MRI at The University of Vermont MRI Center for Biomedical Imaging: A Tool for Neuroscience and Beyond

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Philips 3 Tesla Achieva dStream

Functional Magnetic Resonance Imaging (fMRI)
Pre-Study Setup (Julie Dumas and Jay Gonyea)

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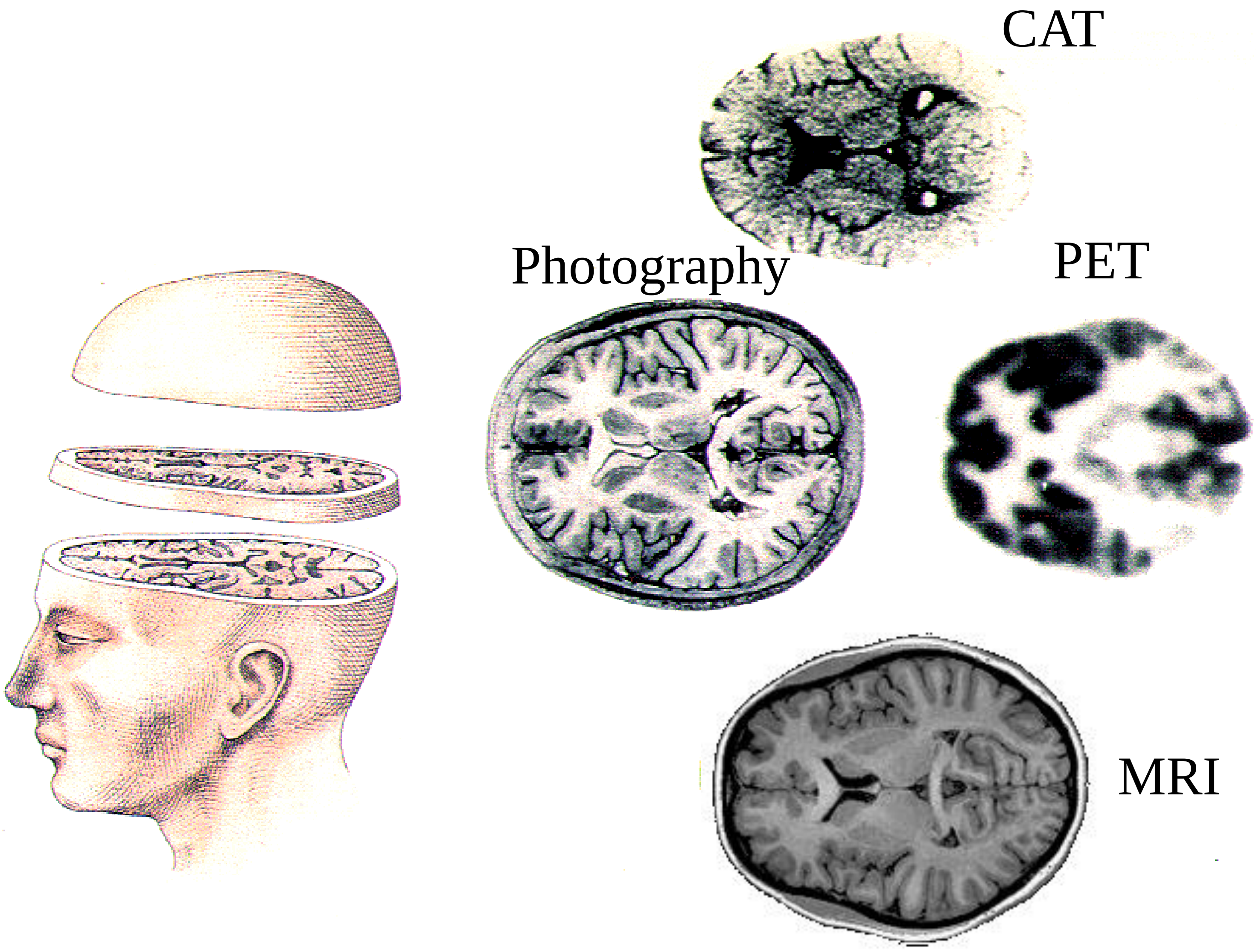
Imaging Methods



Source: modified from Posner & Raichle, Images of Mind

What is MRI and how does it work?

- Magnet
- RF Transmitter-(amplifier/coil)
- Receiver Coil
- Computers-reconstructor/operating system
- Gradient Coils X, Y, Z (noise makers)
- Magnet Cooling (superconducting) System

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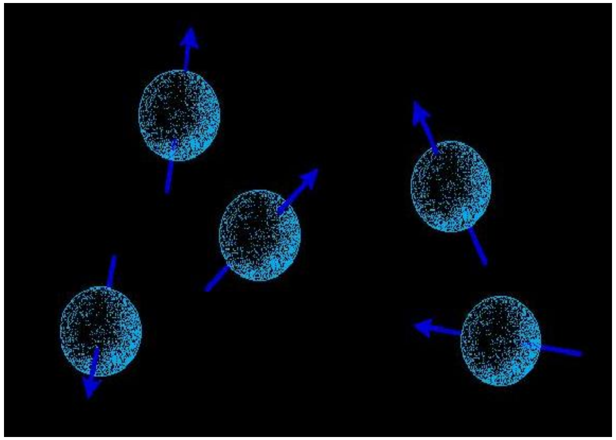
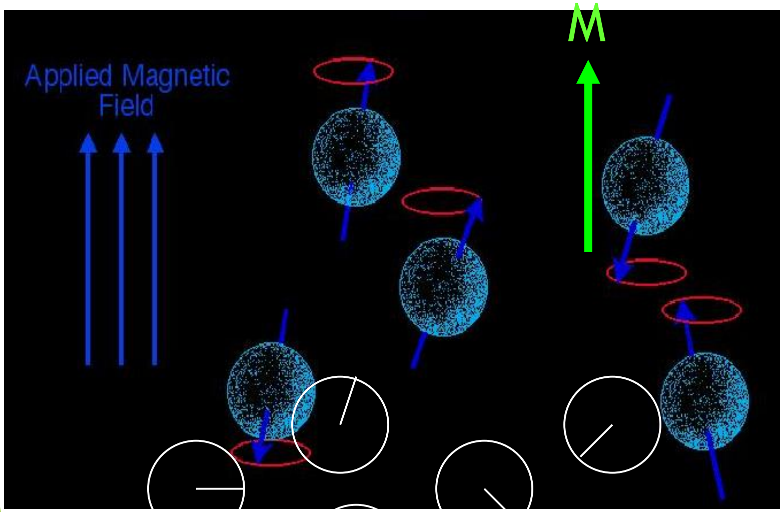
Protons align with field

Outside magnetic field



- randomly oriented

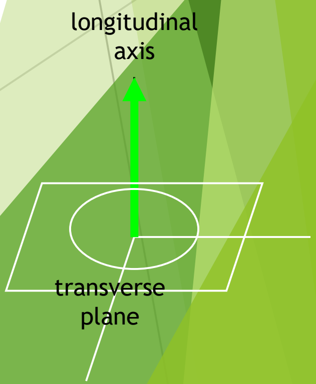
Inside magnetic field



M = 0

- spins tend to align parallel or anti-parallel to B_0
- net magnetization (M) along B_0
- spins precess with random phase
- no net magnetization in transverse plane

Longitudinal magnetization



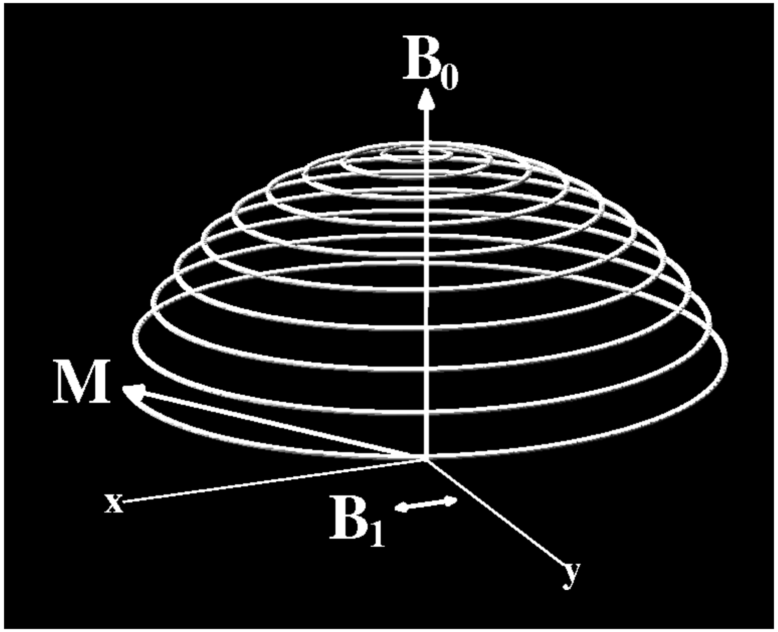
Mark Cohen's web slides

Robert Cox's web slides

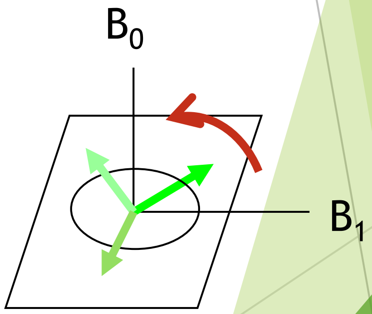
RF Excitation

Excite Radio Frequency (RF) field

- transmission coil: apply magnetic field along B1 (perpendicular to B_0) for ~3 ms
- oscillating field at Larmor frequency
- frequencies in range of radio transmissions
- B_1 is small: ~1/10,000 T
- tips M to transverse plane – spirals down
- analogies: guitar string (Noll), swing (Cox)
- final angle between B_0 and B_1 is the flip angle



