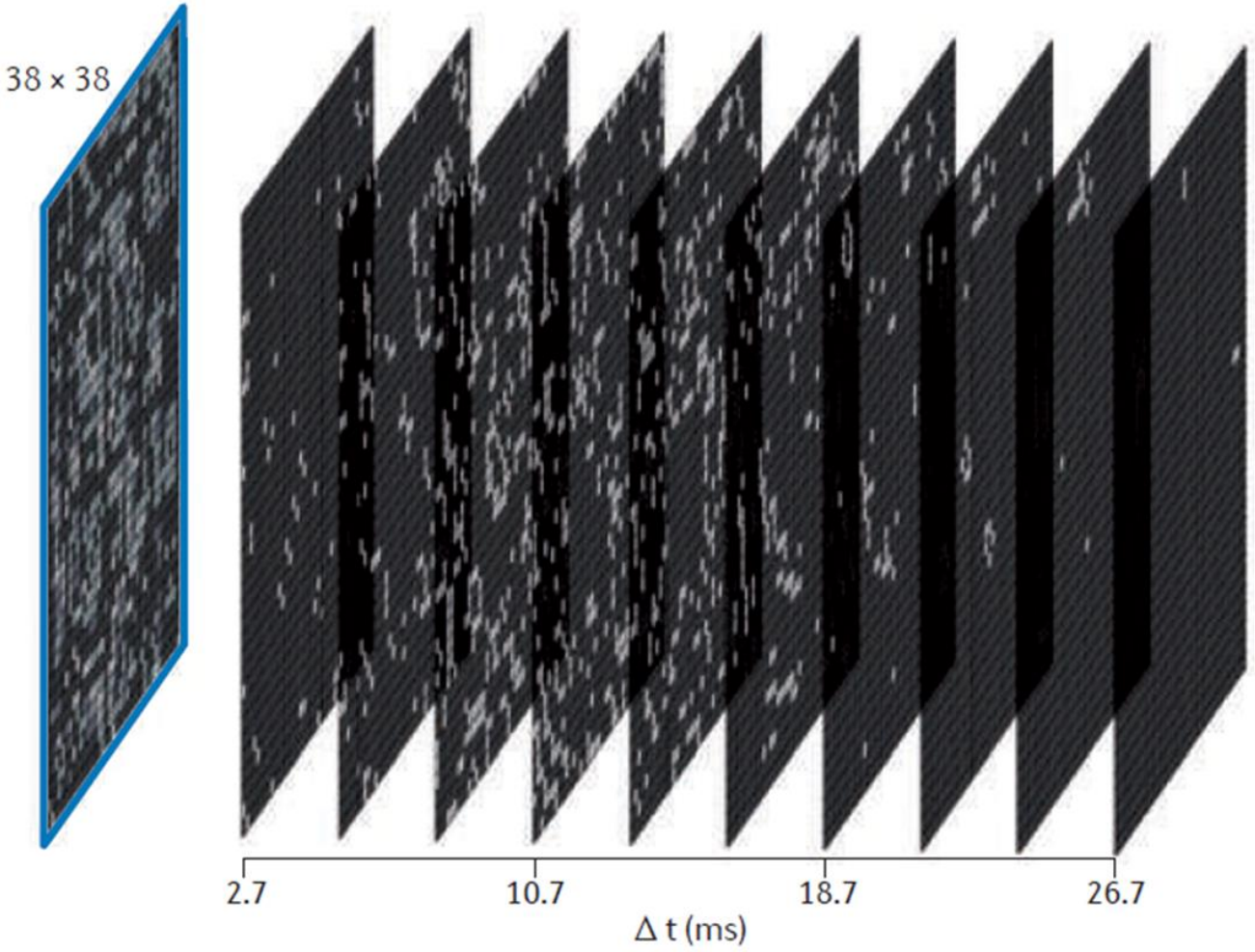
Martinos Imaging Center, MGH

What is a task fMRI?

