# fMRI: Workhorse of Cognitive Neuroscience

# Upcoming

- Today: Lecture
  - Finishing up PET, then focusing on fMRI
  - Readings:
    - Poldrack & Farah, 2015 and Dimsdale-Zucker et al., 2018 (Section 1 only)
- Tuesday, Jan. 21st:
  - Readings:
    - Passingham: Chapter 2
    - Article: How AI helps us understand human vision

# PET (**P**ositron **E**mission **T**omography)

- Early PET measured glucose metabolism
- Now radioactive tracers mostly tag neurotransmitters
- Increasingly used in clinical studies
- Cool but expensive and invasive and very slow
- Low spatial resolution (1 cm) but can measure molecular processes!

# The tracers used are literally under your feet!

https://www.youtube.com/watch?v=eMTZvA8iFgI

# Two kinds of mechanistic insight

**Mechanistic insight**: Insight into brain mechanisms

| **Strength of Causal Evidence** | **Level of Mechanism** | | | |
|---|---|---|---|---|
| | Molecules | Cells | Populations | Networks |
| Purely observational (no causality) | **Correlations of PET imaging with psychological traits** | | | |
| Manipulate psychological processes & observe brain | **Task modulation studies using PET w/ neurotransmitter ligands** | Intracerebral recording in surgical patients | Task activation studies (EEG/MEG) | Task-based functional connectivity (EEG/MEG) |
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| | | | | |



The first characteristic is the level of mechanism captured by the method: columns. The second characteristic is the ability of each method to elucidate the mechanistic role of brain molecule, cell, region or network in a mental function of interest.

# Summary

- Change the brain, measure behaviour
  - Lesion studies
  - Neuromodulation (Transcranial stimulation)
  - Can infer **causality**!
- Change behaviour, measure the brain
  - EEG/MEG: Electrical activity at the scalp tells you when but not where
  - ECoG/s-EEG: Tells you when and where but invasive!
  - ALL: Allow measurement of oscillations as *mechanistic* signals of communication
  - PET allows you to measure neurochemical activity
- **We can use multiple methods to triangulate on a process of interest!**

A.We first looked at methods where you change the brain and measure behavior.
1.Lesion studies tell us what cognitive processes are disrupted when there is damage to a particular brain region, which gives us insight into what those regions do. We can infer causality but a limitation is that lesions are messy and we don't know if it's the region or the network disruption that's causing the damage. Luckily we can now do lesion network mapping to get a more sophisticated view.
2.Transcranial stimulation allows us to ramp brain activity up and down to infer causality non-invasively but it's a bit crude with regard to location.
3. With both approaches - we can conclude a region or network is necessary for a cognitive process or behaiour.
B. We also looked at methods for measuring brain activity while manipulating cognitive processes or behaviour.
1.EEG/MEG – though we can make models of where the activity is coming from there is always more than one model that will explain what's going on at the scalp.
2. Implanted electrodes are great but you can't control where they are put and epileptic brains are different from healthy brains.
4. PET is invasive and slow.

Since all of these methods have their strengths and weaknesses, it can be useful to use them to triangulate on a process of interest.

In the next class, we're going to talk about fMRI, which Poldrack & Farrah call the workhorse of cognitive neuroscience.

# Learning objectives

After this lecture, you should be able to:

- Describe in general terms what functional magnetic resonance imaging (fMRI) measures
- Explain the difference between **encoding** and **decoding** approaches to analyzing fMRI data
- Define structural and functional connectivity and outline some ways they are measured

# Brain imaging: Inferring causation

- Experimental manipulation causes brain activation
- Brain activation causes psychological process

But first, before we get into the how and the what of fMRI, let's start by hammering a point that Poldrack and Farah make about causality that applies to all fMRI -- and EEG and MEG and PET --- studies. So according to the paper by Poldrack and Farah, can we say that our experimental manipulation causes the brain activation patterns we measure? [click] Yes we can make that kind of inference about causality. Now, can we say that the brain activation causes the psychological process we're measuring? [click] No. This is a correlation. And correlation is not causation. Ok, now that's out of the way let's look at what fMRI can do.

# Two kinds of mechanistic insight: The table so far

**Mechanistic insight**: Insight into brain mechanisms

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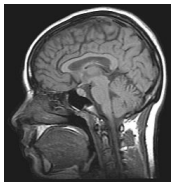
## What if we could really read the brain?

