Neuroimaging with MRI:
Some of the Things We Can See

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Preview of Coming Attractions

- Quick overview of MRI physics (all on one slide!)
- Some images and their applications
  - T1-weighted = gray/white/CSF delineation
  - T2-weighted = detection of tissue abnormalities
  - T2*-weighted = venography
  - Contrast agents
    - Enhancement of signals from various tissue types/conditions
    - DCEMRI & tumor quantification
  - Diffusion weighted imaging = white matter quantification
- Imaging brain function with MRI
- Brain atlases and statistical neuroanatomy
Synopsis of MRI

1) Put subject in big magnetic field [and leave him there]
   ⇒ Magnetizes the H nuclei in water ($\text{H}_2\text{O}$)

2) Transmit radio waves into subject  [about 3 ms]
   ⇒ Perturbs the magnetization of the water

3) Turn off radio wave transmitter

4) Receive radio waves re-transmitted by subject’s H nuclei
   ⇒ Manipulate re-transmission by playing with H magnetization with extra time-varying magnetic fields during this readout interval  [10-100 ms]
   ⇒ Radio waves transmitted by H nuclei are sensitive to magnetic fields — those imposed from outside and those generated inside the body:
   ⇒ Magnetic fields generated by tissue components change the data and so will change the computed image

5) Store measured radio wave data vs time
   ⇒ Now go back to 2) to get some more data [many times]

6) Process raw ("k-space") radio wave data to reconstruct images
T1-Weighted Images

• Images whose design (timing of radio pulses and data readout) is to produce *contrast* between gray matter, white matter, and CSF

Three axial (AKA transaxial or horizontal) slices:
- Spatial resolution is about 1 mm$^3$
- Acquisition time for whole head is 5-10 minutes
Zooming In

- Can follow GM cortex fairly well
  - Can measure thickness of cortex and try to quantify vs age and/or disease and/or genes

- Bright spots and lines: arterial inflow artifact
  - Leads to idea of MRA = Magnetic Resonance Angiography = acquire images to make arteries stand out even more

- Higher spatial resolution is possible
  - At the cost of scan time
A single acquisition is somewhat noisy
Previous T1-weighted image was actually average of 4 separate acquisitions (to average out noise)
MRI can be a 2D or a 3D acquisition technique
Some Bad MR Images

- Subject moved head during acquisition
  - Ghosting and ringing artifacts
  - Might be OK for some clinical purposes, but not much use for most quantitative brain research
MRI vs CT in the Brain

• Skull gets in the way of X-ray imaging:
  ▪ Bone scatters X-rays much more than soft tissue
  ▪ MRI radio waves pass unimpeded through bone
Brain Slice Animations

- Fun to watch (brain soup)
- More useful if movement through slices is under your direct interactive control
3D Visualization

- MR images are 3D, but screens and retinas are 2D
- Understanding 3D structures requires looking at them in different ways

Volume rendering of T1-weighted image showing how corpus callosum spreads into hemisphere
T2-Weighted Images

- Often better than T1-weighting in detecting tumors and infarcts (usually radiologists look at both types of scans)
T2*-Weighted Images

- Designed to make venous blood (with lots of deoxy-hemoglobin) darker than normal tissue = *venography*

Output image

minIP ±1 slice

minIP ±2 slices

Images post-processed to enhance small effects
MRI Contrast Agents

• Chemicals injected into blood, designed to alter MRI signal by affecting magnetic environment of H nuclei
  ▪ Developed starting in late 1980s (and still continuing)
  ▪ Used millions of times per year in USA
  ▪ Designed to be biologically inert (only “active” magnetically)
    • About 1 person in 100,000 has allergic reaction
  ▪ Purpose is to increase contrast of some tissue type

• Most commonly used is Gd-DTPA (Magnevist™)
  ▪ Gadolinium ion (highly magnetizable) chelated to a molecule that won’t pass an intact blood-brain barrier
  ▪ Makes T1-weighted images brighter where it accumulates and makes T2- and T2*-weighted images darker

• Deoxy-hemoglobin is an endogenous T2* agent
Tumor: T2 and T1+contrast

T2-weighted

T1-weighted post-contrast
T2* MRV on a Seizure Patient

Gd-enhanced T1-weighted

Gd-enhanced T2*-weighted

Bad
DCE-MRI and Brain Tumors

• DCE = Dynamic Contrast Enhancement
  ▪ Inject contrast agent rapidly ("bolus") and take rapid images of brain repeatedly to observe its influx
  ▪ Cost of taking such rapid images: coarser spatial resolution and limited spatial coverage and more noise
  ▪ Below: rapid T1-weighted images (20 s per volume)
    • 12 slices at 5 mm thickness (0.9 mm in-slice resolution)
Time Series of Images