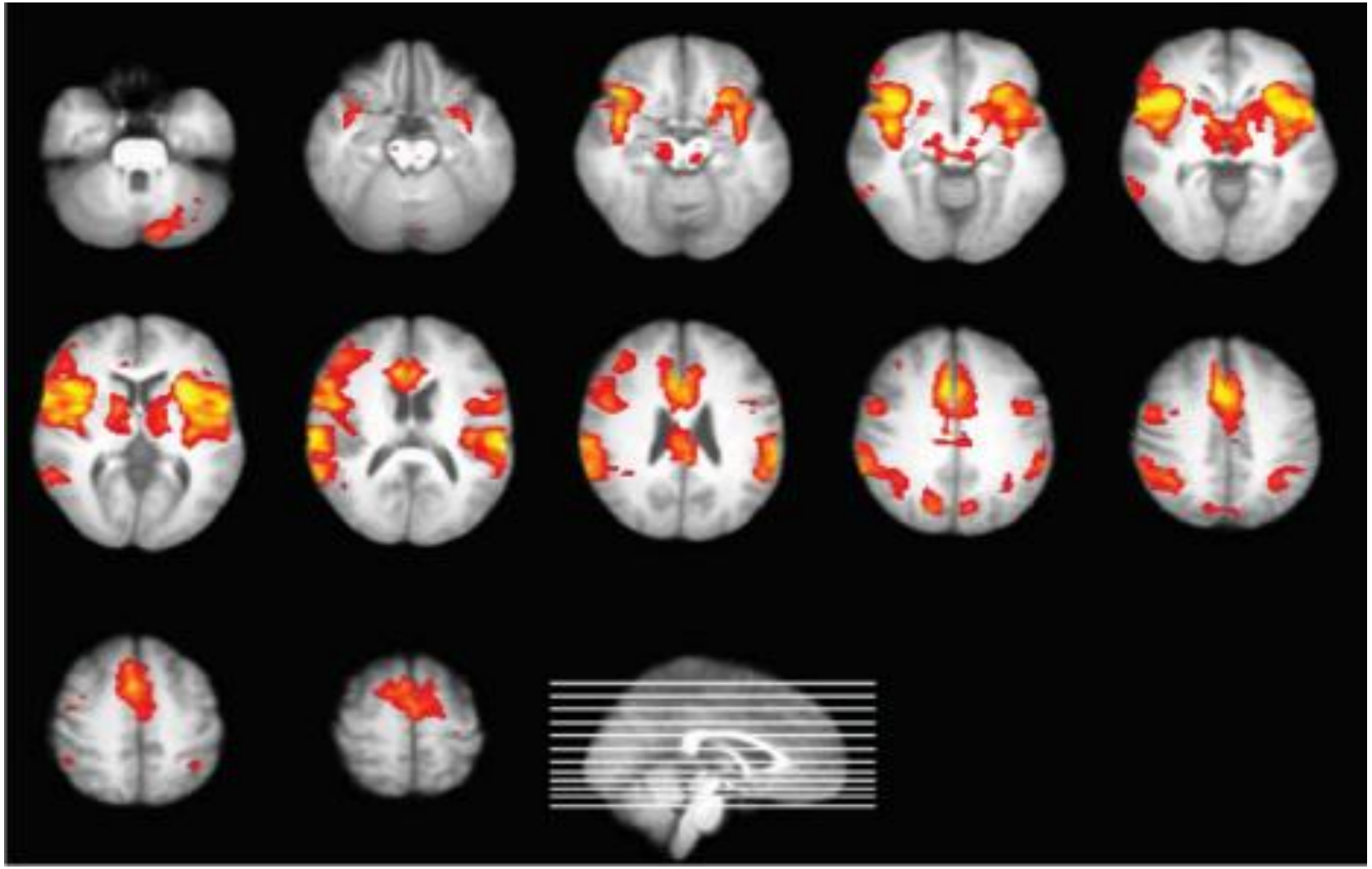


Huettel, 2004

Space-Time Structure of Couplings

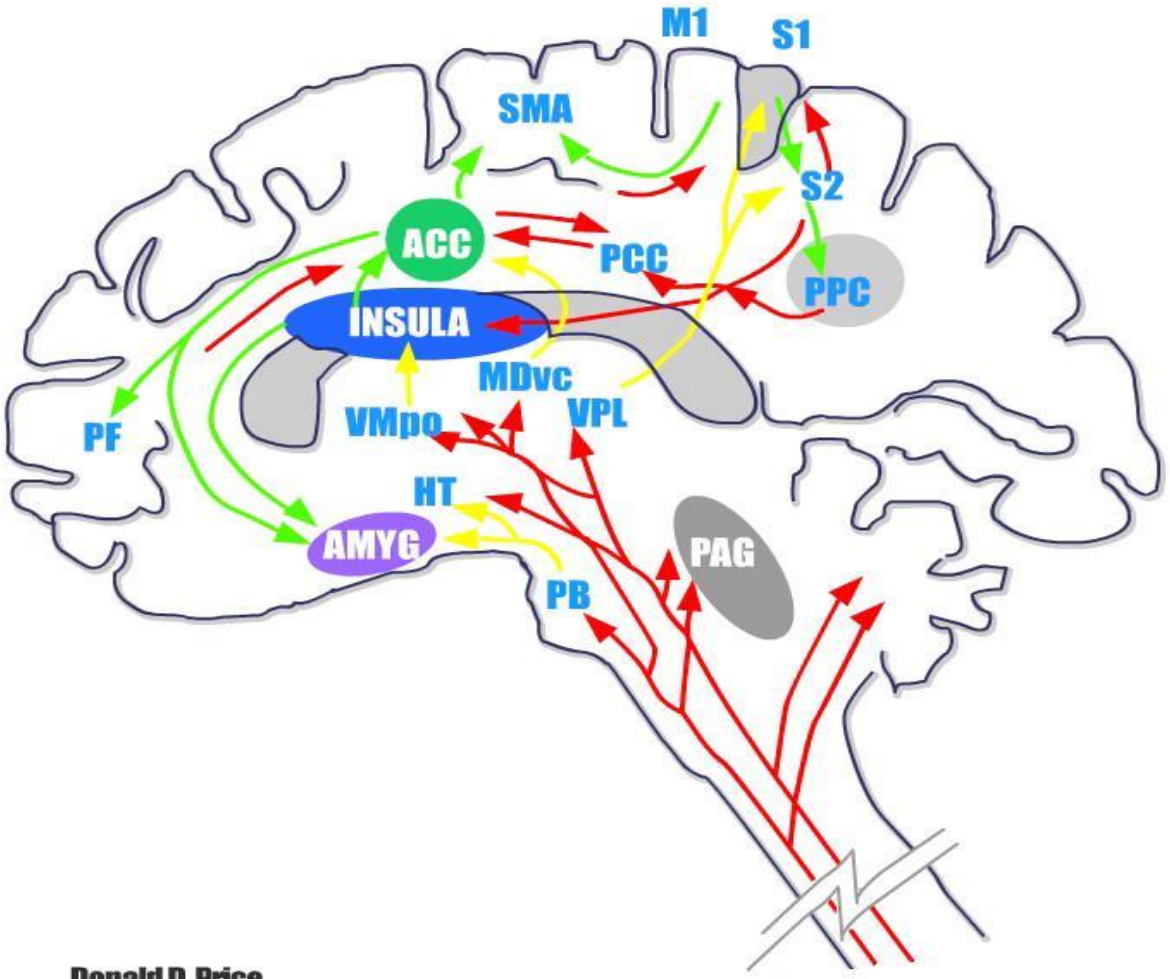


fMRI Acute Pain (Salience) Network



Tracey, 2008

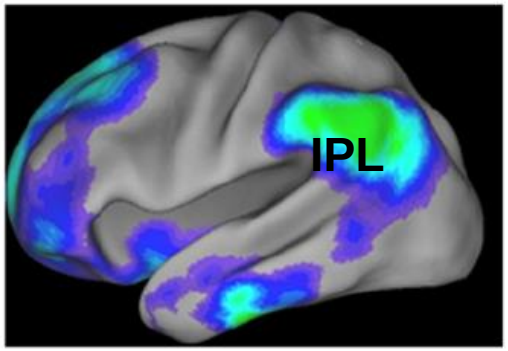
Nociceptive Processing Network

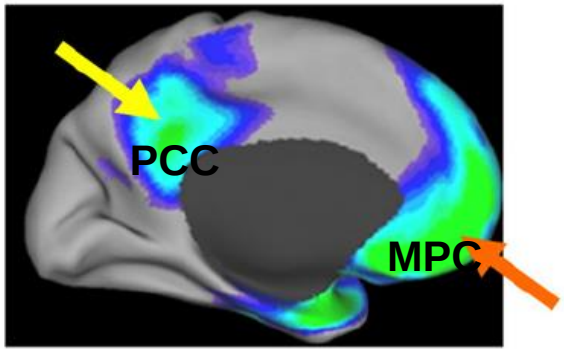


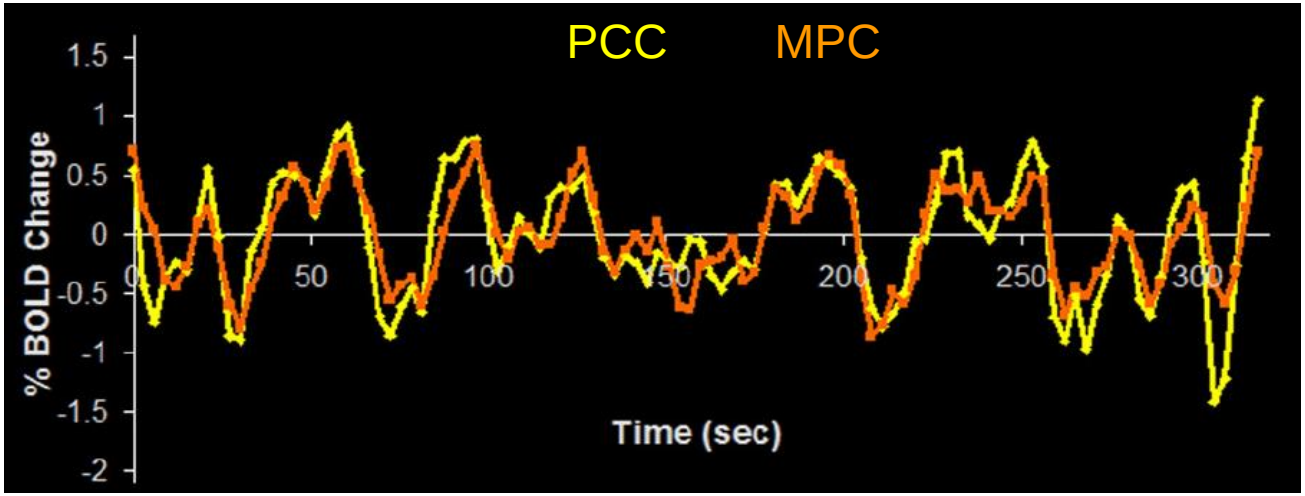
Donald D. Price
Science 9 June 2000 288: 1769-1772

Resting State Default Mode Network

Brain regions more active at rest (internal focus) than during externally focused tasks (e.g. visual, motor, somatosensory) includes inferior parietal lobule (IPL), posterior cingulate cortex / precuneus (PCC), medial prefrontal cortex (MPC)







Shulman et al., 1997
Fox et al., 2005

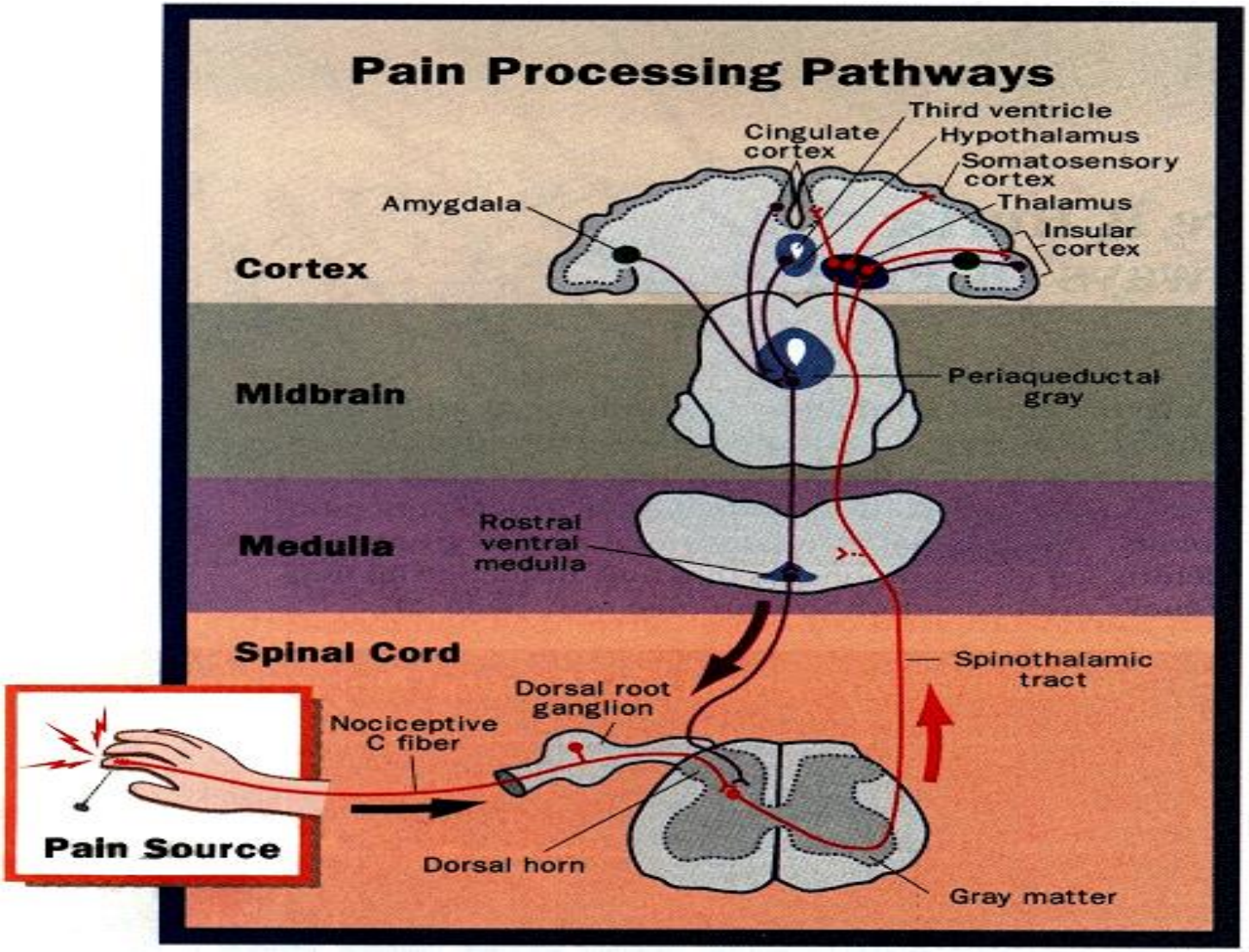
The Pain Revolution

Melzack R, Wall PD: Pain mechanisms: a new theory.

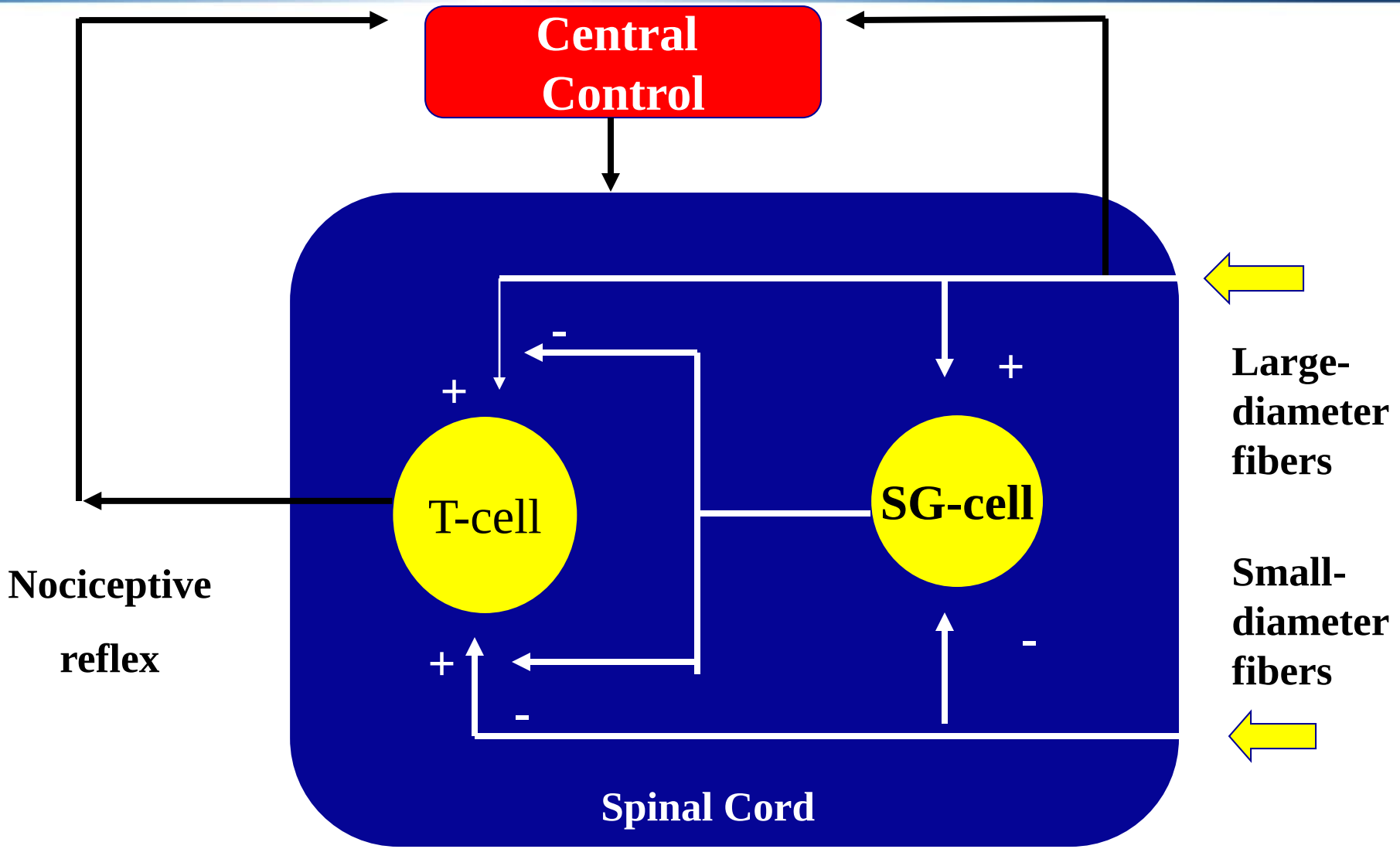
Science. 1965 Nov 19;150(699):971-9

Engel GL: The need for a new medical model: a challenge for biomedicine. Science. 1977 Apr 8;196(4286):129-36