Transverse magnetization



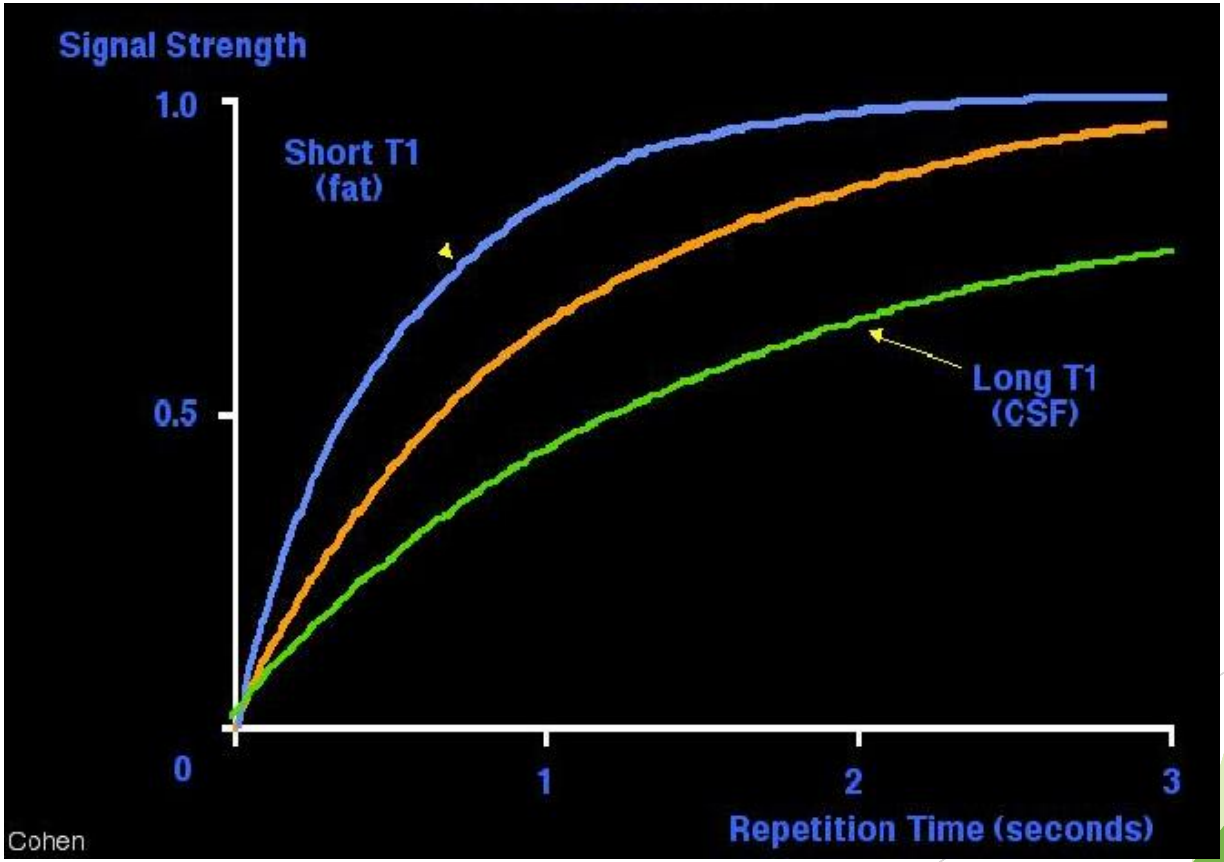
Source: *Robert Cox's web slides*

T1 and TR

T1 = recovery of longitudinal (B_0) magnetization

- used in anatomical images
- ~500-1000 msec (longer with bigger B0)

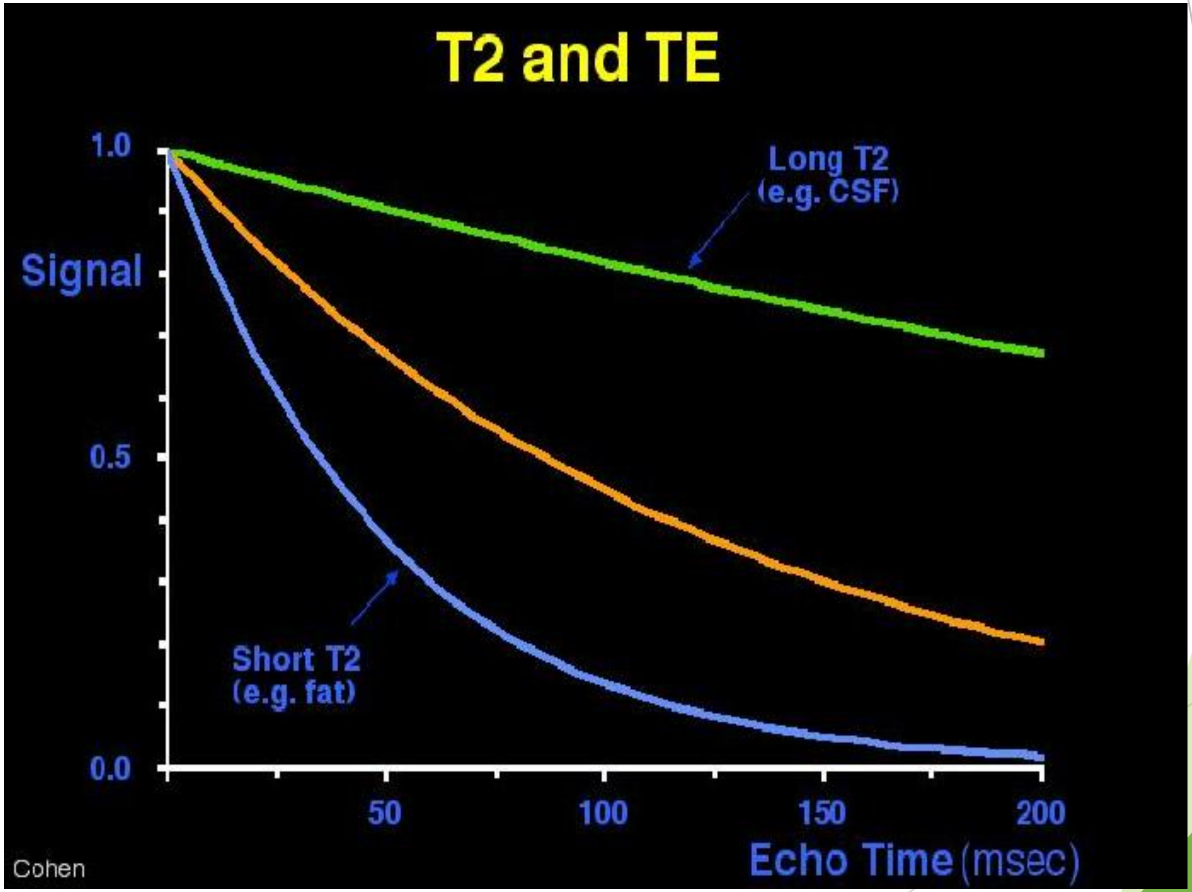
TR (repetition time) = time to wait after excitation before sampling T1



Source: *Mark Cohen's web slides*

T2 and TE

T2 = decay of transverse magnetization
TE (time to echo) = time to wait to measure T2 or T2* (after refocussing with spin echo or gradient echo)

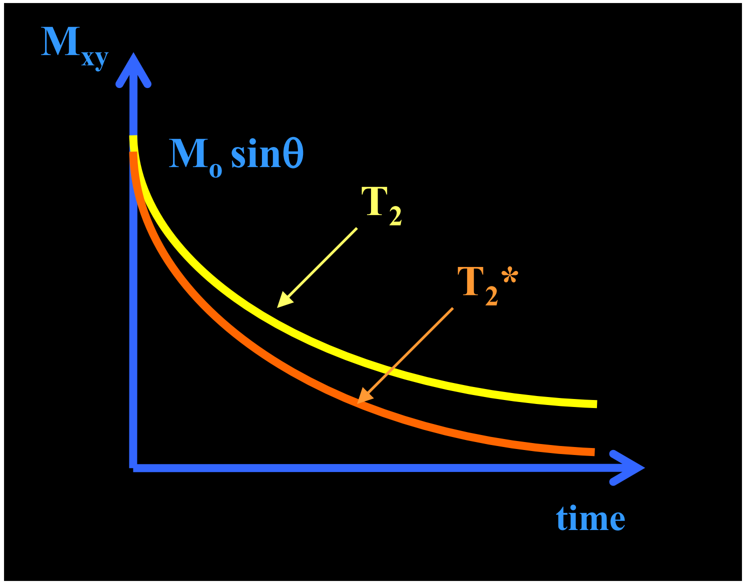


Source: Mark Cohen's web slides

T2*

T_2* relaxation

- dephasing of transverse magnetization due to both:
  - microscopic molecular interactions (T_2)
  - spatial variations of the external main field ΔB
    (tissue/air, tissue/bone interfaces)
- exponential decay ($T_2^* \approx$ 30 - 100 ms, shorter for higher B_o)



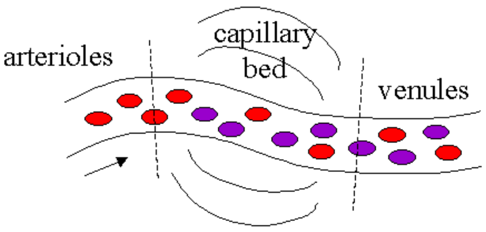
Source: Jorge Jovicich

BOLD signal

Blood Oxygen Level Dependent signal

↑neural activity ➔ ↑ blood flow ➔ ↑ oxyhemoglobin ➔ ↑ T2* ➔ ↑ MR signal

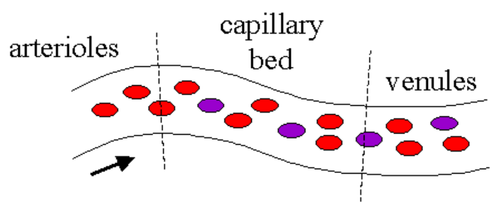
<u>Basal state</u>



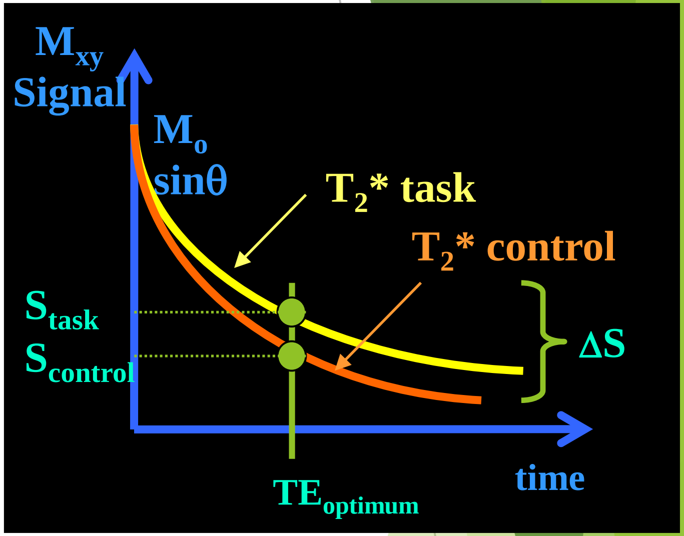
- normal flow
- basal level [Hbr]
- basal CBV
- normal MRI signal