- https://www.youtube.com/watch?v=APgMXDjLcT4



START AT 3:19? Ok – fMRI. Can do lots of very nifty things. Note that in the second part of the talk he is talking about what the Poldrack paper refers to as representational analyses, and nicely illustrates some of the things the paper talks about. But let's make sure we're clear on what we're actually measuring. Questions?

# Looking at brain **structure**: MRI



- **Magnetic Resonance Imaging**
- Protons in nuclei of hydrogen atoms in water naturally "vibrate" (*resonate*) when direction of *magnetic* field is suddenly changed
- Different tissues alter the resonance to produce images of white and gray matter, and cerebrospinal fluid
- Able to produce very good spatial resolution *anatomical* or *structural* images

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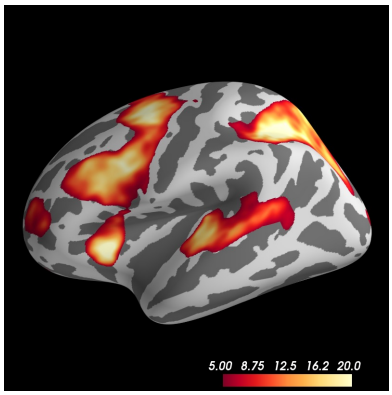
# **Function**: Putting the *f* in *fMRI*

- *Functional* Magnetic Resonance Imaging
- Index of cognition in action
- Measures differences in activity between groups or experimental conditions
- Does **not** directly measure neuronal activity

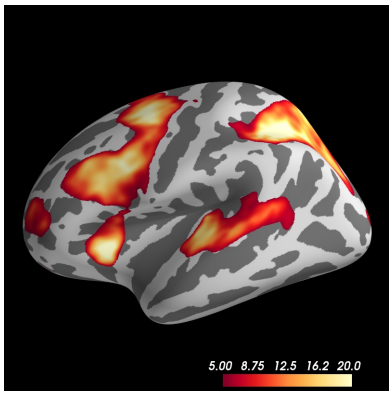


## fMRI: How it works

- When a part of the brain is active, it requires more oxygen
- More oxygenated blood is delivered
- This affects the blood's magnetic properties
- Which affects the brain's magnetic signal
- Which is measured by fMRI:
  - BOLD: Magnetic properties associated with changes in ratio of oxygenated: deoxygenated blood

# The Blood Oxygen Level Dependent (BOLD) response

- Dependent variable of an fMRI study
  - changes in ratio of oxygenated: deoxygenated blood
- Not a direct measure of your neurons firing
- Much signal processing is done on fMRI signal
- Then statistics produce blobs
- What you are looking at is a statistical map!



# Question:

If fMRI doesn't directly measure neuronal activity, then what does it measure?

# Strengths and limitations of fMRI

**Strengths**

- Good spatial precision
- Non-invasive

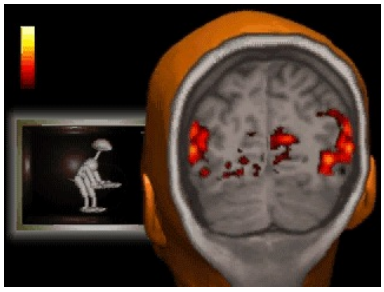
**Weaknesses**

- Expensive
- Poor temporal precision
- Indirect measure of brain activity
- Correlational relationship between activation and cognition

# fMRI analysis: Encoding & decoding

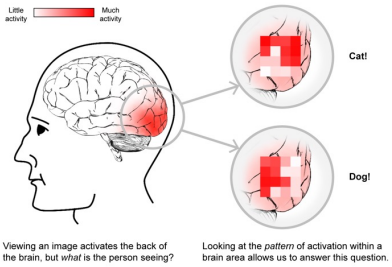
**Encoding:** *Standard*

"Brain Mapping": Use a stimulus or experimental task and measure activity that is evoked.