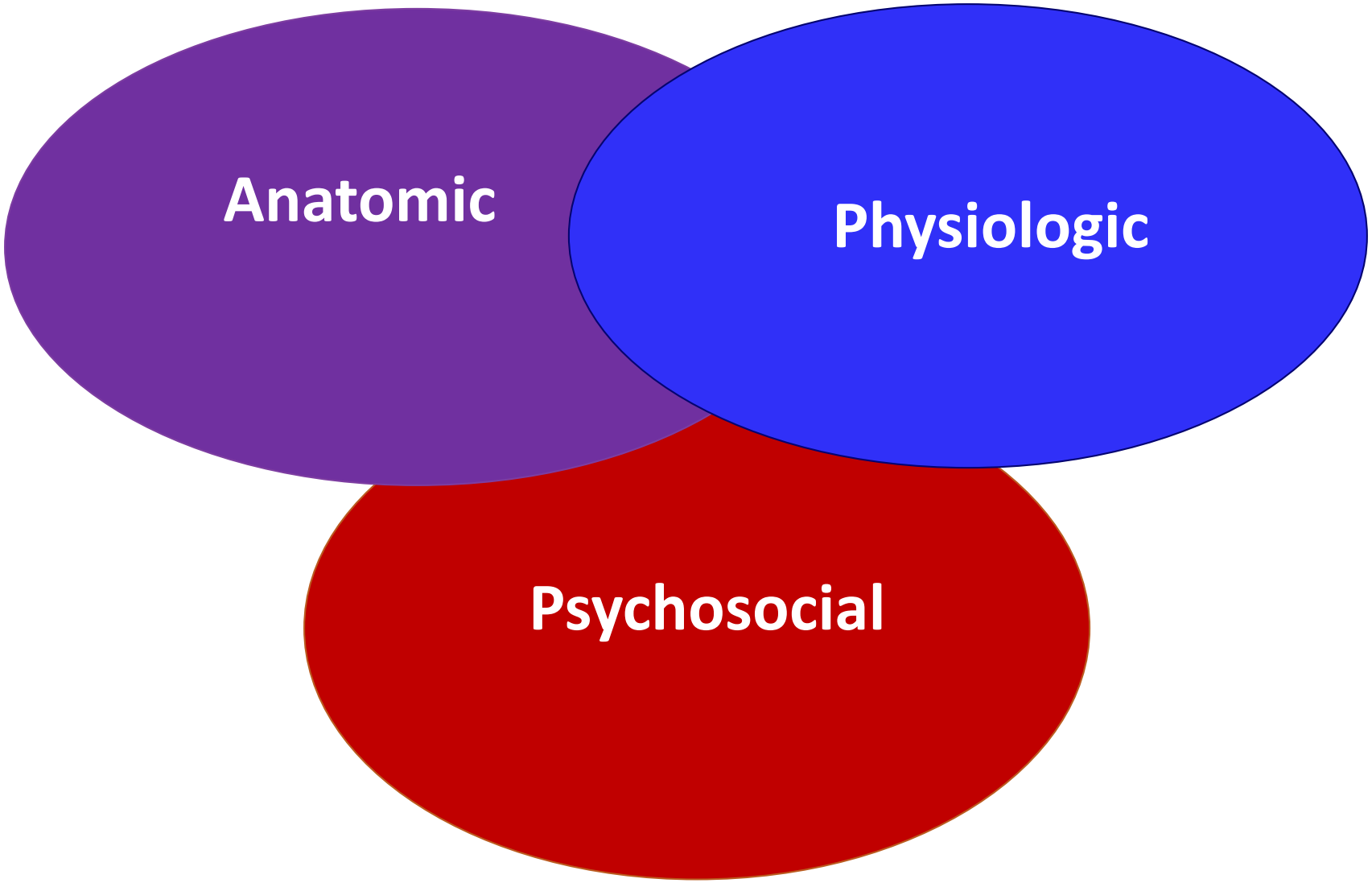
Pain Processing Pathways



Gate Mechanism of Anti-nociception



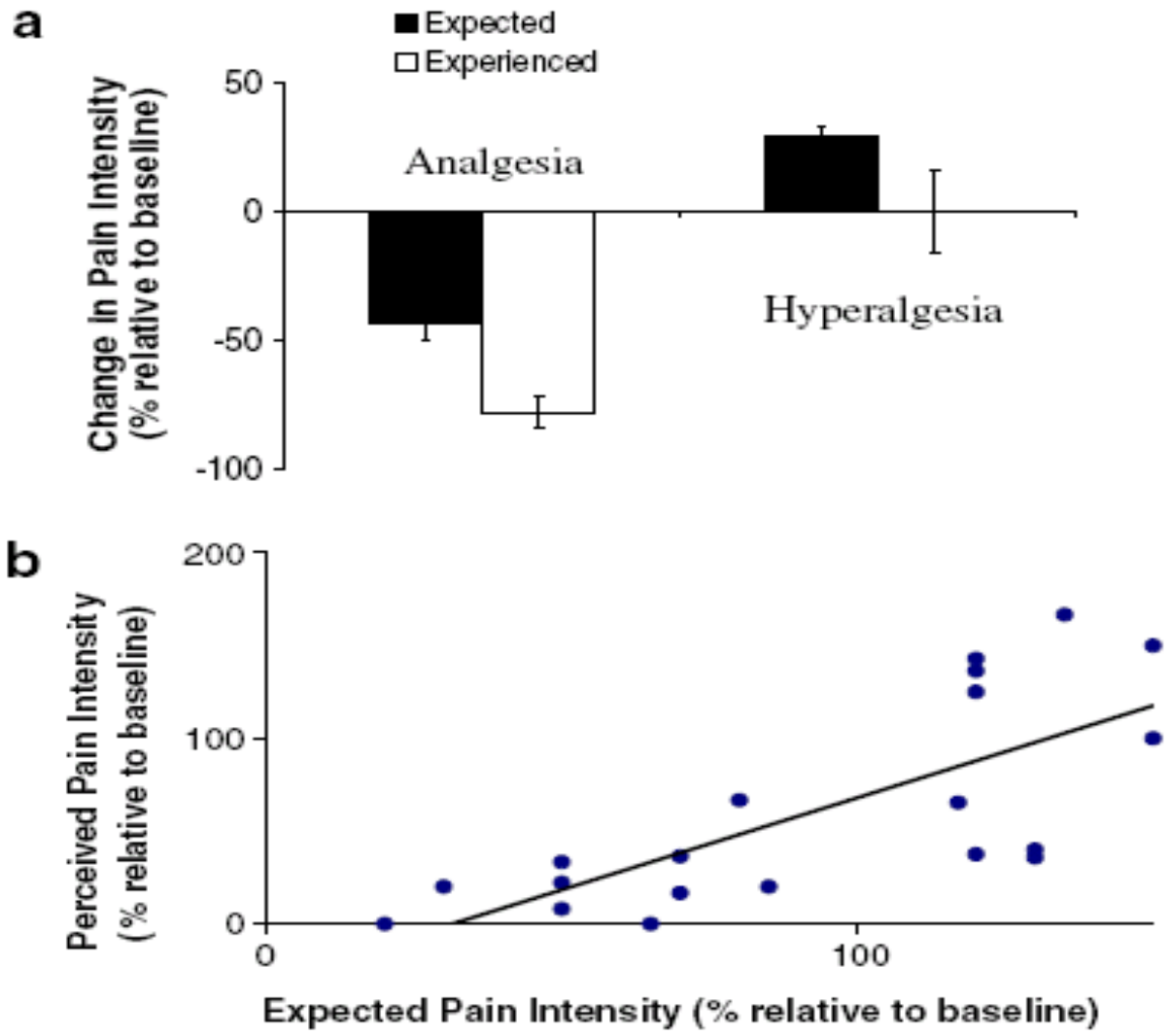
Biopsychosocial Model



Chronification of Pain

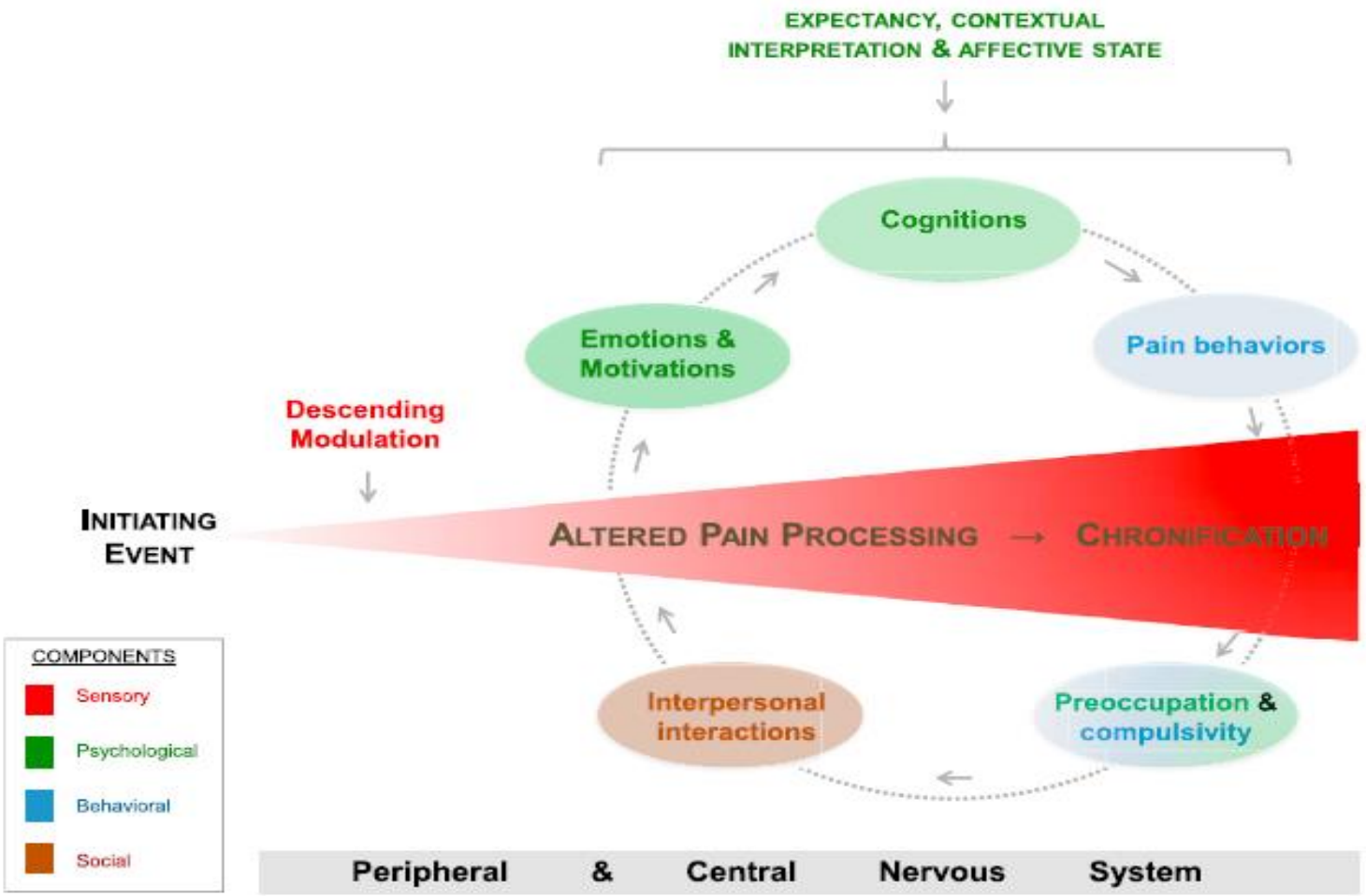
Acute pain (transient)	→	Chronic pain (spontaneous)
Bio	→	Psychosocial
Peripheral	→	Central sensitization
Objective findings	→	Subjective reports
Structural injury	→	Functional syndrome
Components	→	Inter-relationships (systems biology)

Expectancy Effects for Pain



Goffaux, et al

Evolution of a Chronic Pain Syndrome



Elman I, Borsook D: Neuron, 2016

Neural Correlates of Chronic Pain

Spontaneous pain intensity is encoded:

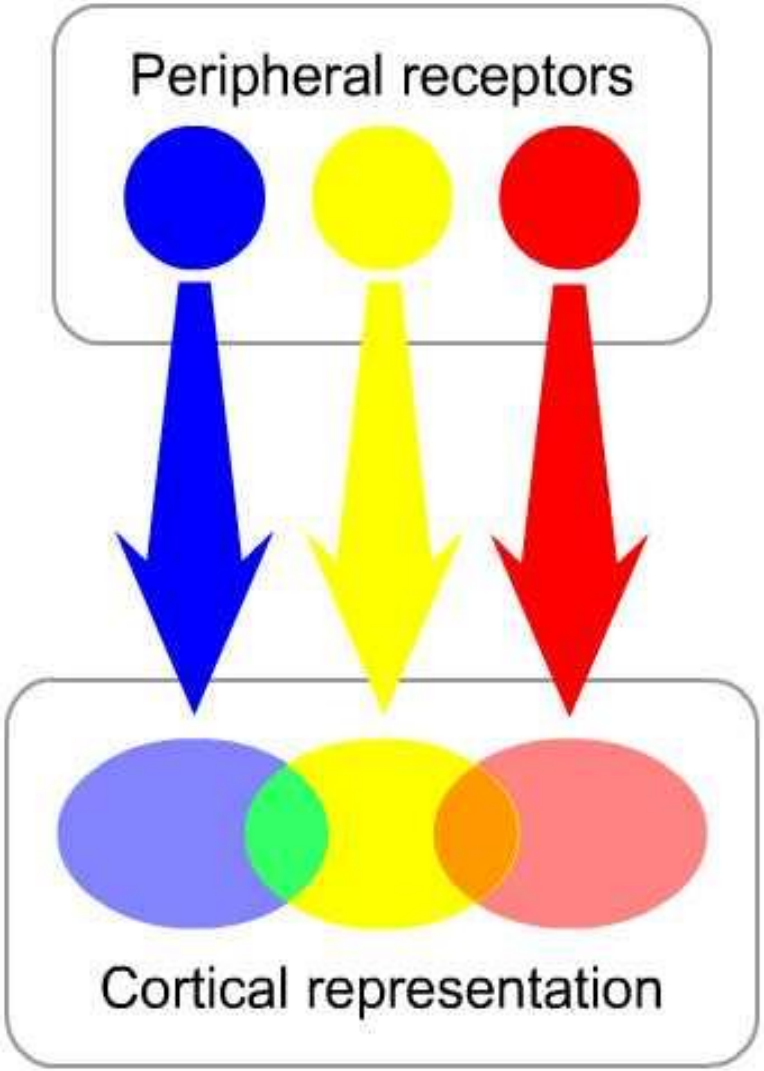
hedonic and emotional learning
(medial PFC, rACC, orbitofrontal cortex)

reward and goal direction
(striatum)

fear behavior
(amygdala)

Apkarian, 2008

Neuromodulation of Cortical Plasticity

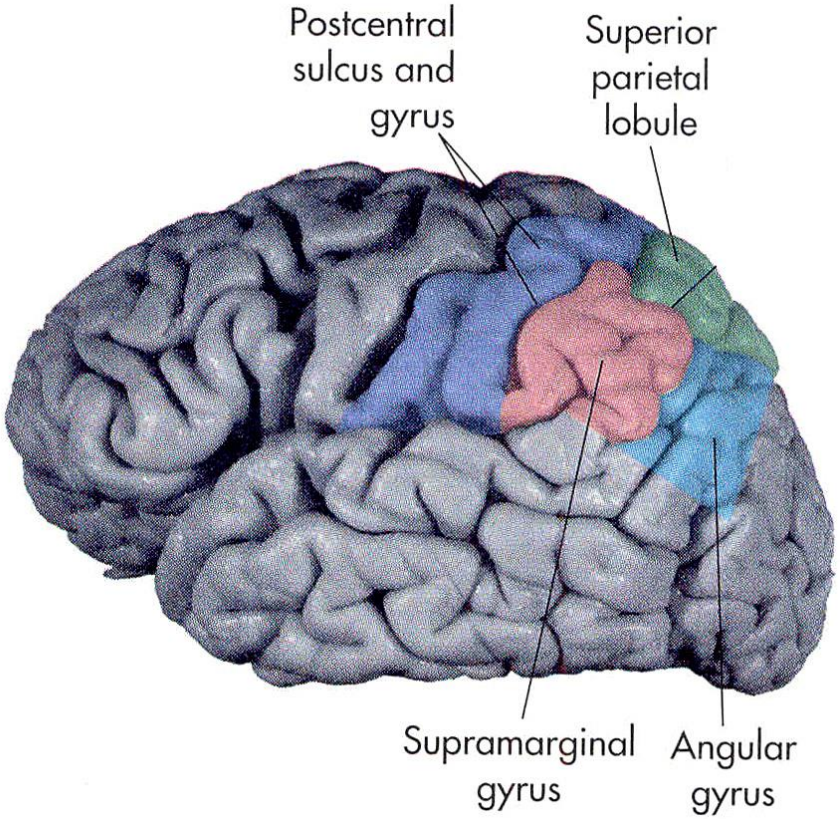


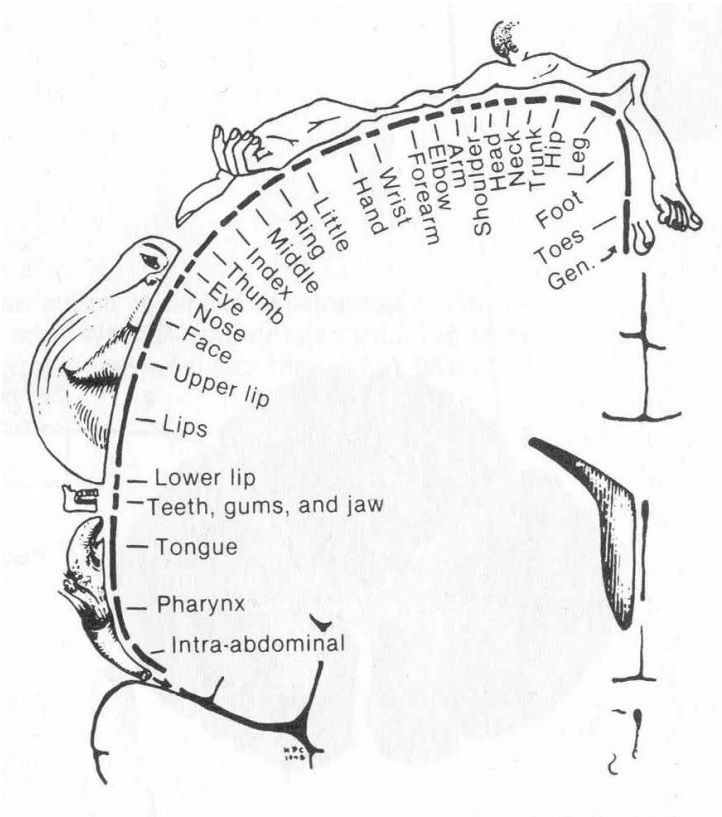
Nelson, 2003

Bruce Rosen, MD, PhD
Athinoula A Martinos Center
HMS MGH MIT

Digital Mapping S1 Somatotopy

The somatotopic digit homuncular organization in the human primary somatosensory cortex (S1) was originally mapped by Penfield in 1937.





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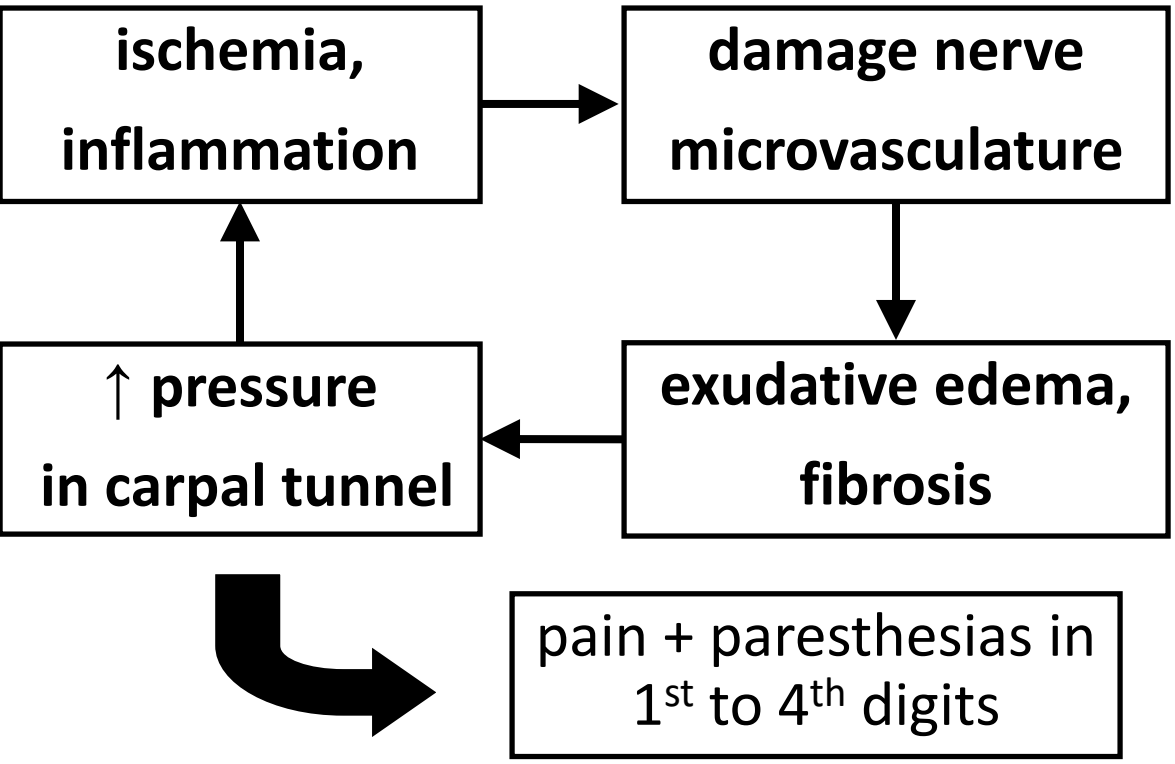
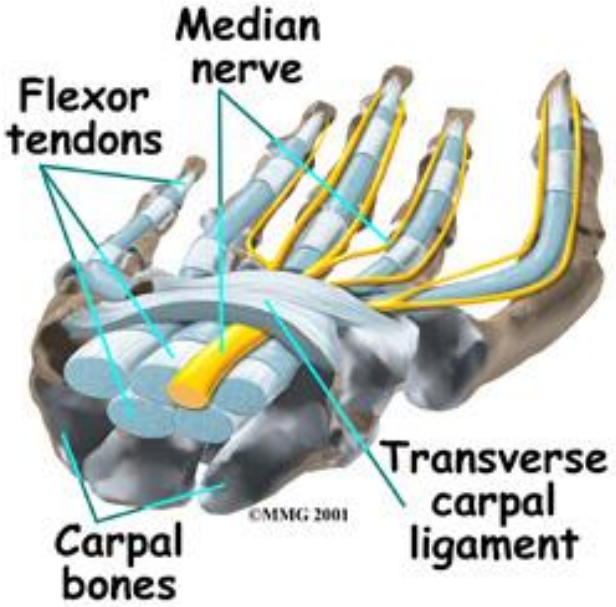
Acupuncture and Carpal Tunnel Syndrome

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy → U.S. prevalence 3.72%[1].