= HbO_2
= Hbr

<u>Activated state</u>



- increased flow
- decreased [Hbr] (*lower field gradients around vessels*)
- increased CBV
- increased MRI signal (*from lower field gradients*)



fMRIB Brief Introduction to fMRI

Source: Jorge Jovicich

MRI is extremely flexible and can be applied to virtually all body regions. Some of the MRI techniques used to generate quantitative data include:

- fMRI
- Diffusion
- Perfusion
- T1rho mapping
- T1 mapping
- T2 mapping
- Structural Volumetric Analysis

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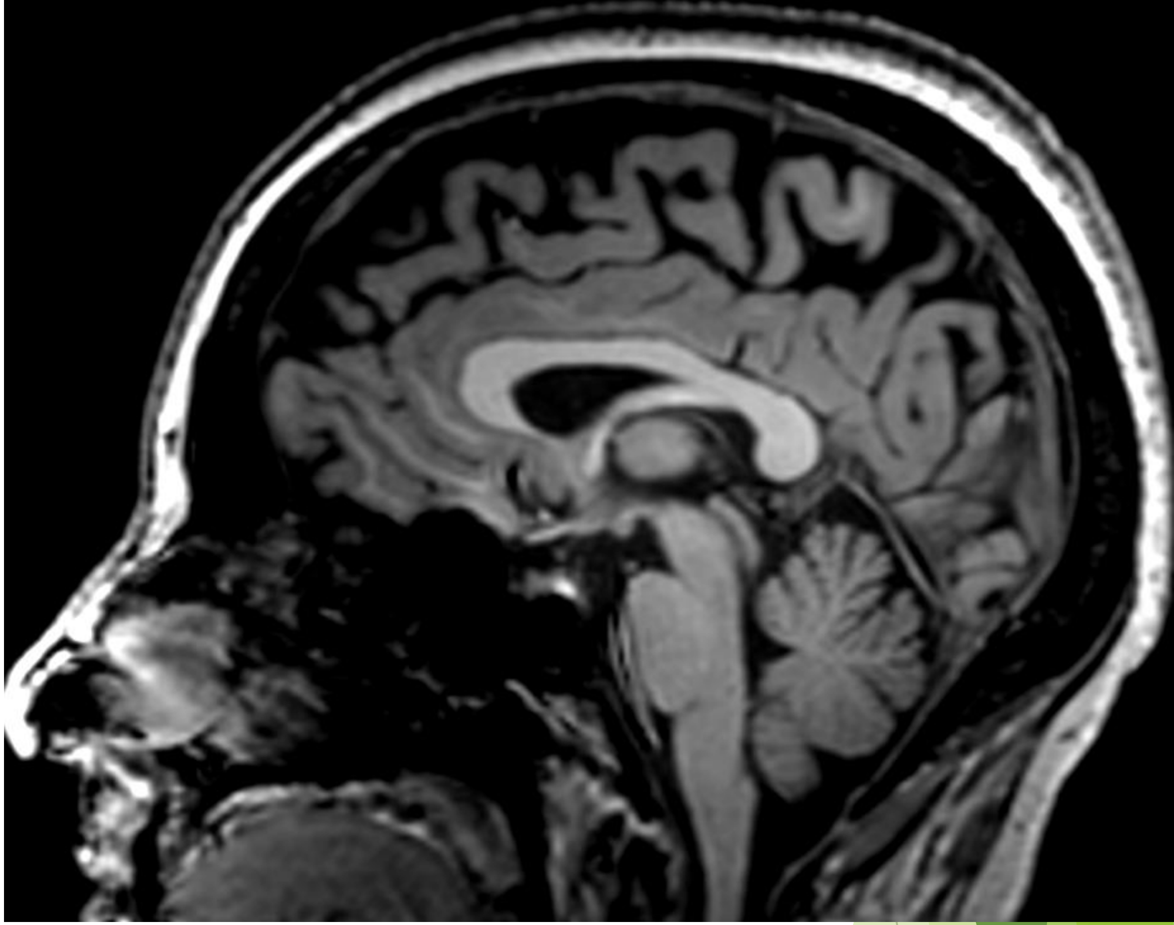
Neuroscience Applications of MRI

MRI provides exceptional tissue contrast and is especially useful for brain imaging



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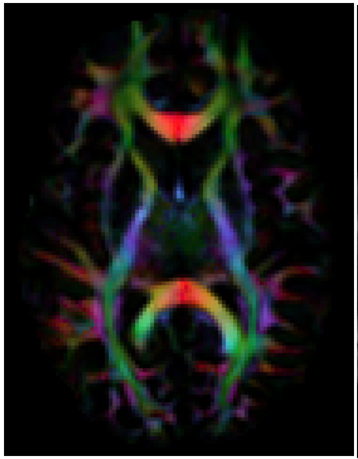
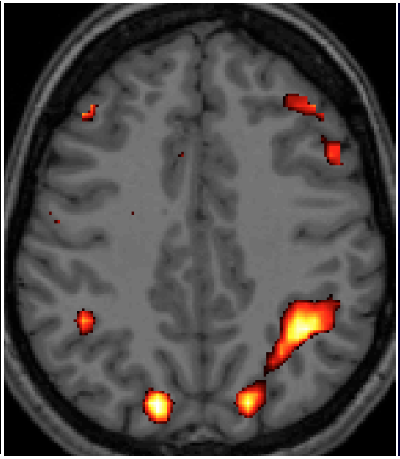
Applications of MRI in the Brain

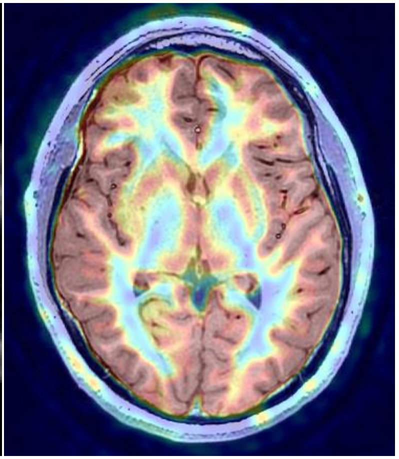
Contrasts due to
- Proton density
- Magnetic relaxation properties (T1, T2, T2*)
- Water motion (diffusion)
- Blood oxygenation (fMRI/BOLD)
- Blood flow/perfusion(CBF)