**Decoding:** *Representational*

Look at brain activity to predict what the stimulus or cognitive process producing it is



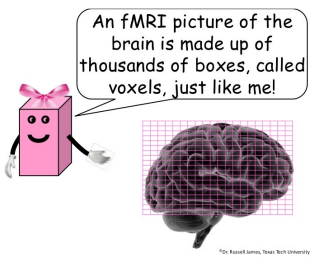


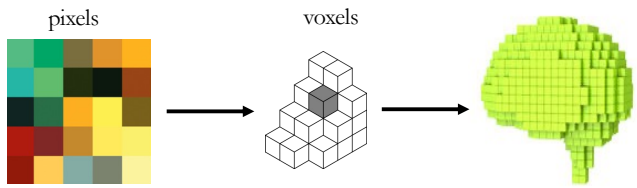

I'm going to tell you about two approaches to fMRI analysis, described in the Poldrack and Farah paper. These are not opposing approaches but are often used to together in a complementary way. In the **encoding approach**, or what Poldrack and Farah call standard analysis. you use a stimulus or experimental task to measure the activity that is evoked, or results from the manipulation. Specifically, you give a participant a stimulus or experimental task in the scanner and look for activity where there is more activation in one condition than another. The result is brain mapping – we can see brain regions that "light up" or are more active for one type of stimulus or cognitive process than another. As the Passingham text points out in Chapter 1, it's a contrast or comparison. In this example they showed people visual gratings and that odd creature doing something with a tool and what we see lighting up is regions that activate preferentially to visual gratings vs. living things doing purposeful action. We're looking at the brain from behind. A "coronal" view. Blobs = more vs less activation (purposeful tool manipulation vs. striped gratings, for example). More activity laterally -- on the outside of the occipital cortex for purposeful action and more activity medially, in the middle, for gratings. So when we see the regions more active for the creature, we can say this is the part of the brain that **encodes** animate action more than low level vision. **Encodes** – the stimulus is there and

we see where the brain responds to that stimulus. So,  the standard approach shows us what regions prefer one experimental condition from another, and we infer that that those regions are involved in the cognitive process our experiment has manipulated.
[click] With a **decoding** or **representationa**l approaches we look at patterns of brain activity to predict or decode what stimulus or cognitive process is producing itIn this case, we can zoom in to  look a little closer at the pattern of activity within a region where we already know the general function.  We can then ask how this part of the brain represents content. So we know what regions of the brain are sensitve to animate relative to inanimate objects.  But now we can go a step further and look at the *patterns* of BOLD activity in those regions of  the brain to see how it represents individual animals.  Beyond knowing this region is important for encoding animate objects, this approach can actually allow us read out  or *decode* which kind of animal they're looking at from the brain activity itself. Here we can read out the pattern across the visual cortex, like morse code, and say that not only are they looking at something that's alive,  actually the person is looking at a cat or a dog.  In this way can not only read mental content from brain activity, but we can can tell what they are looking at with much more precision.
So, in sum,with the encoding or standard approach we use an experiment to manipulate what the brain has to do  and then see what parts of the brain light up.  With a decoding or representational approach we treat the fMRI signal as code to read out and tell us what information the brain is represeting.  As in the video you watched last class describing the study of reading dream imagery from brain activity.  But to understand these methods better --- and to understand the descriptions of them in the Poldrack and Farah paper, there is a bit of key information.  You first have to understand what a "voxel" is.

# What is a voxel? Why do we care?

- MRI and fMRI images are composed of units called **voxels**
- A **voxel** is a "volumetric pixel"



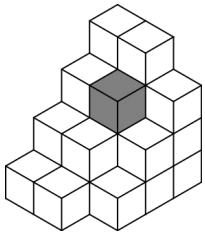



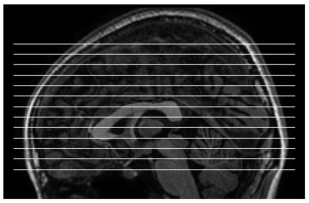



You'll be hearing a lot about voxels from here on in. MRI and fMRI are composed of these units we call voxels. What are they? What is their role in analysis of fMRI data? For measurement purposes we divide the brain into grids of cubes that have no relationship to anatomical divisions. The word voxel is just volumetric plus pixel. It's a 3D pisxel Think of a digital photograph. It's a 2d image that captures patterns of light to represent objects in the world. So just as a photo is a 2D image of light, think of an MRI image as a 3d photograph of magnetic activity (which corresponds to tissue type or blood oxygen levels). Then just as you can break up a 2D digital photo into pixels on your screen, you can break up a 3D MRIor fMRI image into voxels. A 2D digital photograph is made up of pixels, and an fMRI image is made up of 3D pixels, or voxels. Pixels don't correspond to the boundaries of the objects in your photo – they're just the unit by which we divide up a screen. Same with voxels. They don't correspond to the anatomy of the brain.