The CTS vicious cycle

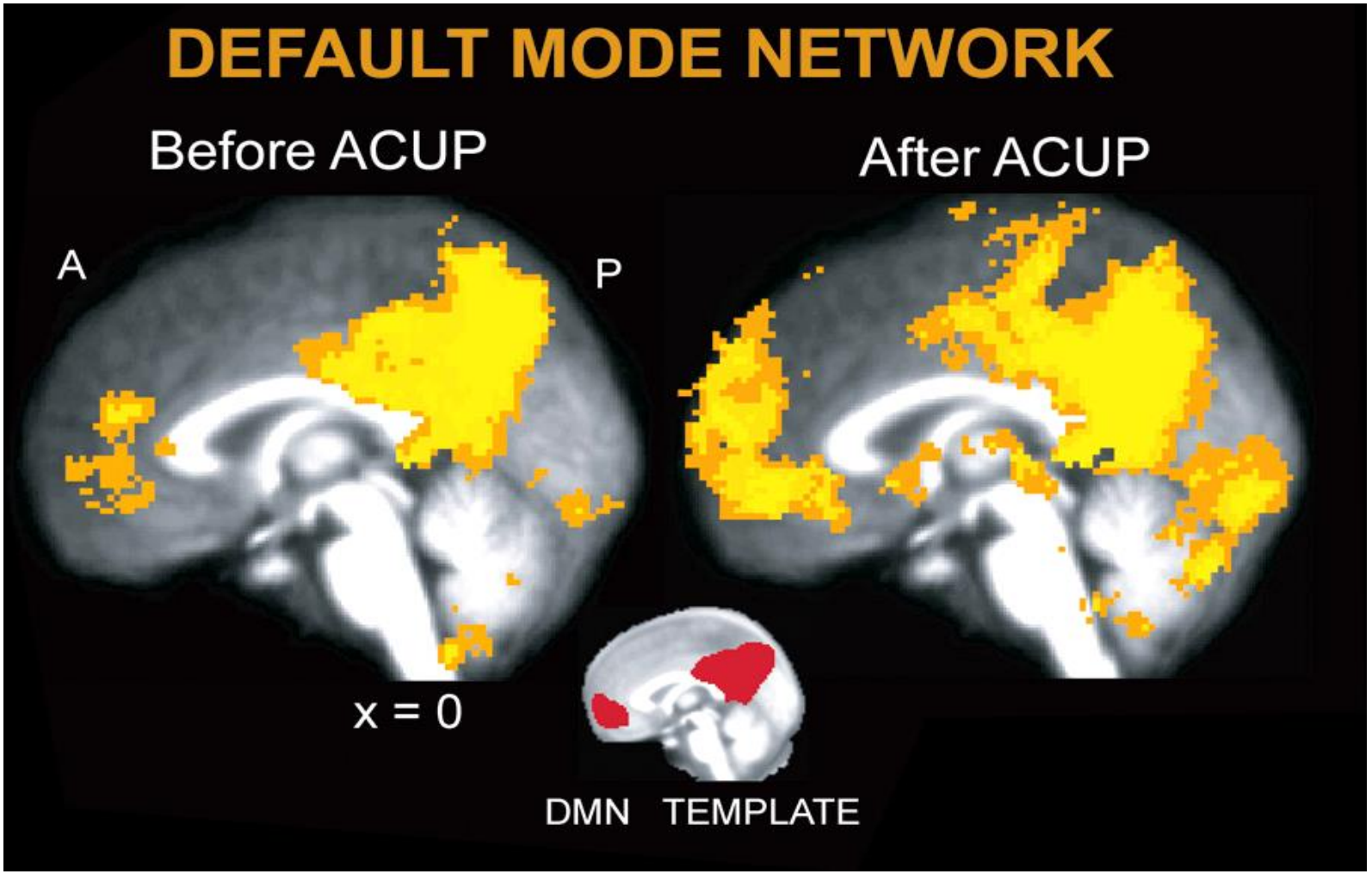




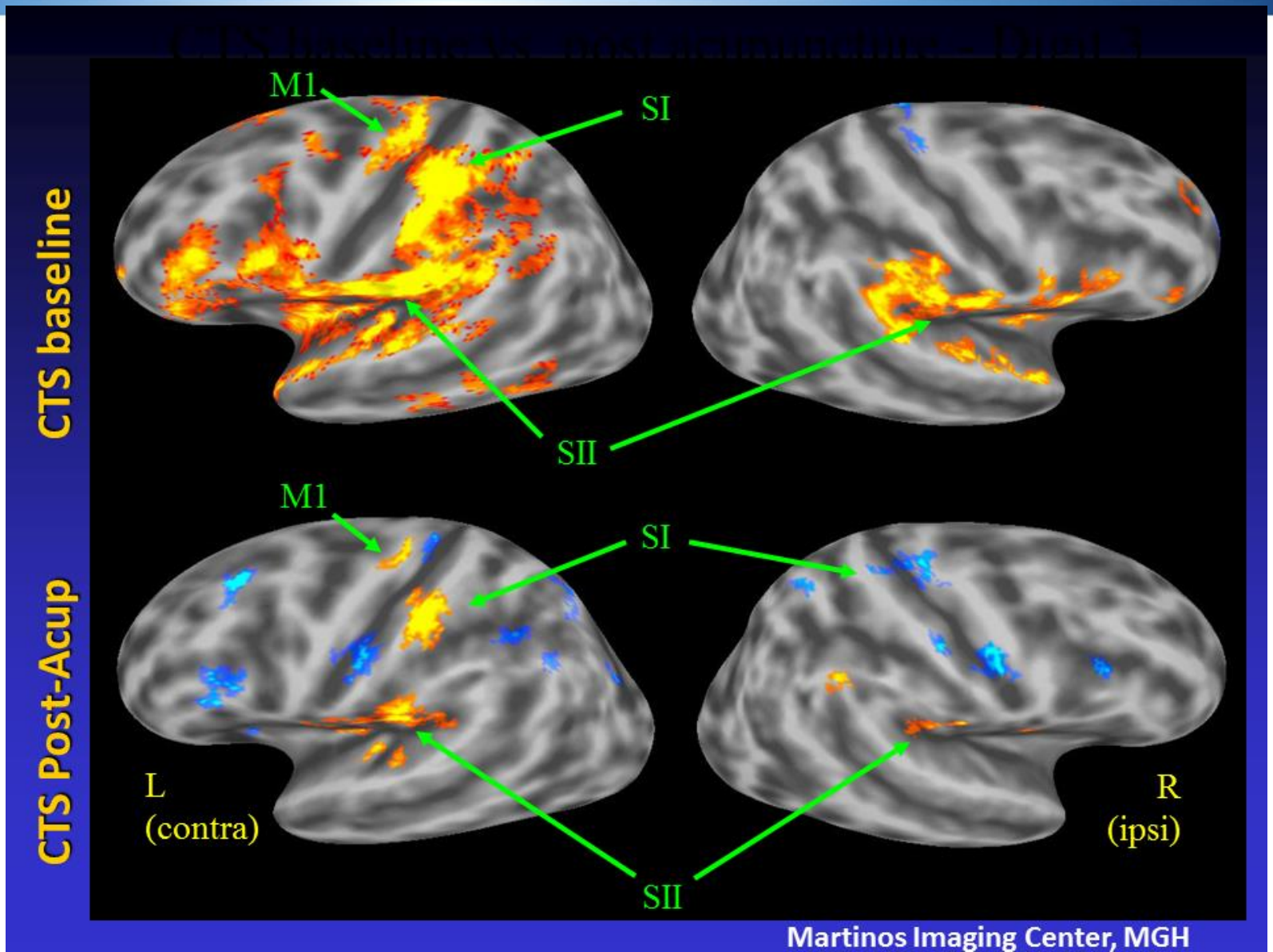
Martinos Imaging Center, MGH

[1]Papanicolaou, et al. J Hand Surg. 2001; 26(3):460-6

Maps for Resting DMN Connectivity



CTS Baseline vs. Post-Acupuncture – Digit 3



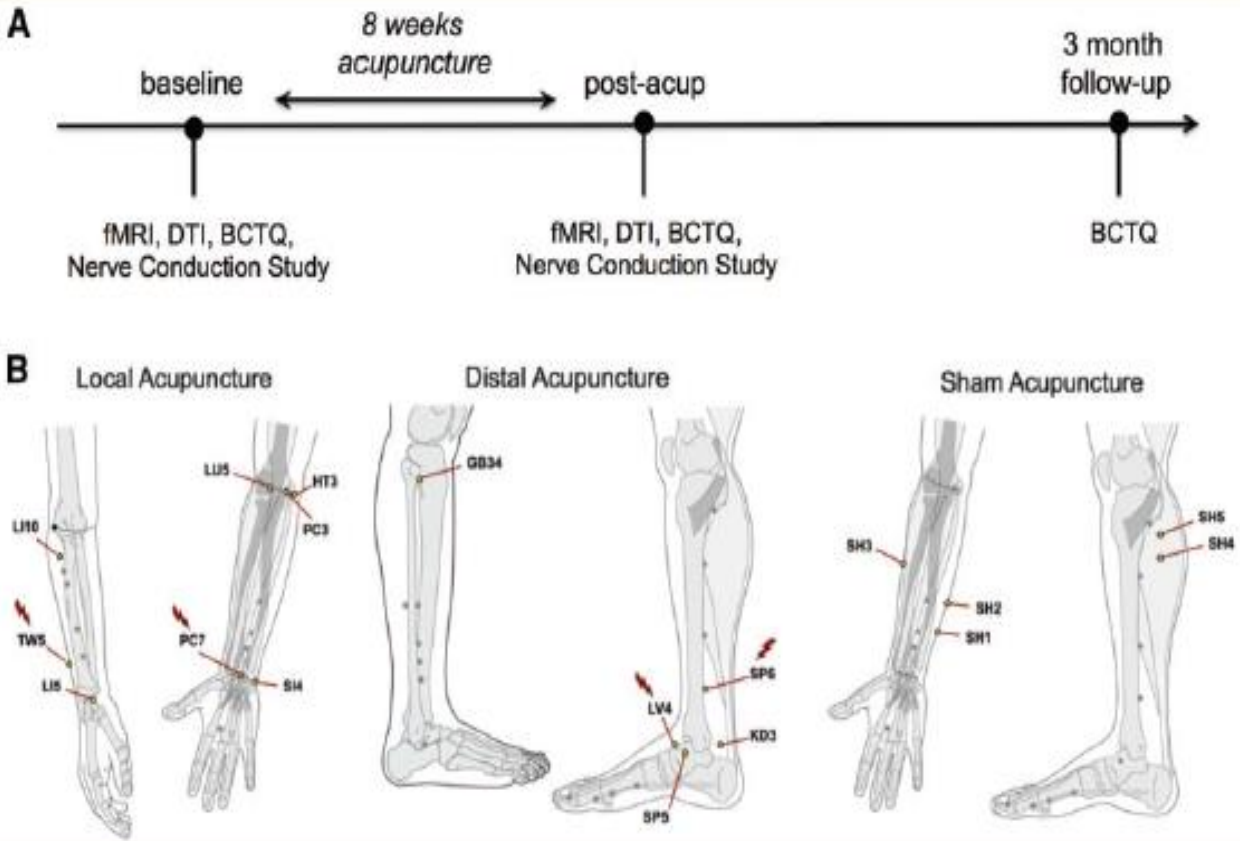
doi:10.1093/brain/awx015

BRAIN
A JOURNAL OF NEUROLOGY

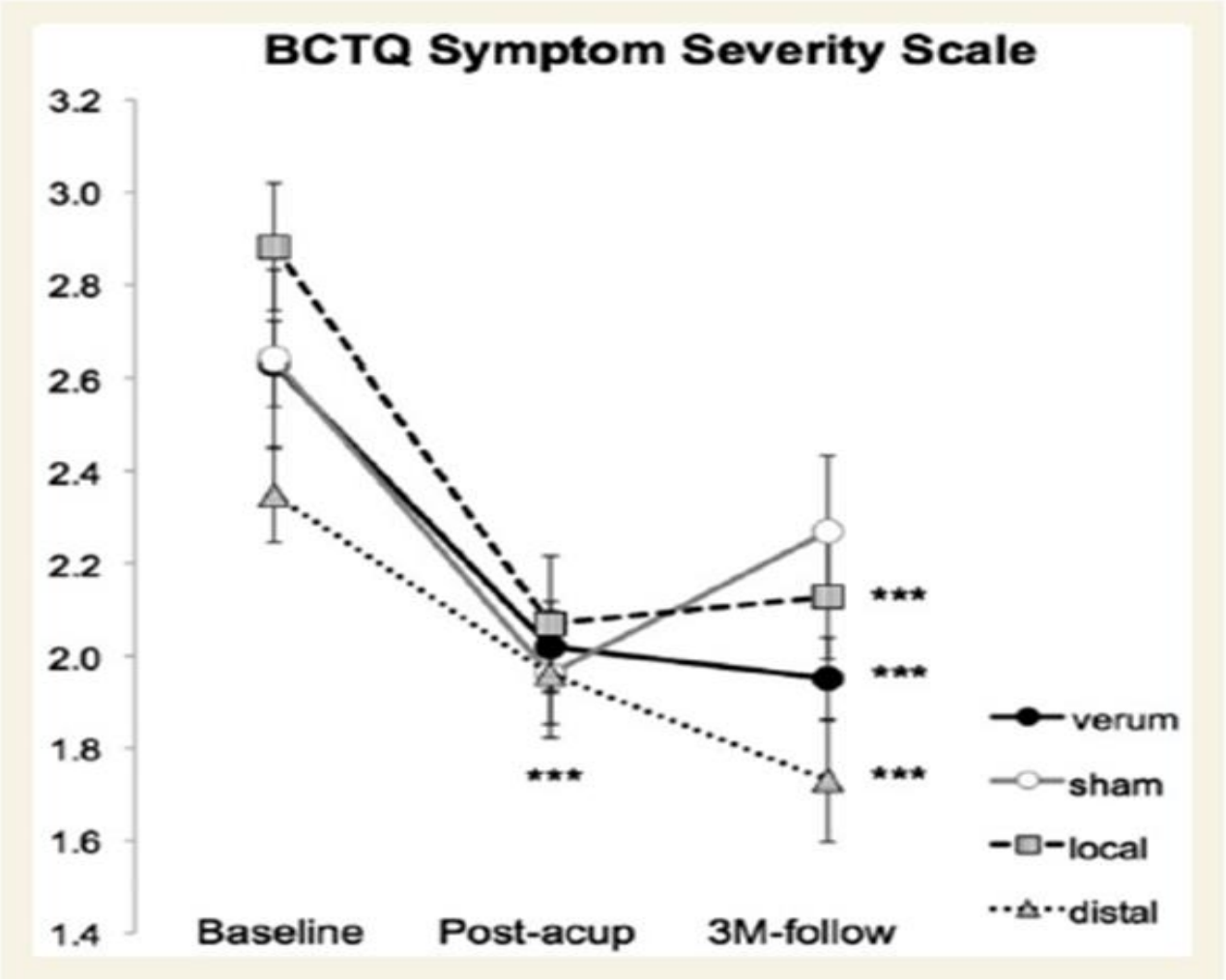
Rewiring the primary somatosensory cortex in carpal tunnel syndrome with acupuncture