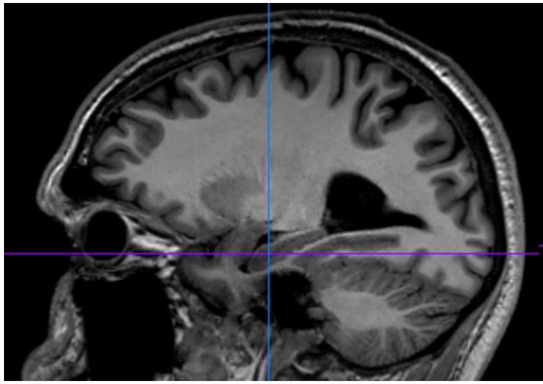
DTI Color Map



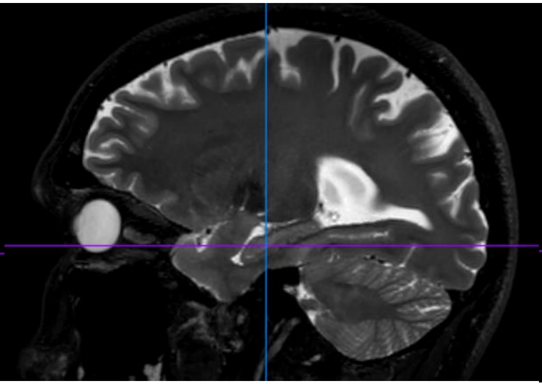
fMRI Activation Map



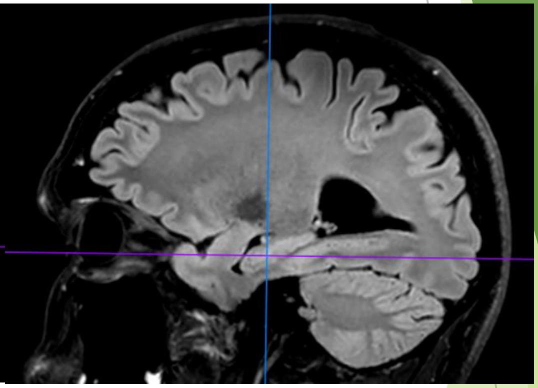
Perfusion (CBF) Map



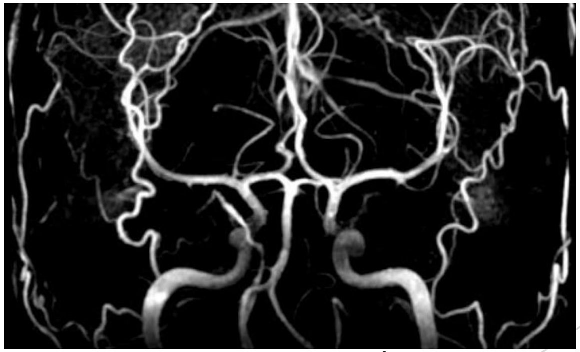
T1-weighted image



T2-weighted image



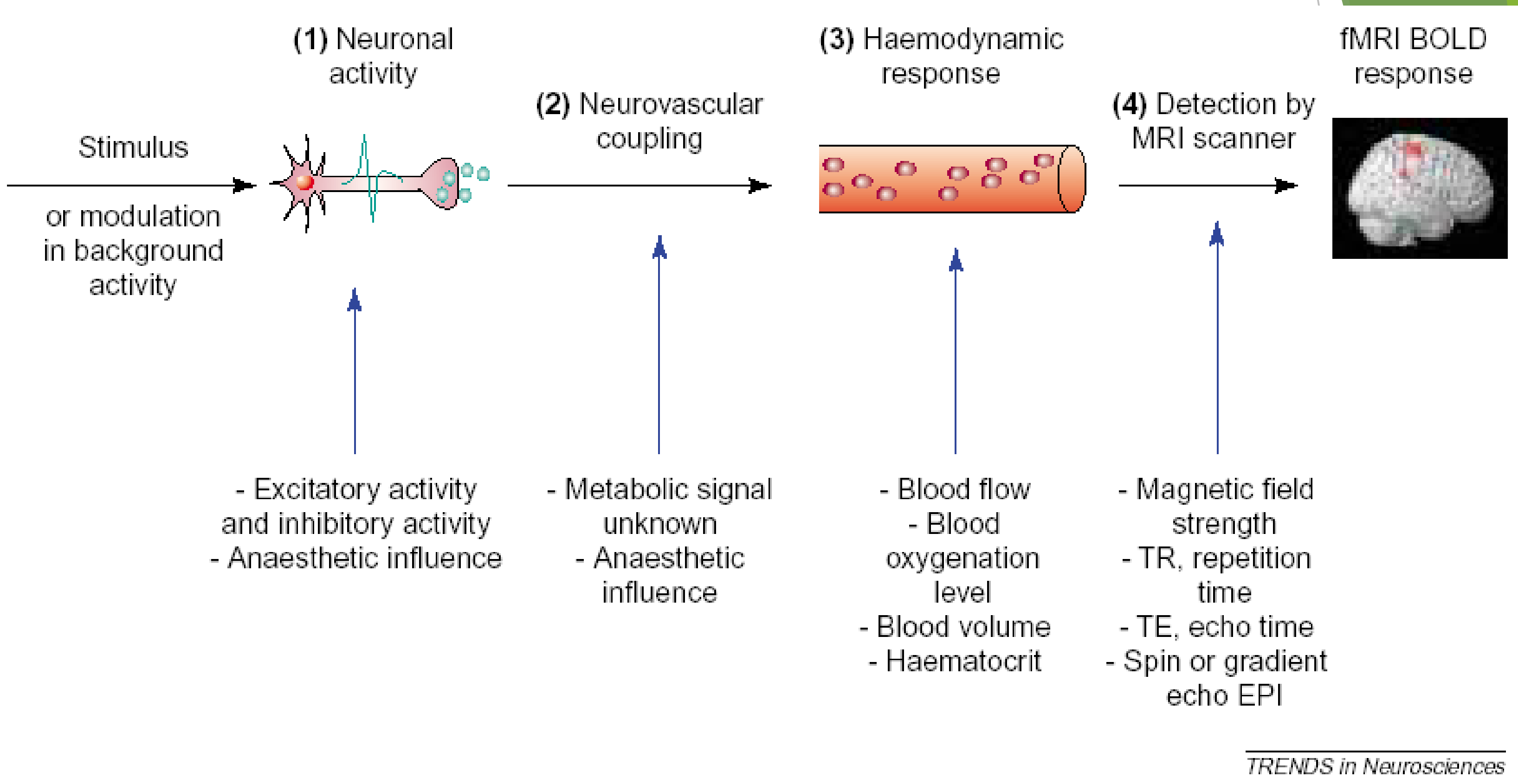
T2-FLAIR image



MR Angiography
(Non-Contrast)

Functional MRI (fMRI, BOLD)

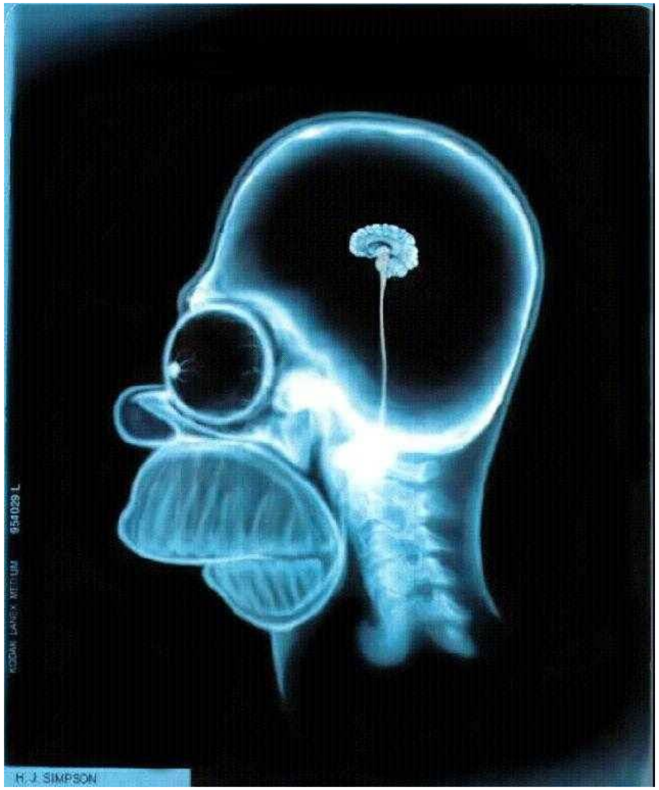
Blood Oxygenation Level Dependent Imaging (BOLD)



The BOLD Effect is the result of the Hemodynamic Response to Brain Stimuli

MRI vs. fMRI

MRI studies brain <u>anatomy</u>.



<u>Functional</u> MRI (fMRI) studies brain <u>function</u>.

Culham 2006

Is fMRI better than phrenology?

Phrenological Chart of the Faculties.

What can fMRI tell us about cognition?

- Brain regions involved in cognition
- Brain regions that work together as a network during a cognitive process
- How the localization of a cognitive process changes over time, training, illness, medication, etc.

fMRI Studies by LCOM Investigators

- Adolescent Brain Cognitive Development (ABCD)
  U01 DA041148 MPIs Garavan and Potter
- The Nicotinic Cholinergic System and Normal Cognitive Aging
  R01 AG05071 PI Dumas
- Fatty Acid Effects on Normal Aging
  R56 AG062105 PI Dumas
- Health of the Cholinergic System and Risk for Alzheimer's Disease in Postmenopausal Women
  R01 AG066159 MPIs Dumas and Newhouse
- Tobacco Center on Regulatory Science (TCORS)
  PI Higgins
- Cannabis and Schizophrenia
  R01 DA034699 UVM PI Garavan and Mackey
- Investigator of Opioid Exposure and Neurodevelopment (IOPEN) R34 DA050283 MPIs Potter, Garavan, Heil

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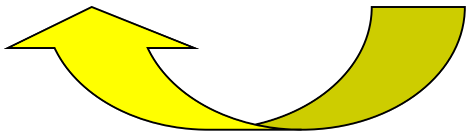
An Example: Pharmacological fMRI

Functional Neuroimaging (fMRI) + Psychopharmacology

Localization of neural correlates of cognitive function

Neurochemical modulation of cognitive function

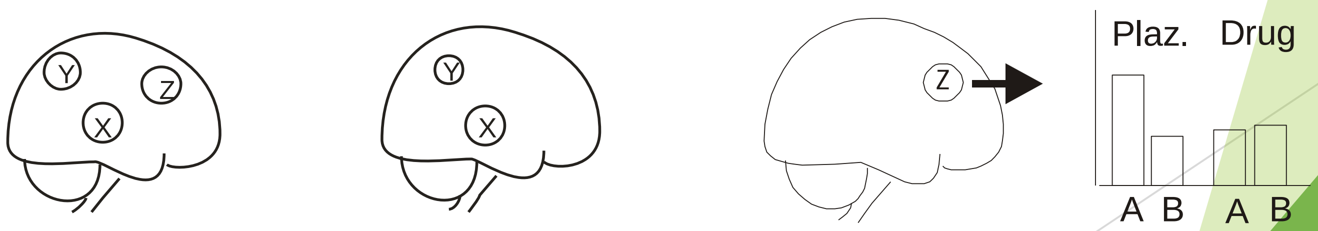


Modulation of task-related activity

Placebo A-B

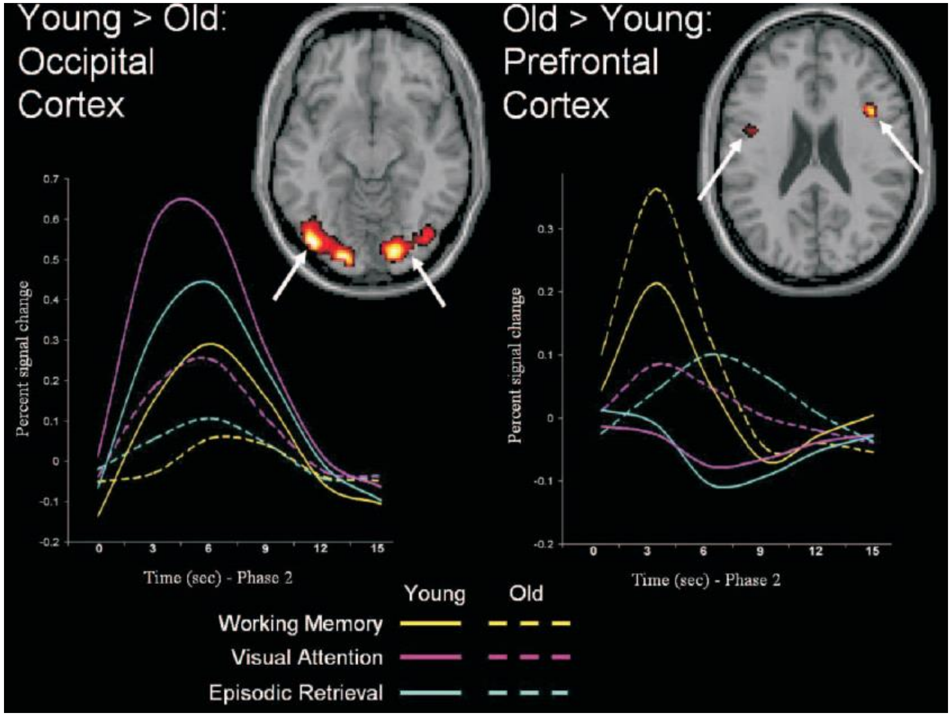
Drug A-B

(Placebo A-B) - (Drug A -B)