# The voxel is a unit of measurement

- BOLD data collected in “slices” and “volumes”
- These are chopped further into cubes, or voxels
- Voxels can be different sizes:
- ~150,000 in a whole brain
- fMRI: BOLD activation level for every brain voxel





# Higher resolution MRI

- Most scans are at a field strength of 3 Tesla (3T), including here at UBC
- More scanners are now imaging at 7T or beyond
- We can use higher resolution scanners to image activation in thin cortical layers (layer fMRI)

# Standard vs. representational approaches

**Standard**

- Basic functional map of the brain
- Assumption: An area codes for a stimulus if it activates more
- But maybe coding depends on *pattern* of high and low activation instead

**Representational**

- Information is in the pattern of activation across voxels
- Decode *representations* of psychological states from these patterns

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# Question

According to Poldrack & Farah, two recent approaches, MVPA and RSA are good for:

a. ”Brain mapping” – seeing what parts of the brain “light up” for a given psychological process

b. Relating the contents of the mind to the activity of the brain more directly

c. Understanding the role of neuronal action potentials in human cognition

d. Understanding how the brain responds to pictures of bears



b. Going beyond comparing 2 experimental conditions and “reading” the brain to see what a person is looking at. O

## Multi-voxel pattern analysis

- Allows for the identification of *representative patterns* for categories, visual objects, cognitions, etc. within a brain region.
- This information can be used in different ways:
  - ***Classification Analyses***

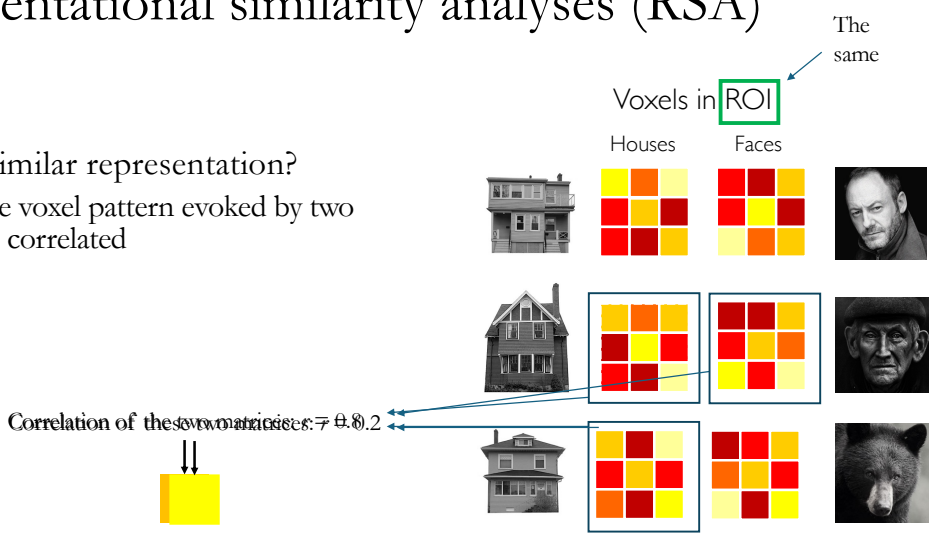
    -> Can the brain (region) dissociate this information?
    - Searchlights, ROIs, RFE
  - ***Representational Similarity Analyses***

    -> What does the brain group together?

    *OR* What shares a representational space?