Yumi Maeda,[1,2,*] Hyungjun Kim,[1,3,*] Norman Kettner,[2] Jieun Kim,[1,3] Stephen Cina,[1] Cristina Malatesta,[4] Jessica Gerber,[1] Claire McManus,[4] Rebecca Ong-Sutherland,[4] Pia Mezzacappa,[1] Alexandra Libby,[1] Ishtiaq Mawla,[1] Leslie R. Morse,[5] Ted J. Kaptchuk,[6] Joseph Audette[7] and Vitaly Napadow[1,2]

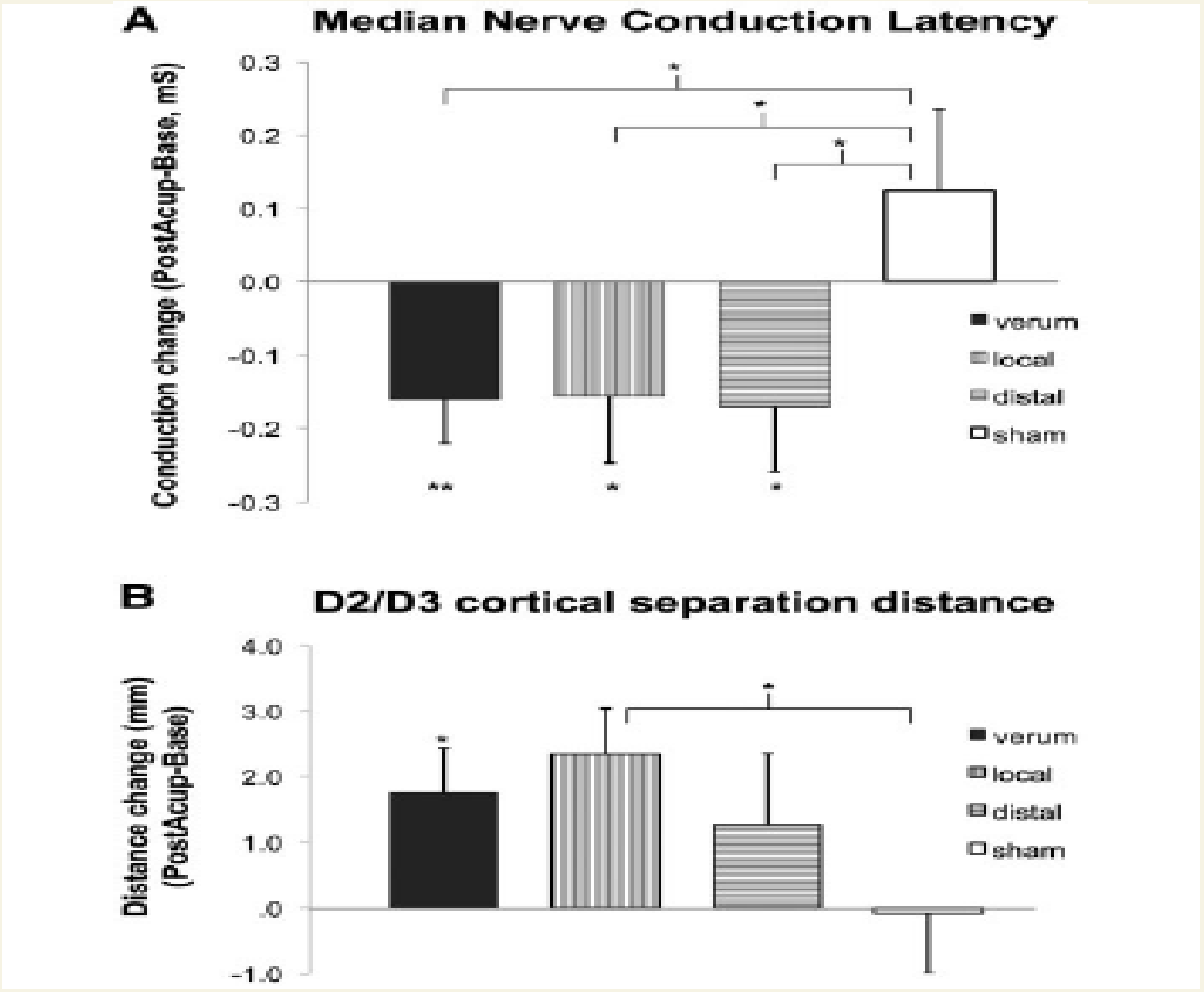
Rewiring S-1 in CTS with Acupuncture



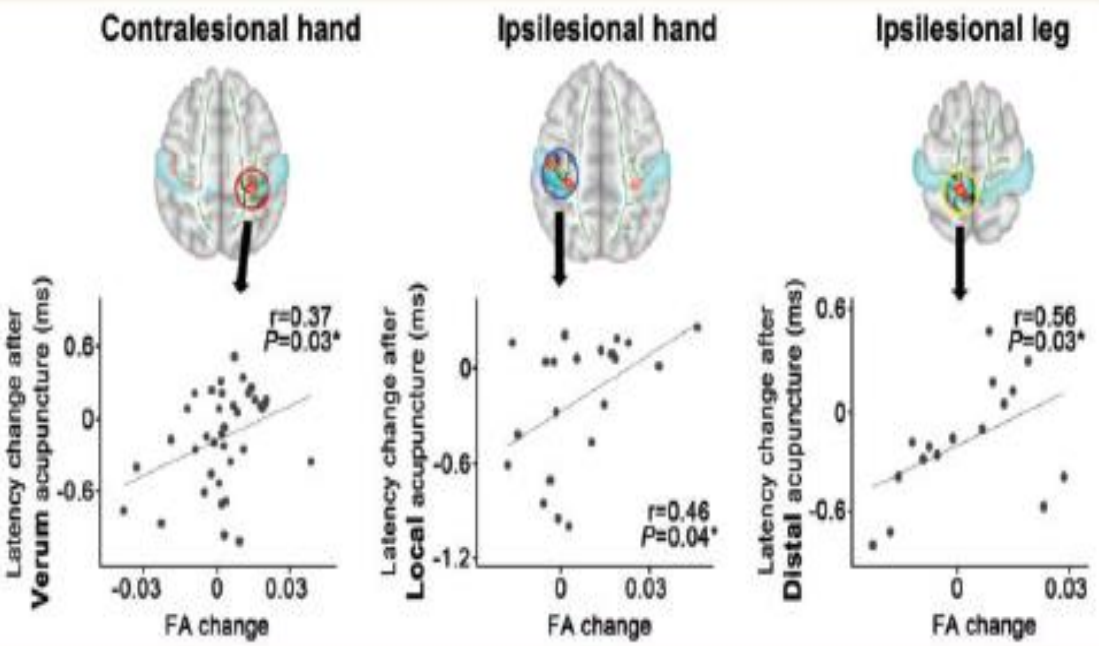
Acupuncture Clinical Measures



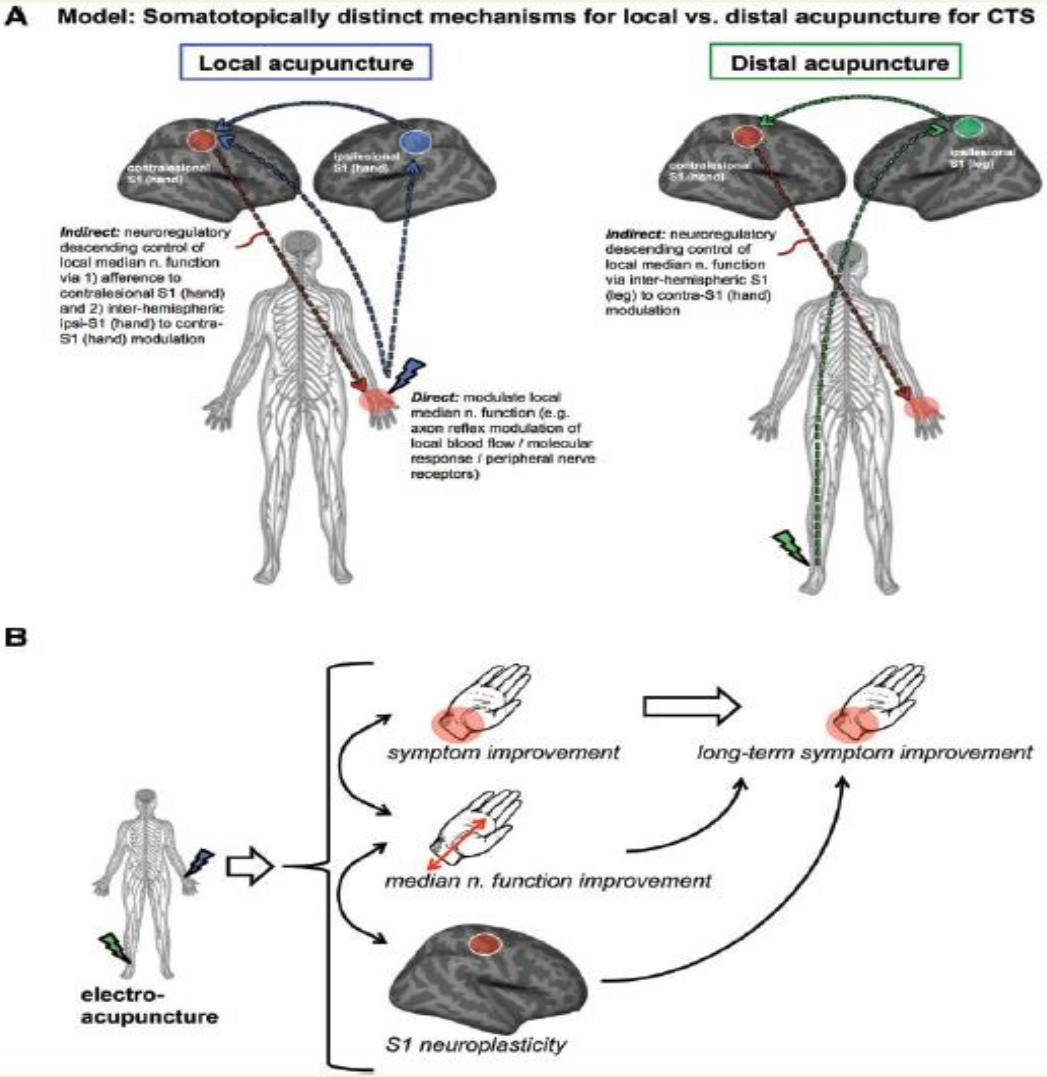
Acupuncture NCV Improvement



S-1 DTI (white matter)