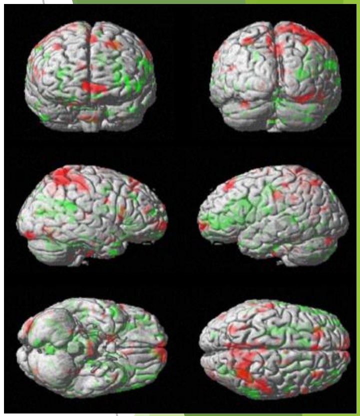
Drug by task interactions

Cognitive Aging and Cholinergic System



Cabeza et al. (2004)

RED: MECA> PLC
GREEN: SCOP>PLC



Dumas et al. (2008)

PHYSO > PLC

Bentley et al. (2003)

Working Memory Task

- Working memory task
  - Visual verbal N-back

Verbal N-back task

1-back

A B C C D E E F G

2-back

A B C B D E F E G

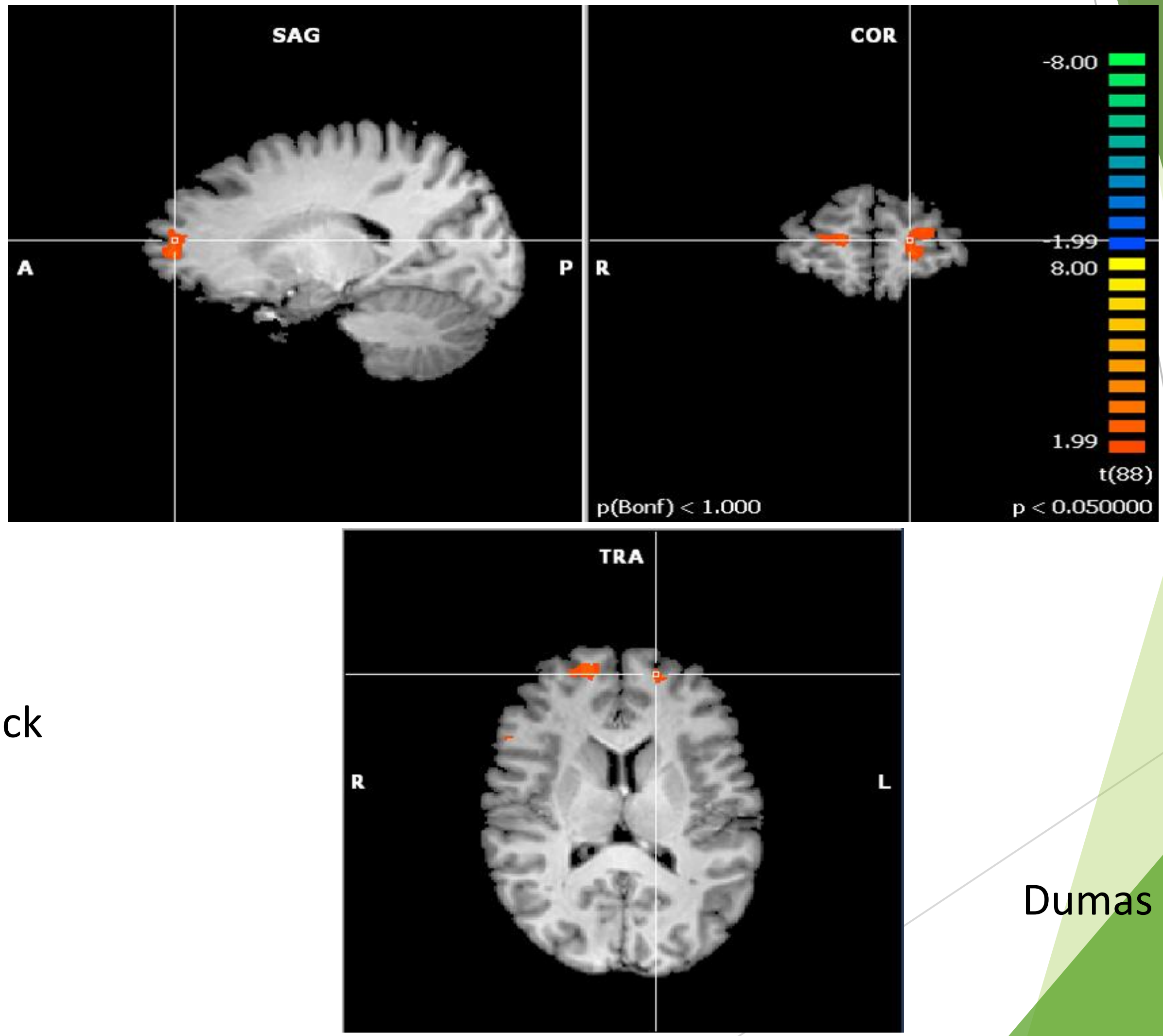
3-back

A B C A D E F D G

0-back

A B X C D X F G X

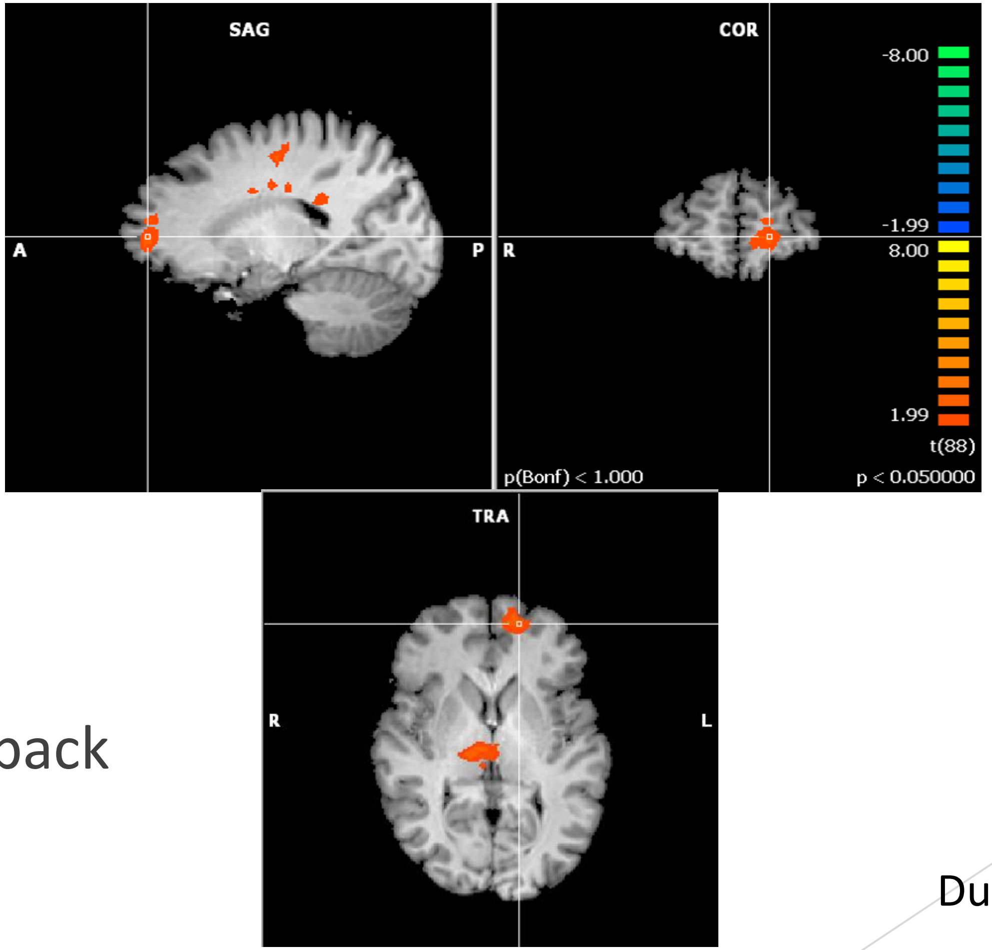
Cholinergic modulation of Working Memory Networks



MECA – PLC
3-back – 0-back

Dumas et al. (2012)

Cholinergic modulation of Working Memory Networks

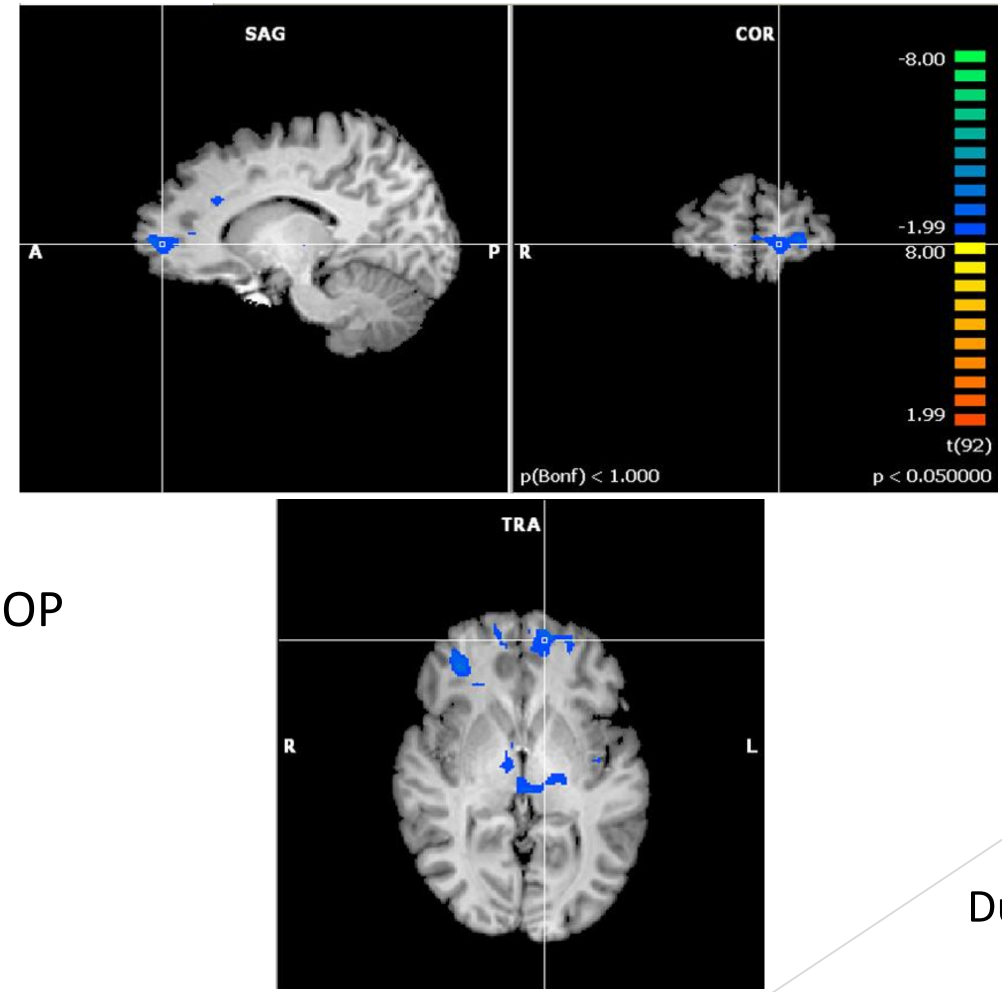


SCOP – PLC

3-back – 0-back

Dumas et al. (2012)