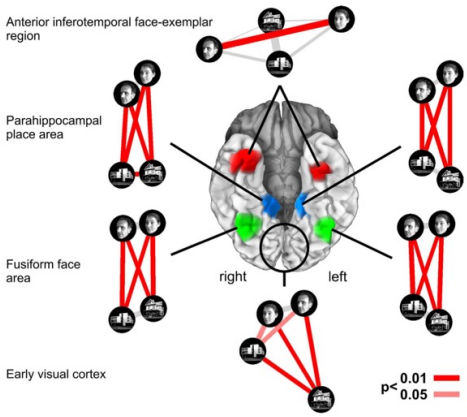
# Representational similarity analyses (RSA)

- What is a similar representation?
  - When the voxel pattern evoked by two stimuli is correlated



# Representational similarity analyses (RSA)

- A comparison of patterns of voxels at different time points in the task
- Evaluate how much the representations correlate with each other



## Summary: 3 approaches

- **Standard Encoding**: Brain mapping. Where do clusters of individual voxels light up more for animate vs inanimate objects?
- **MVPA**: Decode individual psychological states. Based on multivoxel patterns are you looking at a bird or a piece of furniture?
- **RSA**: How are patterns of brain activity evoked by different stimuli related to each other? How are mental representations instantiated in the brain? Do multivoxel patterns tell us that our brains represent a robin as more like a parrot or a chair?



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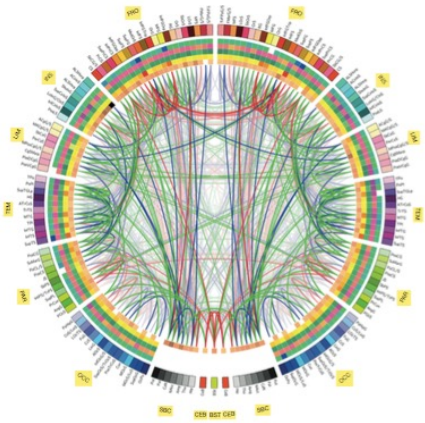
# The connectome!

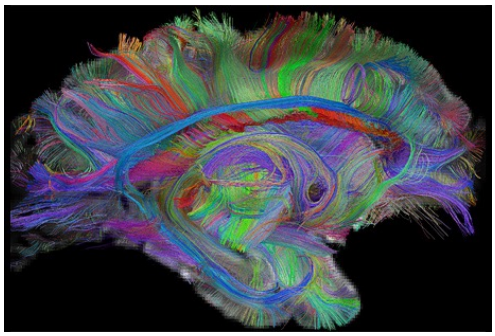
Connectogram



Connectobear

# How do we Measure Structural Connectivity?

- Anatomical/structural connectivity
  - Presence of axonal connections
  - Example: Diffusion Tensor Imaging (DTI)





One way it's been measured is in post-mortem brains. But now we have ways of imaging it in live people. Think of an image of a neuron. The axon is the long stringy part covered in a sheath that allows for better long distance conduction. We can measure these axonal sheaths using forms of imaging. DTI is a form of imaging that measures direction of diffusion of water, which flows like streams along white matter. Myelin imaging is another method, developed at UBC measures the myelin sheath. So that's structural connectivity.

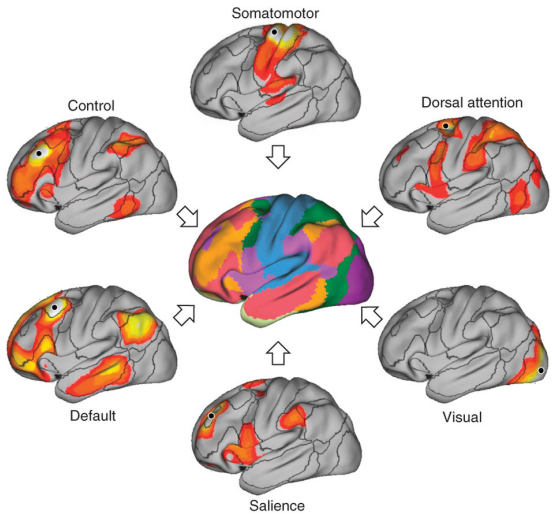
# Functional Connectivity

## Functional connectivity

- Correlation in *activation* between BOLD activity in different areas over time
- Examined while doing an experimental task or lying in the scanner "at rest." Or watching movies!