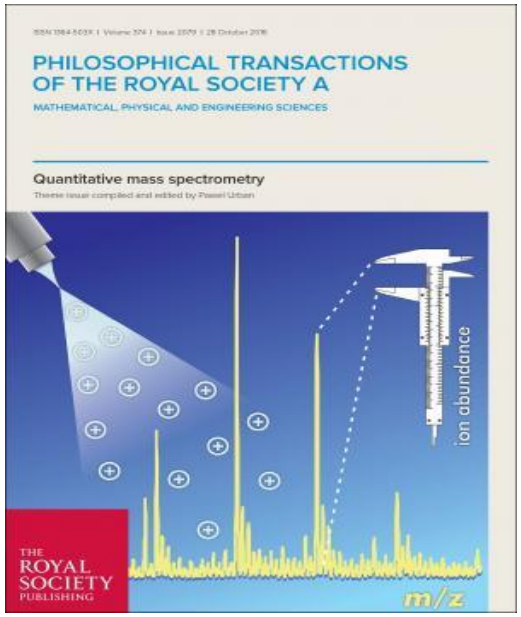
Neural Mechanism of Acupuncture



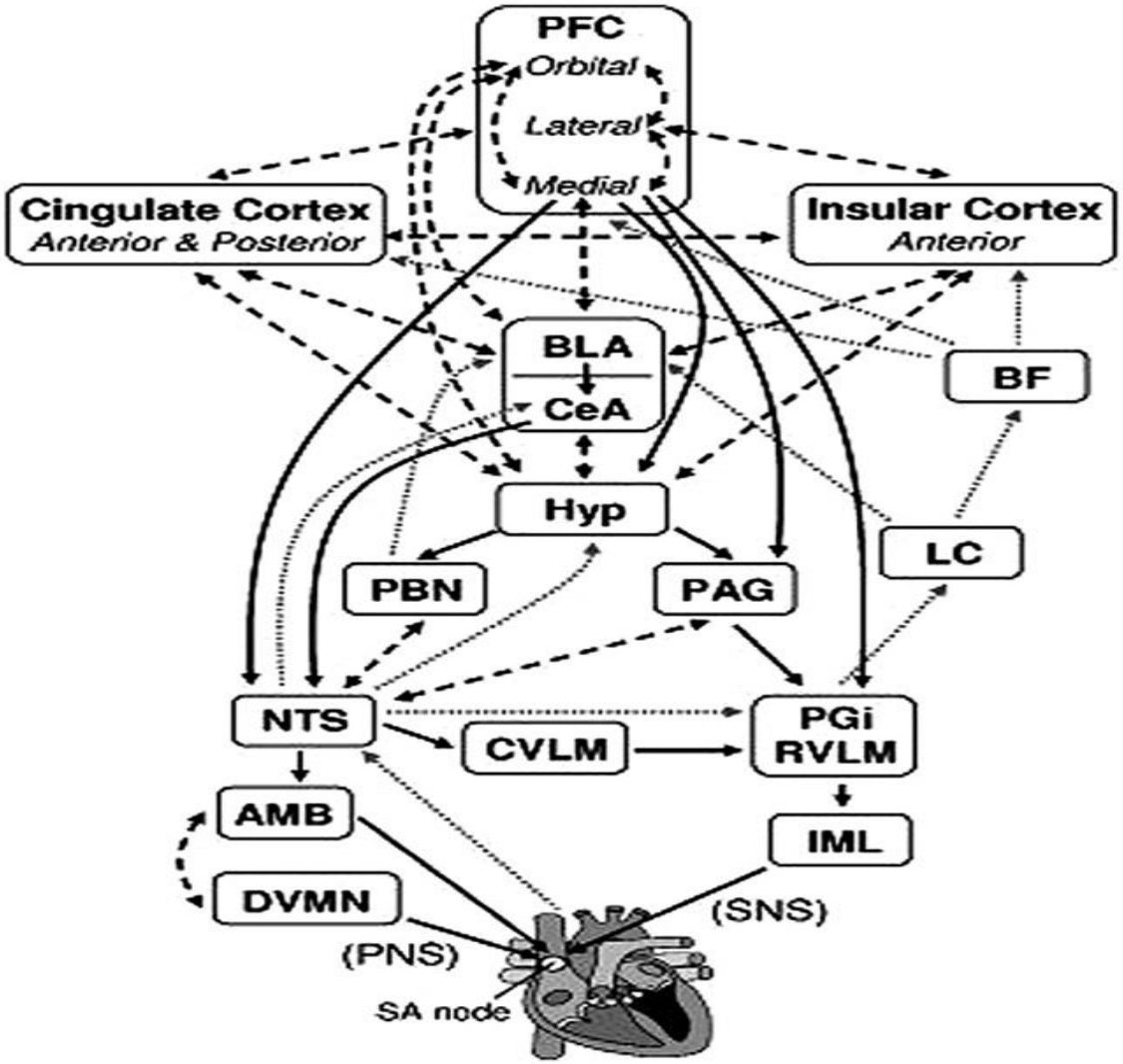
Brainstem autonomic nuclei

Neuroimaging brainstem circuitry supporting cardiovagal response to pain: a combined heart rate variability/ultrahigh-field (7T) functional magnetic resonance imaging study

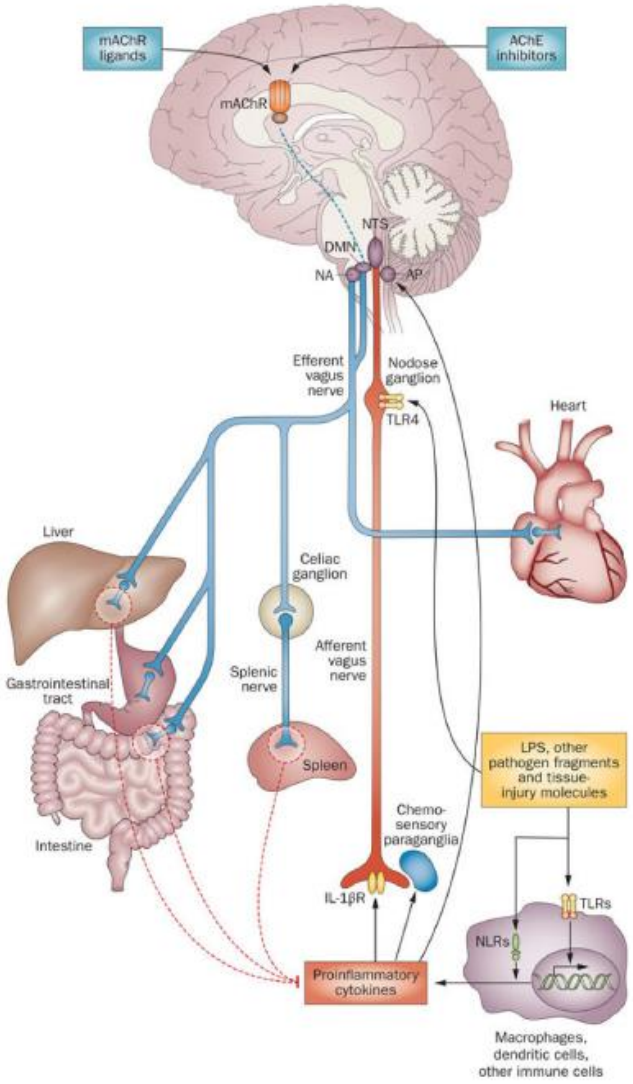
Philos Trans A Math Phys Eng Sci. 2016 May