Estradiol modulation of cholinergic activity

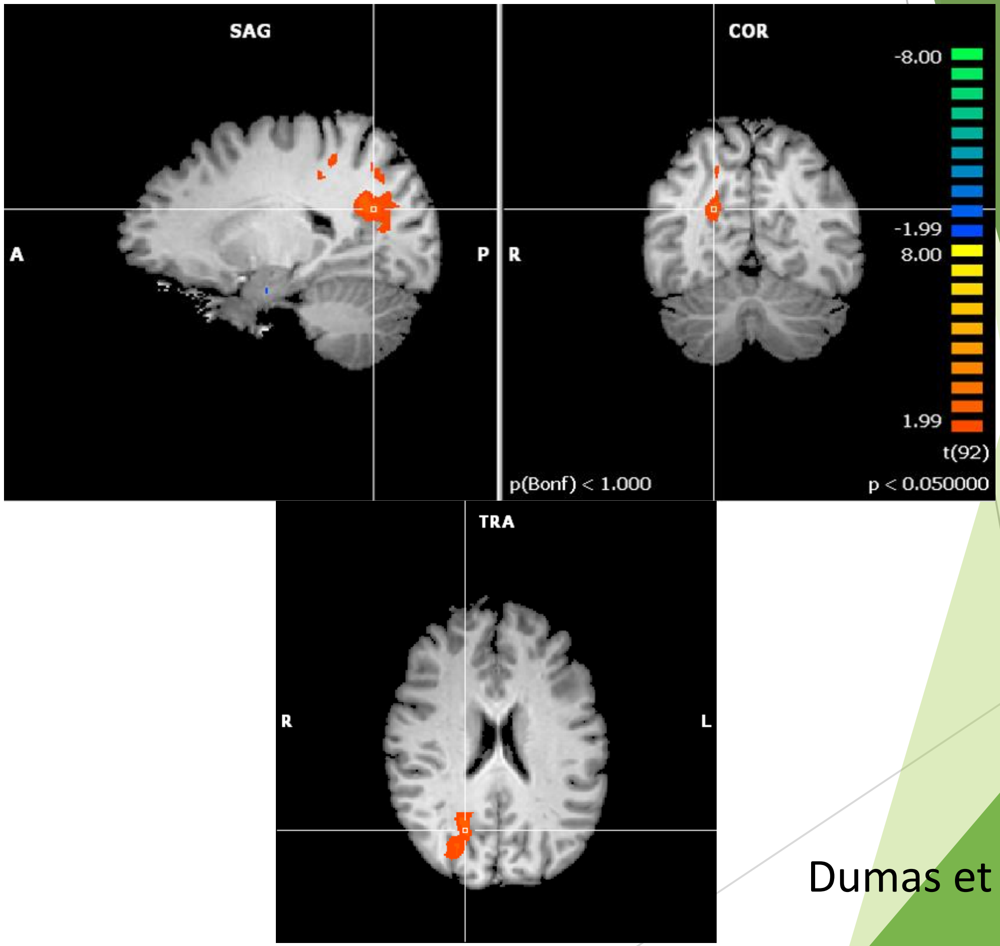


E2 – PLC during SCOP challenge

3-back – 0-back

Dumas et al. (2012)

Estrogen modulation of cholinergic activity

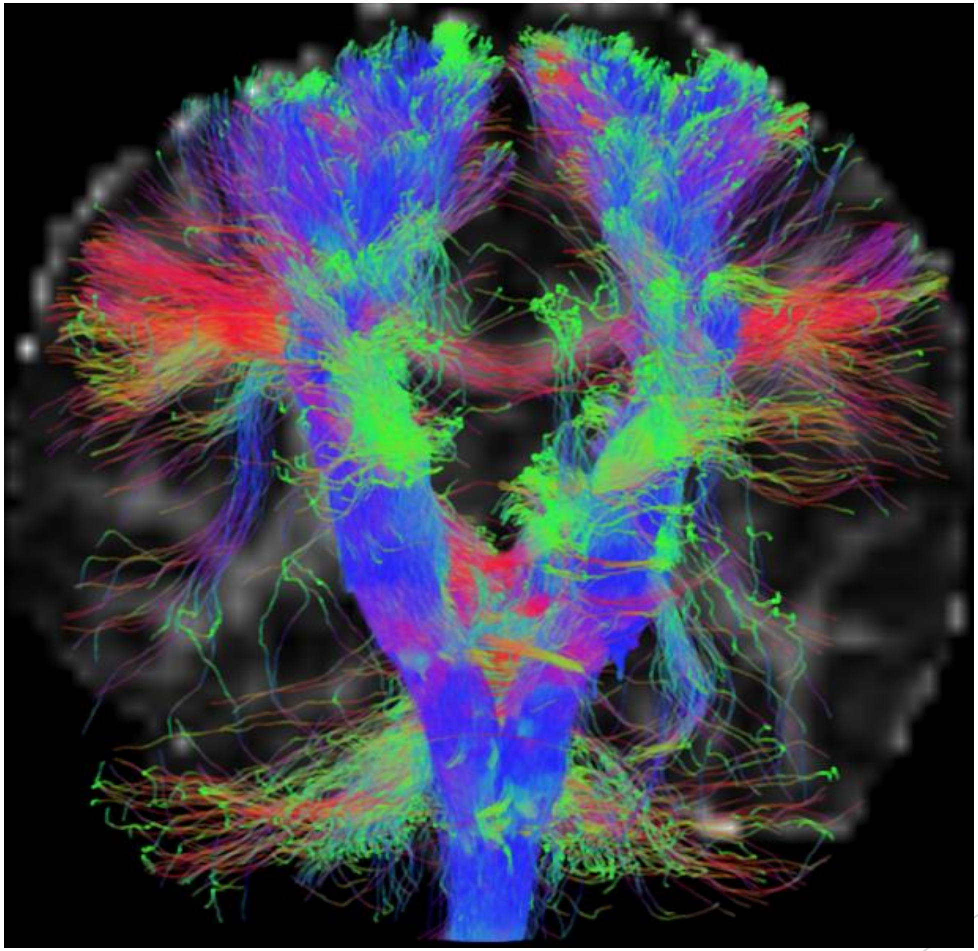


E2 – PLC during MECA challenge

3-back – 0-back

Dumas et al. (2012)

Brain diffusion (DTI) demonstrates axonal diffusion and directionality or anisotropy of water along white matter tracts. (Blue=Superior to Inferior (CST), Red=Left to Right (CC), Green=Anterior to Posterior



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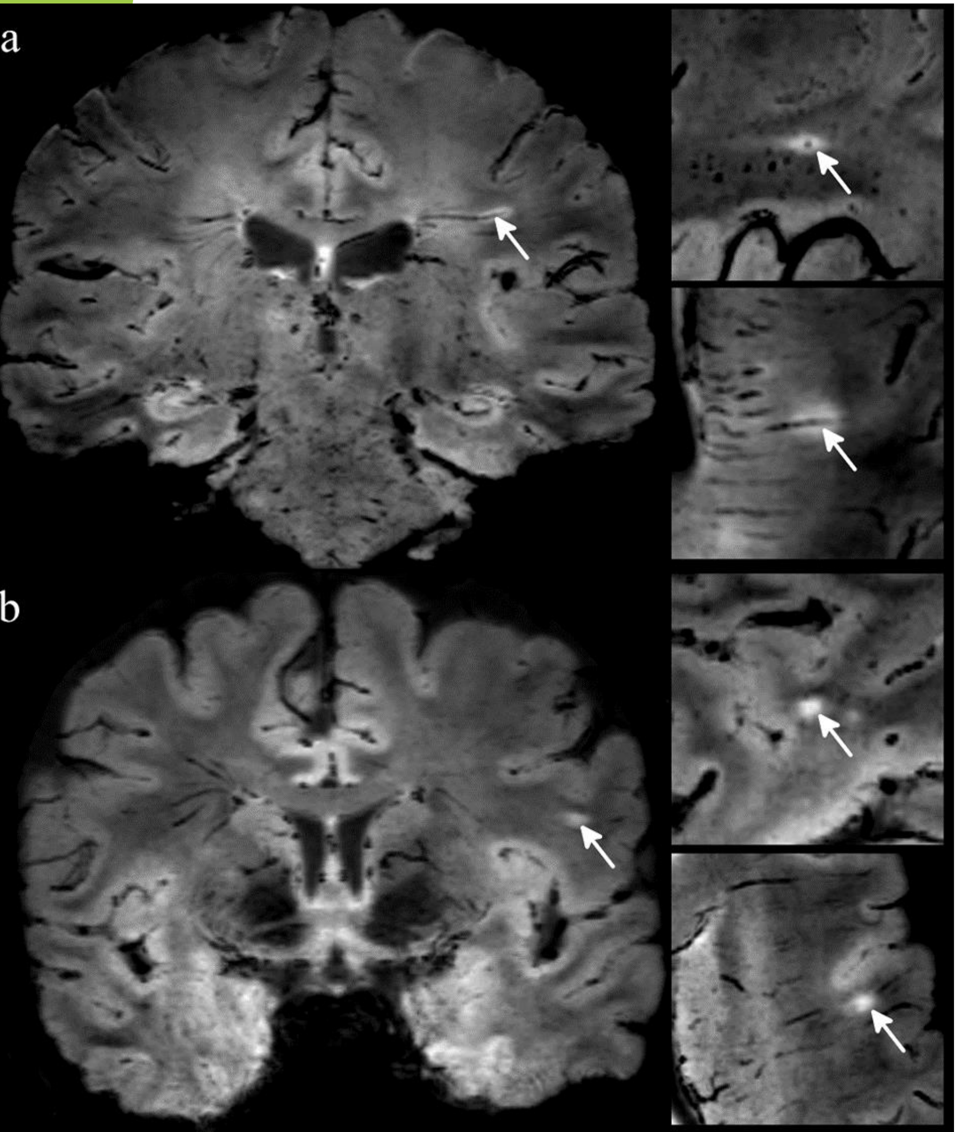
T2*-FLAIR
Central Vessel in Multiple Sclerosis (MS)