Time Point #7: Before Gd hits (bright spot = sagittal sinus)

Time Point #9: Gd into vessels

Time Point #23: Gd leaks into tumor (now mostly gone from vessels)

From John Butman’s group in NIH/CC
**Time Courses of Voxel Intensities**

- **Voxel in vessel**
  - This data is used as “arterial input function” for math model below

- **Voxel in tumor**
  - Can fit math model of Gd infiltration to quantify “leakiness”
  - Tumor grade?
  - Necrosis?
  - Treatment effects?
Diffusion Weighted Imaging

- Water molecules diffuse around during the imaging readout window of 10-100 ms
  - Scale of motion is 1-10 microns ≈ size of cells
  - Imaging can be made sensitive to this random diffusive motion (images are darkened where motion is larger)
- Can quantify diffusivity by taking an image without diffusion weighting and taking a separate image with diffusion weighting, then dividing the two:
  \[
  \text{Image(no DWI)} \div \text{Image(with DW)} = e^{b \cdot D}
  \]
  where \( b \) is a known factor and \( D \) is a coefficient that measures (apparent) diffusivity
  - Can thus compute images of ADC from multiple (2+) scans
DWI in Stroke

• ADC decreases in infarcted brain tissue within minutes of the vessel blockage
  - Causes thought to include cell swelling shutting down water pores that allow easy H$_2$O exchange between intra- and extra-cellular spaces
  - Cell swelling also causes reduction in extra-cellular space which has a higher ADC than intra-cellular space

• Stroke damage doesn’t show up on T1- or T2-weighted images for 2-3 days post-blockage

• DWI is now commonly used to assess region of damage in stroke emergencies
  - And whether to administer TPA (clot dissolving agent with many bad side-effects)
MRI and Acute Stroke

4 hours

T2-wt.

DWI

From Mike Mosely (Stanford Radiology)
Diffusion Tensor Imaging

• Diffusive movement of water in brain is not necessarily the same in all directions — not isotropic
• In WM, diffusion transverse to axonal fiber orientation is much slower (3-5 times) than diffusion along fibers
  ▪ This anisotropic diffusion is described mathematically by a tensor \(= 3 \times 3\) symmetric matrix \(= 3\) perpendicular directions with 3 separate diffusion coefficients \(D\) along each one
• Diffusion weighted MR images can be designed to give more weight to diffusion in some directions than in others
• By acquiring a collection (7+) of images with different directional encodings, can compute the diffusion tensor in each voxel \(\Rightarrow\) WM fiber orientation
DTI Results

Unweighted (baseline b=0) image

Fractional Anisotropy (FA): Measures how much ADC depends on direction

FA Color-coded for fiber directionality:
- x = Red
- y = Green
- z = Blue
Other Types of MR Images

- **MR Angiography** = designed to enhance arterial blood (moving H$_2$O) — sometimes with Gd contrast
  - Much more commonly used than MRV
  - Useful in diagnosing blood supply problems

- **Magnetization Transfer** = designed to indirectly image H in proteins (not normally visible in MRI) via their magnetic effects on magnetized H in water
  - Useful in diagnosing MS and ALS abnormalities in WM
    - Especially when used with Gd contrast agent
  - Possibly useful in detecting Alzheimer’s plaques

- **Perfusion weighted images** = designed to image blood flow into capillaries only

- **MRI methodology R&D continues to advance ****
Functional Brain MRI - 1

• 1991: Discovery that oxygenation fraction of hemoglobin in blood changes \textit{locally} (on the scale of 1-2 mm) about 2 seconds after increased neural activity in the region

• Recall T2*-weighted imaging: sensitive to deoxy-hemoglobin level in veins
  - Arterial blood is normally nearly 100% oxygenated
  - Resting state venous blood is about 50% oxygenated
  - Neural activation \textit{increases} oxygenation state of venous blood (for various complicated reasons)
  - Since deoxy-hemoglobin makes T2*-weighted image darker, neural activation will make image brighter (because have less deoxy-hemoglobin) \textit{locally}
Functional Brain MRI - 2

- FMRI methodology:
  - Scan brain with T2*-weighted sequence every 2-3 seconds
  - Subject performs task in an on/off fashion, as cued by some sort of stimulus (visual, auditory, tactile, ...)
  - Usually gather about 1000 brain volumes at low spatial resolution
  - Images look bad *in space*, but are designed to provide useful information through *time*
  - Analyze data time series to look for up-and-down signals that match the stimulus time series