Central Autonomic Network

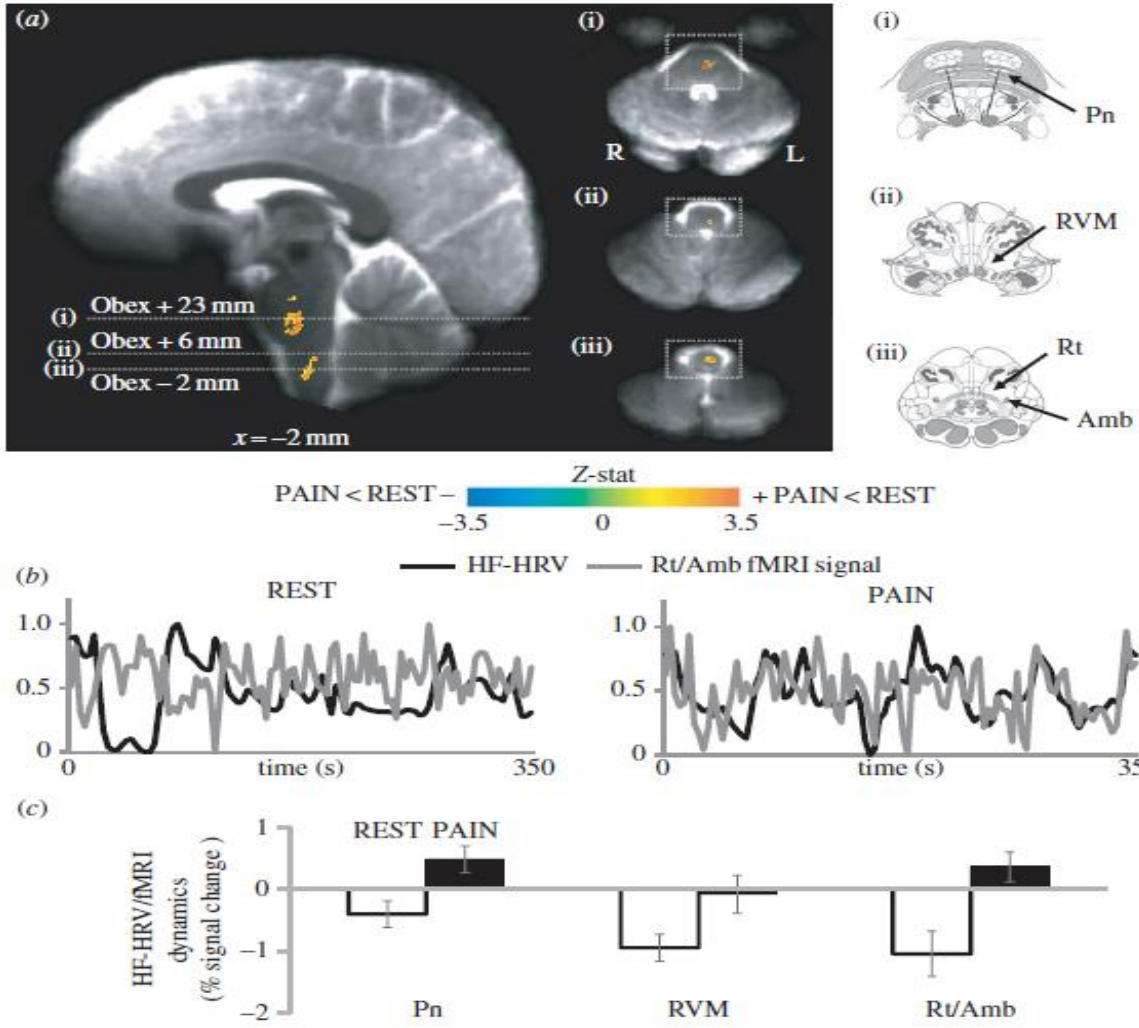


The Functional Anatomy of the Inflammatory Reflex

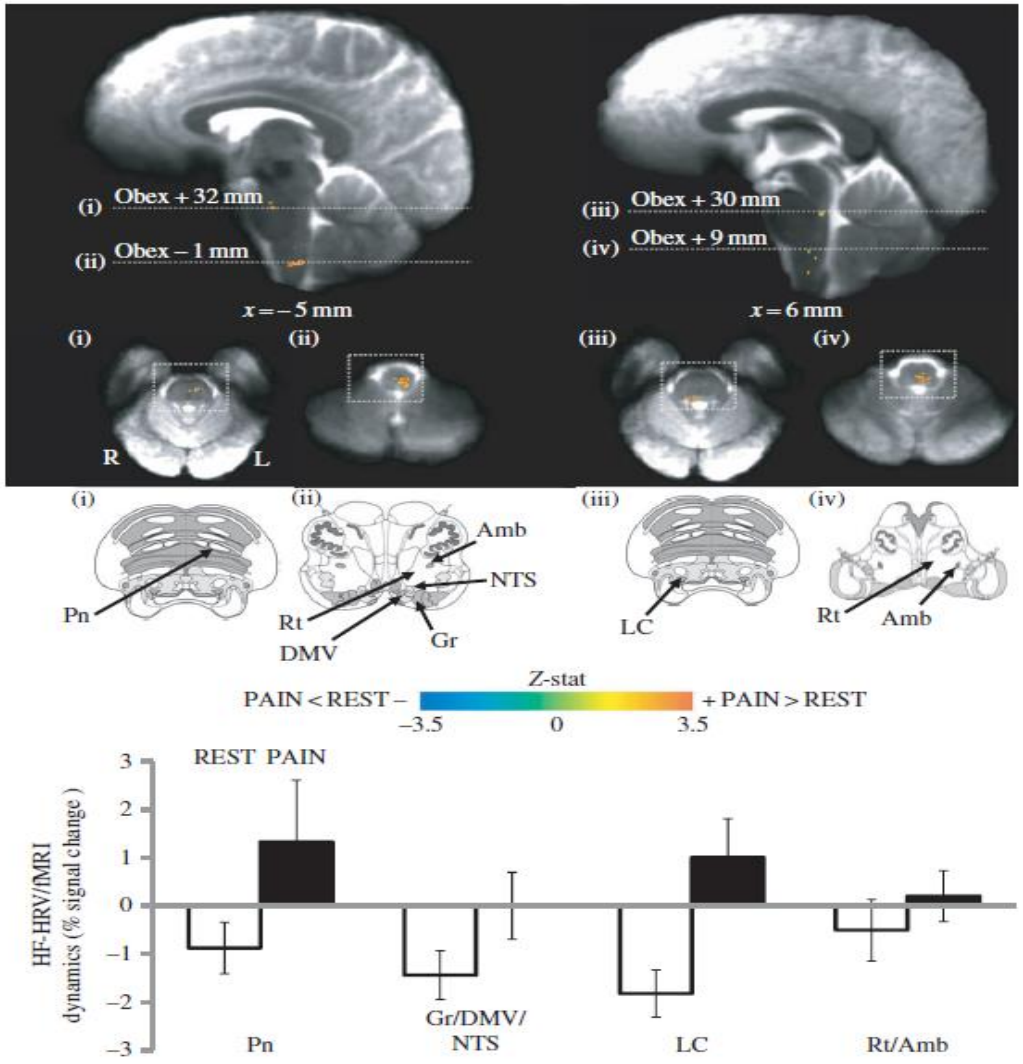


Pavlov, Tracey: Immunol Res. 2015

Brainstem Autonomic Nuclei



Brainstem Autonomic Nuclei



CiPNI
Center for Integrative Pain NeuroImaging

LOGAN UNIVERSITY

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MASSACHUSETTS GENERAL HOSPITAL
Harvard-MIT Health Sciences & Technology

Neural Correlates of Spinal Manipulative Therapy

Norman Kettner[1], Dan-Mikael Ellingsen[2], Ekaterina Protsenko[2], Ishtiaq Mawla[2],Matthew H Kowalski[3], David Swensen[4], Deanna O'Dwyer-Swensen[4], Vitaly Napadow[1,2], Marco L Loggia[2]

[1]Department of Radiology, Logan University, [2]Athinoula A. Martinos Center for Biomedical Imaging; [3]Osher Center for Integrative Medicine, Brigham and Women's Hospital; [4]Melrose Family Chiropractic

Introduction

- Pain perception is generated by a range of experiences from acute tissue injury to ongoing chronic pain. Chronic pain shifts brain resources from nociceptive networks to those involved with cognition, emotion, motivation and autonomic regulation.
- fMRI has identified maladaptive structural and functional neural networks in cognitive and emotional pain processing networks, reinforcing psychosocial factors in chronic pain.
- The neural correlates of many pharmacological and nonpharmacological interventions for chronic pain are still unknown, including Spinal Manipulative Therapy.

Methods

- The principal aim was to assess the brain correlates of pain-related fear, and whether SMT could modulate it.
- A perceptual probe was utilized consisting of a pain-related fear experience (videos) designed to provoke measures of clinical pain and fear in patients with chronic non-specific low back pain.
- fMRI brain mapping was obtained in both patients and controls before and after viewing videos of maneuvers.
- Correlations of clinical and fMRI BOLD were assessed.

Methods

- Lumbar SMT, was delivered by one of three chiropractic physicians.
- Before and after SMT, the participants:
- rated the level of their low back pain and current level of anxiety
- watched videos of gender-matched model perform maneuvers patients had previously identified as pain/fear provoking. After each maneuver video, patients used a button box to rate:
    1. "fear about performing this exercise" (0 - not fearful at all; 100 - extremely fearful)
    2. "pain expected when performing this exercise" (0 - no pain at all; 100 - most intense pain imaginable)
- completed fMRI scans to assess brain BOLD response to video viewing.

Methods

- fMRI data were collected using a “simultaneous multi-slice” sequence (SMS), on a 3T Siemens Skyra scanner equipped with a 32 channel head coil. Whole brain T2*-weighted gradient echo BOLD EPI pulse sequence (TR/TE =1.25sec/33ms, flip angle=90°, voxel size=2x2x2mm, number of slices=75).
- Structural volumes obtained with multi-echo MPRAGE.

Results

DEMOGRAPHICS

	Low Back Pain	Healthy Control
N	15	16
Mean Age	36.9 (9.76)	37.4 (10.2)
Sex	8 F, 7 M	8 F, 8 M

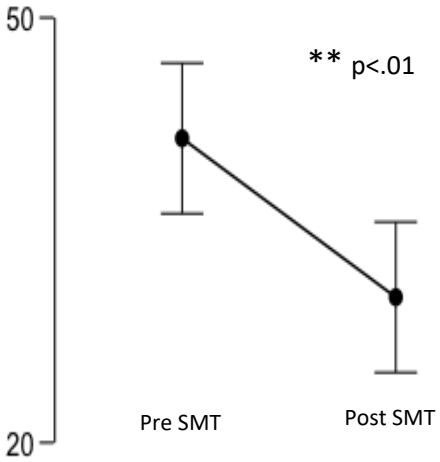
Following **SMT**:

1. patients experienced less clinical pain ($p<0.01$)
2. expected less pain in future back-stressing maneuvers ($p<0.05$).

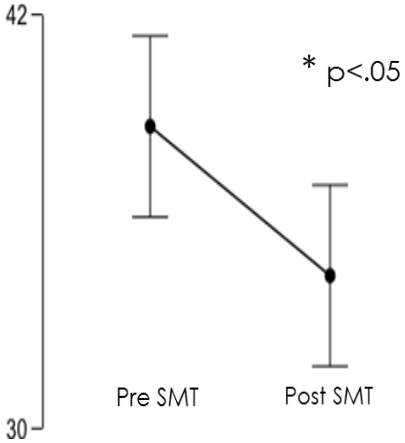
These measures significantly correlated ($p<0.05$).

Results

Clinical Low back pain

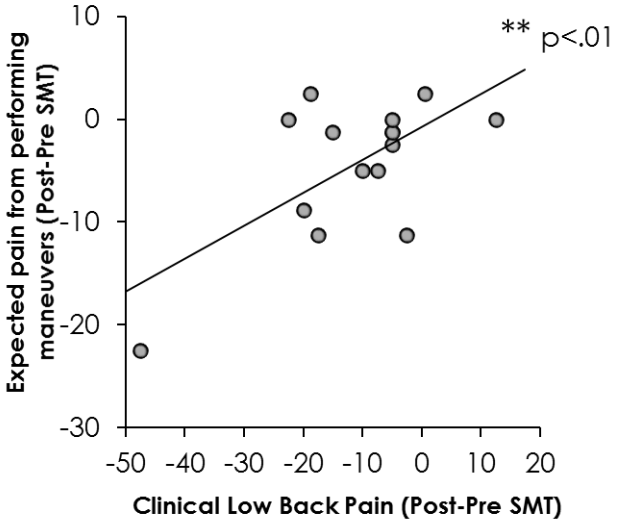


Expected pain from performing maneuvers

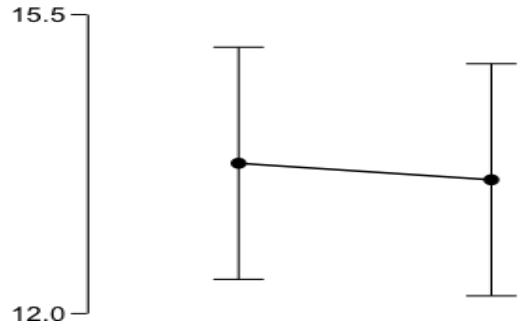


Results

Pain measures were significantly correlated (p<0.01)



Fear of performing maneuvers



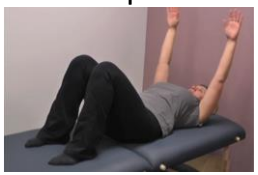
Pre
SMT

Results

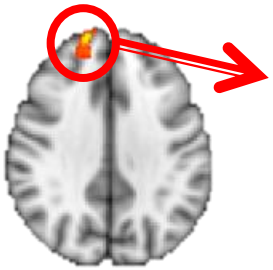
LBP – HC
(Painful-Nonpainful)

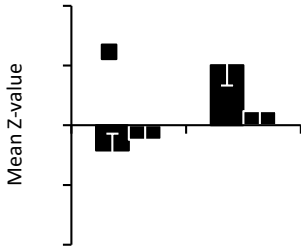
Painful

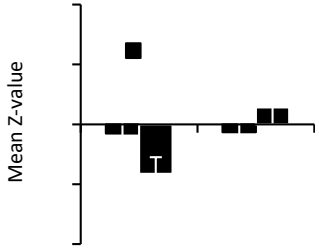
Non-painful



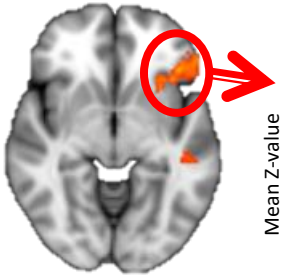
Right
dorsolateral PFC

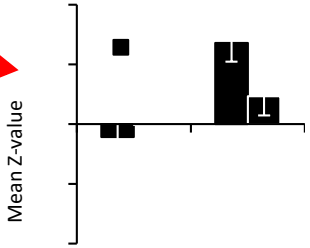


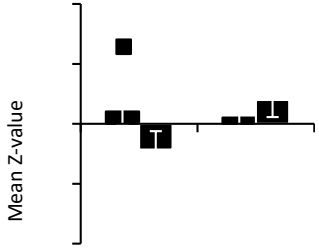




Left anterior insula/
ventrolateral PFC







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Thank You!

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