IMPROVING DIAGNOSIS OF MULTIPLE SCLEROSIS THROUGH THE INTEGRATION OF NOVEL IMAGING AND LABORATORY BIOMARKERS

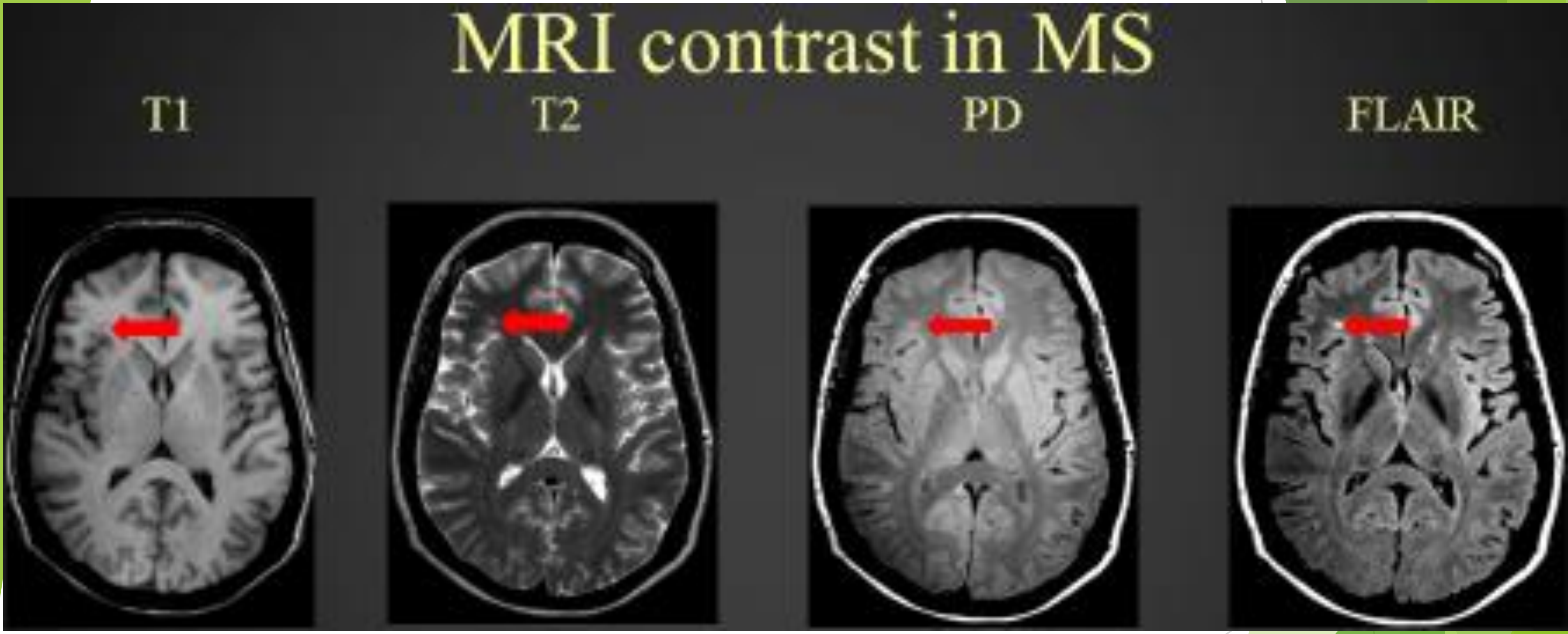
K02 NS109340 PI Solomon

Central vessel sign is a promising (Andy Solomon, M.D. Department of Neurological Sciences)

Note: the blood vessel seen within the multiple sclerosis lesion (arrows)

Various Scan Sequence Types Yield Specific Tissue Contrasts

Note: the varying appearance of the multiple sclerosis (MS) lesion



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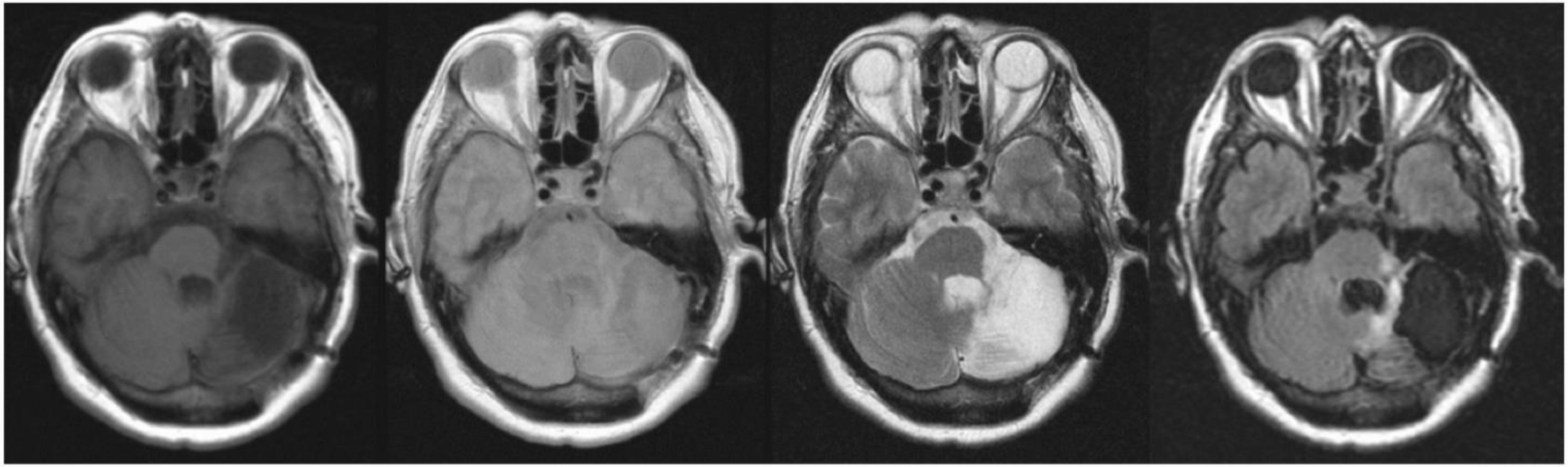
Note: the varying appearance of the cerebrospinal fluid (CSF) in patient s/p brain tumor resection



T1	Proton Density	T2	FLAIR

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Musculoskeletal Applications of MRI

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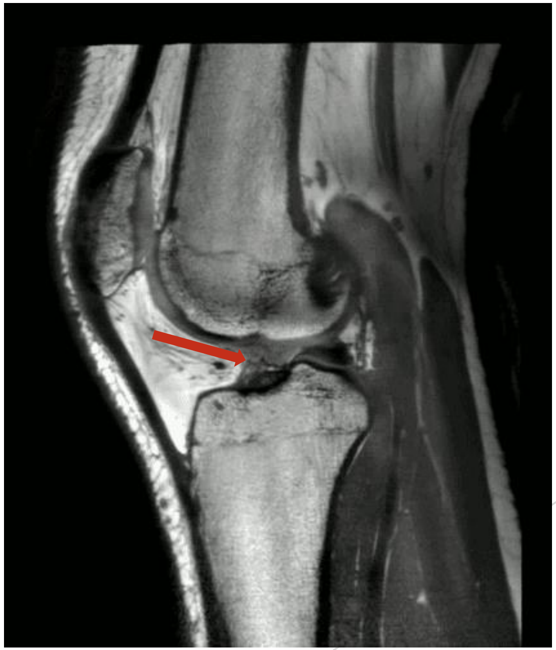
- Dr. Bruce Beynnon and his team are investigating geometric characteristics of the knee to better understand risk factors for anterior cruciate ligament (ACL) injury among young athletes in the contralateral knee following ACL repair.

Knee 3D T1w FFE WATSc
(For Cartilage Segmentation)

Knee 3D PD w TSE
(For Meniscus and Ligaments)
(arrow)