A single fast (100 ms) 2D image
One fast image and a 3×3 grid of voxel time series
Brain Activation Map

Time series analysis results overlaid on T1-weighted volume
Applications of FMRI

- Clinical (in individuals):
  - Pre-surgical mapping of eloquent cortex to help the surgeon avoid resecting viable tissue
  - Can combine with DTI to help surgeon avoid important white matter bundles (e.g., cortico-spinal tract)
  - Measure hemispheric lateralization of language prior to temporal lobe surgery for drug-resistant epilepsy

- Neuroscience (in groups of subjects):
  - Segregation of brain into separate functional units
    - What are the separate functions of the brain pieces-parts?
  - Discover differences in activity between patients and normals (e.g., in schizophrenia)
  - Map functional (i.e., temporal) connectivity
    - vs. anatomical connectivity (e.g., via DTI)
Other Brain Mapping Tools

• Downsides to FMRI:
  ▪ Poor time resolution since we are looking at signal from blood, not directly from neurons
  ▪ Physiological connection between neural activity and hemodynamic signal measured by MRI is complex and poorly understood

• EEG and MEG: signal is from neural electrical activity, so time resolution is great
  ▪ But spatial resolution is bad (and confusing)

• FDG PET: signal is closer to neural metabolism
  ▪ But must give subject radioactive substance — limits repeat studies, etc.
  ▪ Time resolution much worse than FMRI, and space resolution somewhat worse

• Through-the-skull IR: new-ish; hits brain surface region
Digital Brain Atlases

- Attempts to provide statistical localization on MRI scans of brain regions determined by post-mortem histology
  - Statistical because each person’s brain is different in details
  - Major effort by Zilles’ group in Jülich to categorize 10 brains, region by region, using histology
- Also available: Talairach & Tournoux atlas regional boundaries (derived from 1 brain in the 1980s, plus some literature search to clear up ambiguities in the published book) — from Fox’s group at UT San Antonio
- These are the two freely available human brain atlas databases now distributed
  - Also are some privately held databases (corporate & academic)
Cyto-architectonic Atlas

Focus point (LPI)=
40 mm [R], -35 mm [P], 42 mm [S] {T-T Atlas}
40 mm [R], -38 mm [P], 44 mm [S] {MNI Brain}
42 mm [R], -38 mm [P], 51 mm [S] {MNI Anat.}

Atlas TT_Daemon: Talairach-Tournoux Atlas
Focus point: Right Inferior Parietal Lobule
-AND- Right Brodmann area 40
Within 5 mm: Right Supramarginal Gyrus
Within 6 mm: Right Postcentral Gyrus
Within 7 mm: Right Brodmann area 2

Focus point: Area 2
Within 2 mm: hIP2
Within 5 mm: Area 3b
Within 7 mm: Area 3a
-AND- Area 4p

Atlas CA_N27_ML: Macro Labels (N27)
Focus point: Right Inferior Parietal Lobule
Within 1 mm: Right Postcentral Gyrus
-AND- Right SupraMarginal Gyrus

Atlas CA_N27_PM: Cytoarch. Probabilistic Maps (N27)
Focus point: hIP2  (p = 0.20)
-AND- Area 2  (p = 0.80)

Atlas CA_N27_LR: Left/Right (N27)
Focus point: Right Brain

“Where Am I” Navigation
Statistical Neuroanatomy

• Attempts to summarize and describe populations (and differences between populations) from MRI scans
• Example: Voxel Based Morphometry (VBM)
  ▪ Try to characterize “gray matter density” as a function of location in brain, then map differences between patients and normals, …
  ▪ Can also be applied to other measures (e.g., FA)
• Example: Cortical thickness maps
  ▪ Extract gray matter cortical ribbon from images and measure thickness at each location
  ▪ Map vs age, disease condition, …
• Biggest practical issue: Spatial Alignment
Yellow overlay shows regions with gray matter volume reduction in WS (13 WS patients vs 11 normals)
From Karen Berman’s group in NIMH
The End (almost)

• MRI is:
  ▪ Widely available (9000+ scanners in USA)
  ▪ Harmless to subject *if* proper safety precautions are used
  ▪ Very flexible: can make image intensity *(contrast)* sensitive to various sub-voxel structures
  ▪ Still advancing in technology and applications
  ▪ Still in a growth phase for brain research

• Limitations on spatial resolution and contrast types are frustrating
  ▪ e.g., little chemical information is available with even the most sophisticated scanning methods
    • Novel contrast agents making some inroads in this direction
Unfair Pop Quiz

- What are these images of?

- Dolphin brain