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

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

Outside magnetic field

- randomly oriented

Inside magnetic field

- 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

Source: 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 $\sim 3$ ms
- oscillating field at Larmor frequency
- frequencies in range of radio transmissions
- $B_1$ is small: $\sim 1/10,000$ 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

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
$T_2^*$

$T_2^*$ relaxation

- dephasing of transverse magnetization due to both:
  - microscopic molecular interactions ($T_2$)
  - spatial variations of the external main field $\Delta B$
    (tissue/air, tissue/bone interfaces)
- exponential decay ($T_{2^*} \approx 30 - 100$ ms, shorter for higher $B_0$)

Source: Jorge Jovicich
BOLD signal

Blood Oxygen Level Dependent signal

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

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

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

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
Neuroscience
Applications of MRI
MRI provides exceptional tissue contrast and is especially useful for brain imaging.
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)

T1-weighted image  T2-weighted image  T2-FLAIR image
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 **anatomy**.

Functional MRI (fMRI) studies brain **function**.

Culham 2006
Is fMRI better than phrenology?
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
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)

Bentley et al. (2003)

Dumas et al. (2008)

RED: MECA > PLC
GREEN: SCOP > PLC

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)
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

MRI contrast in MS

T1  T2  PD  FLAIR
Note: the varying appearance of the cerebrospinal fluid (CSF) in patient s/p brain tumor resection.
Musculoskeletal Applications of MRI
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.
Quantitative T1$_r$ Map of Knee
Cardiac MRI

Jiming Zhang, Ph.D.

Water movement though sand

George Pinder, Ph.D.
The UVM MRI Center for Biomedical Imaging is supported by the Larner College of Medicine

Thank you!
3 Teslas
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
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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*

TE = time to wait to measure refocussed spins
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

0800  Arrive at GCRC
0900  MECA or plc
0930  SCOP or plc
1100  Cognitive testing/fMRI
1200  lunch
1400  discharge
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).