R01 AR050421
PI Beynnon

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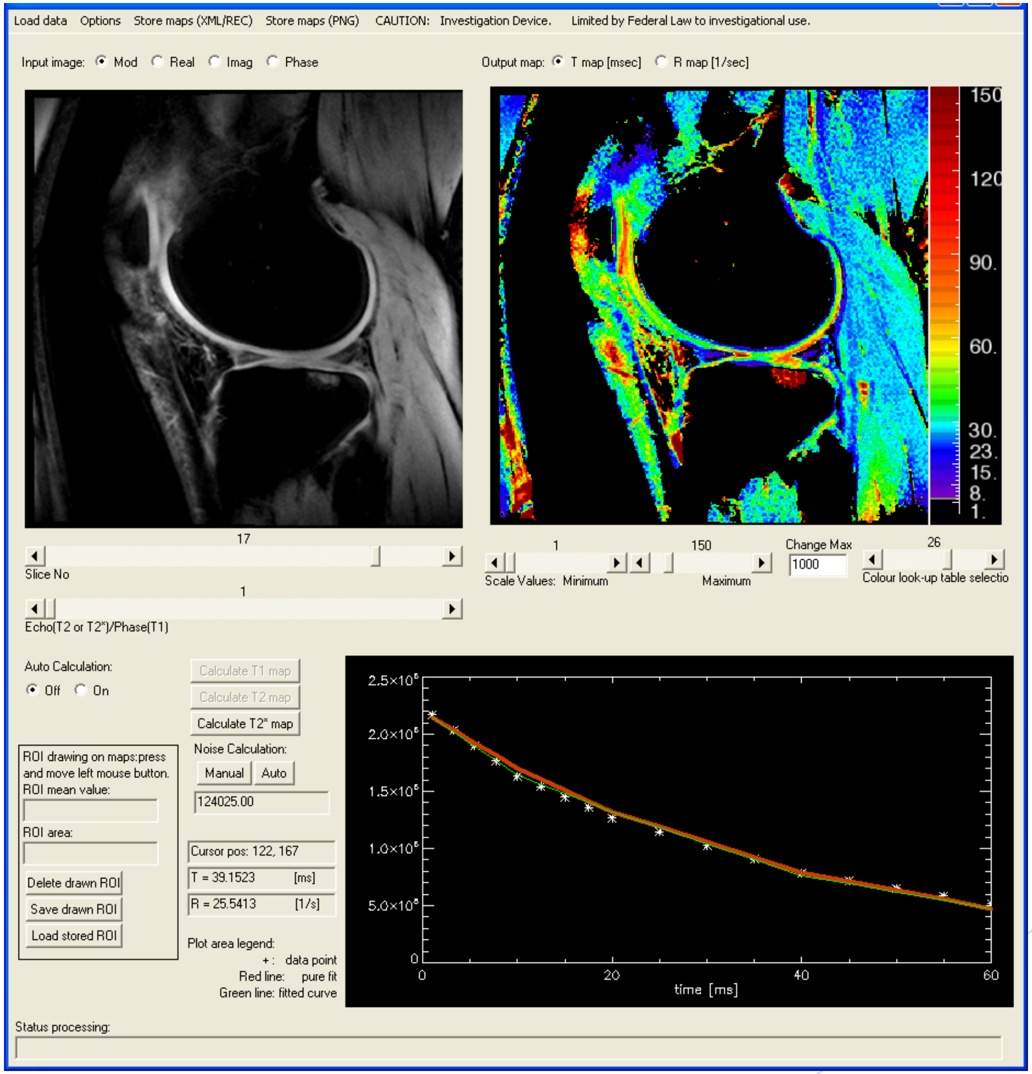
Quantitative $T1_r$ Map of Knee



Cardiac MRI

- Jiming Zhang, Ph.D.

Water movement though sand

- George Pinder, Ph.D.

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The UVM MRI Center for Biomedical Imaging
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Thank you!



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3 Teslas

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References

- **Geometric Characteristics of the Knee Are Associated With a Noncontact ACL Injury to the Contralateral Knee After Unilateral ACL Injury in Young Female Athletes**

James G. Levins,* MD, Erin C. Argentieri,y BS, Daniel R. Sturnick,z MS,
Mack Gardner-Morse,* MS, Pamela M. Vacek,§ PhD, Timothy W. Tourville,|| PhD, ATC,
Robert J. Johnson,* MD, James R. Slauterbeck,* MD, and Bruce D. Beynnon,*{ PhD
Investigation performed at the University of Vermont Robert Larner MD College of Medicine,
Burlington, Vermont, USA

- **Central vessel sign" on 3T FLAIR* MRI for the differentiation of multiple sclerosis from migraine**

Andrew J. Solomon1, Matthew K. Schindler2, Diantha B. Howard3, Richard Watts4, Pascal Sati2,
Joshua P. Nickerson4 & Daniel S. Reich2
1Department of Neurological Sciences, University of Vermont College of Medicine, Burlington, Vermont
2Translational Neuroradiology Unit, Division of Neuroimmunology and Neurovirology, National Institute of Neurological Disorders and Stroke,
Bethesda, Maryland
3Vermont Center for Clinical and Translational Science, Burlington, Vermont
4Department of Radiology, University of Vermont College of Medicine, Burlington, Vermont

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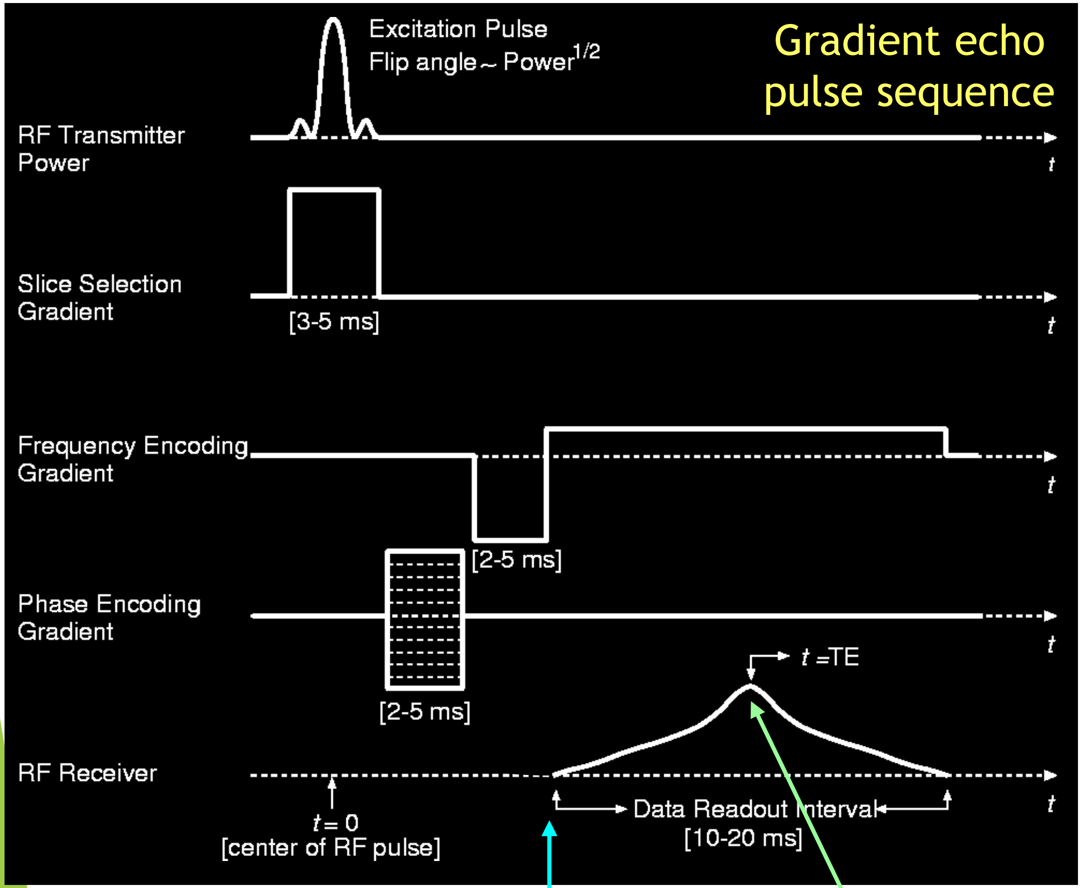
Echos

pulse sequence: series of excitations, gradient triggers and readouts



A gradient reversal (shown) or 180 pulse (not shown) at this point will lead to a recovery of transverse magnetization

TE = time to wait to measure refocussed spins

Echos – refocussing of signal

Spin echo:

use a 180 degree pulse to "mirror image" the spins in the transverse plane

when "fast" regions get ahead in phase, make them go to the back and catch up

- measure T2
- ideally TE = average T2

Gradient echo:

flip the gradient from negative to positive

make "fast" regions become "slow" and vice-versa

- measure T2*
- ideally TE ~ average T2*

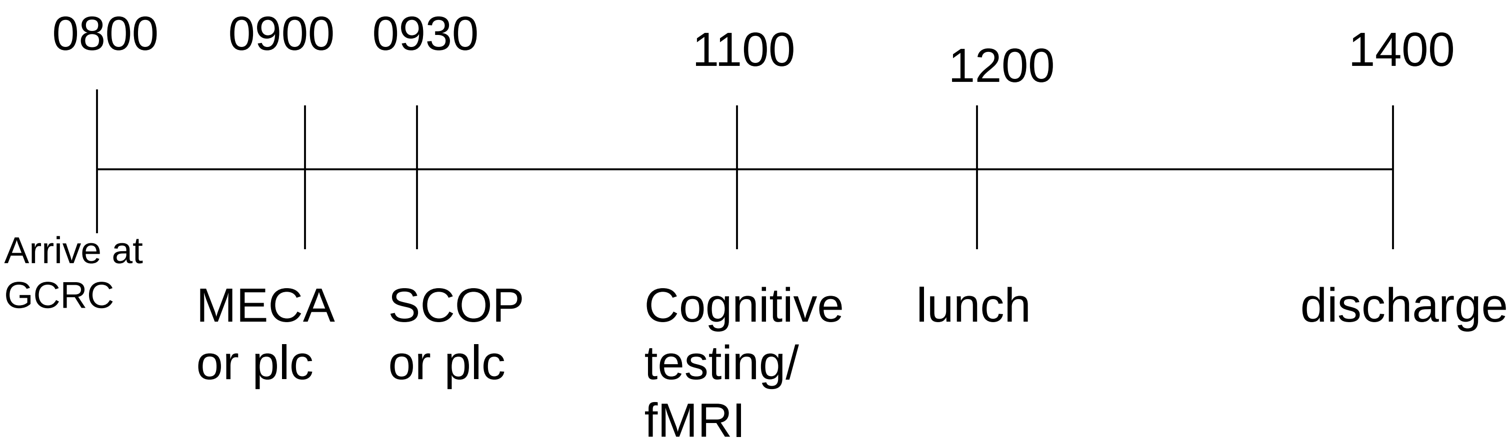
Source: Mark Cohen's web slides

Estradiol and Cholinergic System Interaction and Working Memory in Postmenopausal Women

- Hypothesis – Estradiol will reverse anticholinergic-related brain activation patterns.
- 24 healthy, cognitively normal PMW
- 3 months treatment with 1 mg oral 17-β estradiol per day or placebo
- 3 cholinergic challenge and fMRI study days
  - 2.5 µg/kg SCOP – IV
  - 20 mg MECA – oral
  - Matching placebos

Cholinergic Challenge Day

- Study day timeline



Aging, the Cholinergic System, and Brain Imaging

- Attention, working memory, and episodic memory
  - Prior research shows a shift in brain processing from occipital to a frontal pattern in older relative to younger adults (Cabeza et al. 2004).
  - Cholinergic agonists show posterior increases in activity (Bentley et al. 2003; Furey et al. 2000).
  - Cholinergic antagonists show increased frontal activity older women (Dumas et al. 2012).