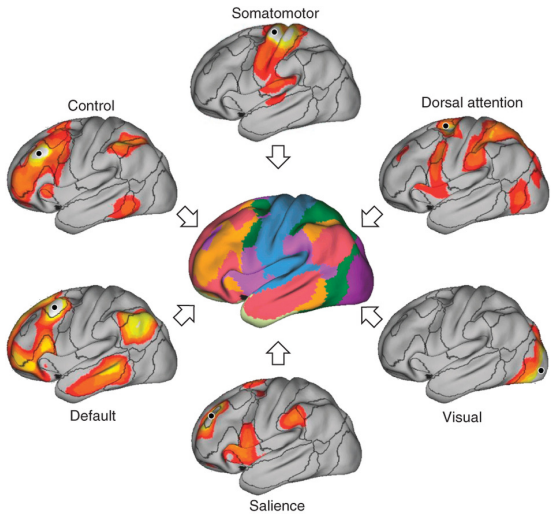
The Poldrack paper talked about discovery that the brain at rest isn't just doing nothing, and the emergence of intrinsic netwoks. Intrinsic networks are networks of regions whose activity pulses slowly up and down together when you're not doing an experimental task. It's correlated activity observed with fMRI –the BOLD signal goes up and down in unison when you're lying in the scanner and you're not focusing on completing a specific task. The Default mode network was the first to be discovered but after that a number of networks, known as intrinsic networks, have been identifiied. Just as we talked about oscillations of different speeds in neuronal activity that allow communication between regions, in fMRI, which is much slower, we can see low frequency slowwww fluctuations that are evidence of communication between regions.

# Functional Connectivity at Rest: Intrinsic Networks



***Intrinsic networks*** are all networks of brain regions whose activity are correlated with each other at rest -- that is when you're just lying in the scanner letting your mind drift [click]. They are networks that have been identified through **resting-state fMRI as described by Poldrack & Farah..** Some of these networks are illustrated on the left and the rise and fall of BOLD response are on the right. Some of these networks are seen across species and they may be altered with brain disorders, such as dementia, and in mental illness – schizophrenia, depression. Beyond rest, a more recent trend is to control for a lot of differences in what people think about by showing movies and measuring network connectivity over time while participants watch. This is referred to as naturalistic viewing, and we observe patterns of functional connectivity in these experiments just as we do when we are observing them at rest.

# *Canonical* Intrinsic Networks




- Default
- Control
- Somato-motor
- Dorsal Attention
- Visual
- Salience



Canonical networks are a specific set of intrinsic networks. ***Canonical*** intrinsic networks are specific intrinsic networks that are observed very commonly at rest and can also be observed during specific types of experimental task. You don't need to memorize all of the canonical networks but you should know what intrinsic networks are. Here's a way of remembering. A definition of "**intrinsic**" is: *originating and included wholly within an organ or part*. In this case intrinsic networks are patterns of brain activity that arise naturally and spontaneously in the brain.

CANONICAL intrinsic networks are networks that a lot of researchers have observed, and we know something about what they do, and the field agrees they are legit.

As mentioned, the activity in these networks rises and falls together at rest, but these networks are also active when doing specific types of task – which is what gives them their names. **Default** – when the mind is left to its own devices to do what it wants or engaged in self-related thoughts or memories. **Control** when you have to exert to effort override a habitual response, for example (not punch your annoying kid brother). **Somatomotor** – when you move or are touched.

**Dorsal attention** – when you deliberately direct your attention to something.
**Visual.** When you're looking at something.
**Salience** – When you attend something relevant.

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## Summary: Brain Imaging Methods

- There are many ways to get an image
- They vary in invasiveness, expense, and temporal and spatial resolution
- The technology is rapidly advancing,
- These methods along with lesion studies, nonhuman animal studies, and computational modeling, allow us to triangulate in on neural underpinnings of human cognition



So in the last two classes we have looked at some very common methods used in cognitive neuroscience. First we talked about lesion studies and transcranial stimulation, where somehow the brain is changed and you measure behaviour. Then we talked about EEG, MEG, PET and fMRI. The take home here is [click[] [click' [ click]They're all limited and imperfect, but with all of them we can make some progress in our understanding of how mind and brain work.

# Questions?

# Questions to ponder

- What are examples of good uses for human neuroimaging in diagnosis and treatment of brain injury or disorder?
- How useful do you think brain imaging can be in predicting behaviour (e.g. neuromarketing?) What is an example of a way you could use it?

## See you next class!

- MRI/fMRI



b. Going beyond comparing 2 experimental conditions and “reading” the brain to see what a person is looking at. O