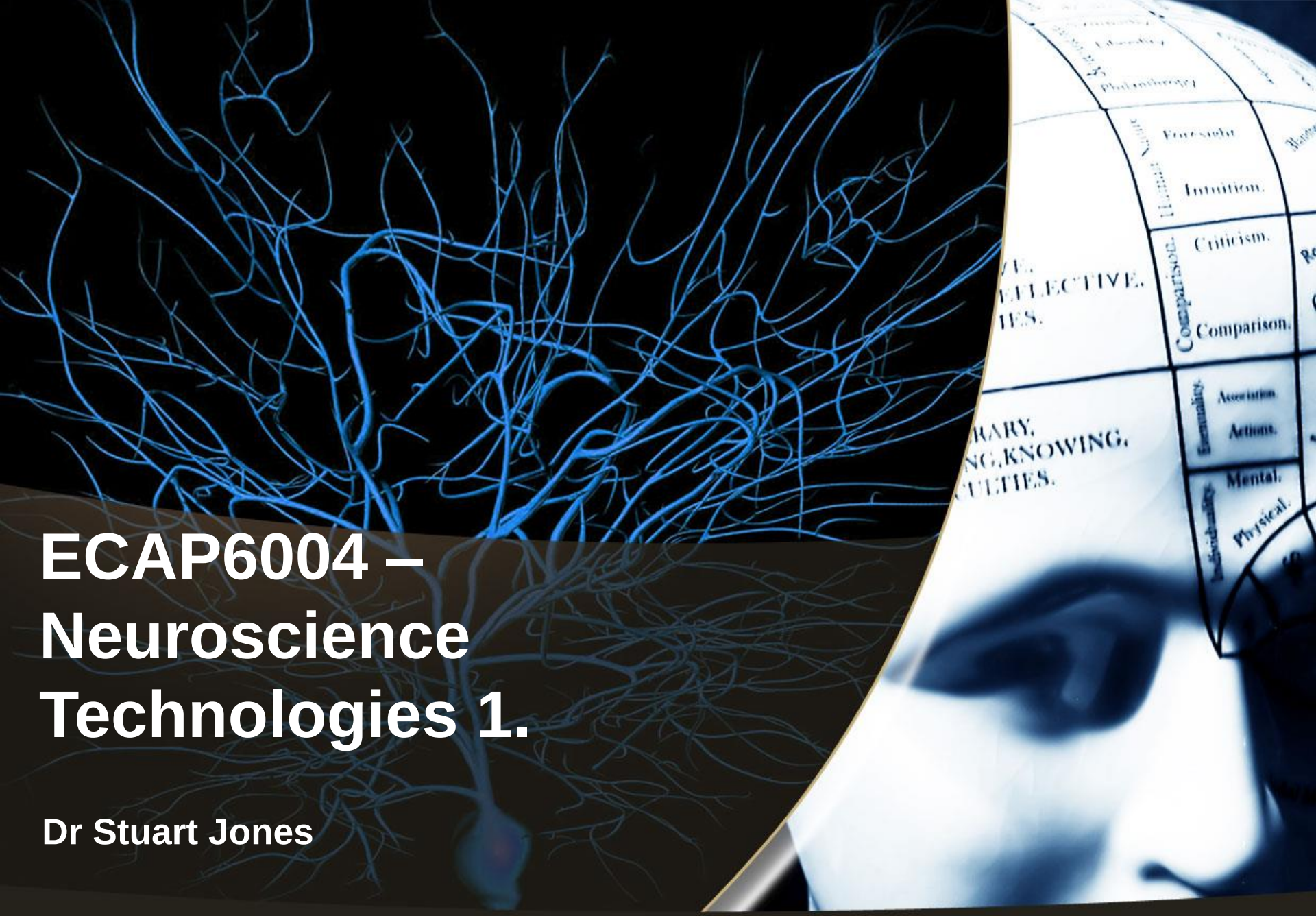

ECAP6004 – Neuroscience Technologies 1.

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Aims of the Lecture

- To discuss the methods of Neuroscience.
- To critically evaluate modern brain imaging techniques.
- To provide scope into how researchers have used tools to make conclusions.

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Last Weeks Lecture.

- Phrenology.
- How technology exposed this theory.
- Technology continually involving.
- Challenging Theories.

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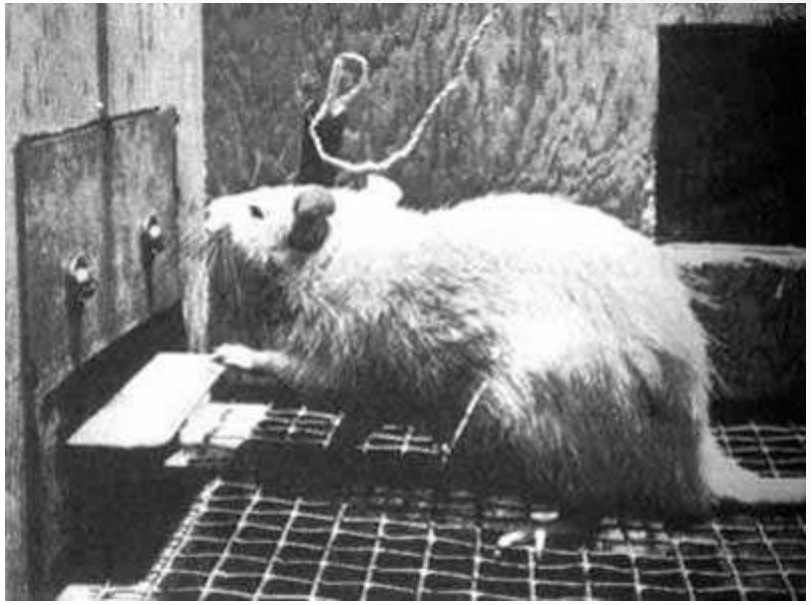
Experiment techniques used with Animals.



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Experiment techniques used with Animals.

- Highly contentious issue.
- Critical role in the medical and biological sciences.
- More experimental approach than studying people with neurological damage.
  - Neural function change?
  - Does damage to one part of Brain disturb function of others?
  - Damage can extend across many neural structures.

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Single Cell Recording.

- Widely considered as one of the most pioneering advancement in neuroscience.
- Prior to Single Cell Recording Neuroscientist described Nervous System action in BROAD regional terms.
- Single Cell Recording – Individual Elements.

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Single Cell Recording.

- Thin electrode is inserted into an animals brain (most often monkeys).
- Electrical Changes can be measured – if electrode is in vicinity of a neural membrane.
- Where is the electrode placed?
  - Intracellularly (inside the neuron).
  - Extracellularly (outside the neuron).
    - Computer algorithms are used to differentiate the contributions form individual neurons.

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Single Cell Recording.

- Used in Experimental situations involving stimulus manipulations with the aim to observe is a consistent change in the response rate of a single cell.

- Does a situation consistently report an increase in firing rate?
- How can the Researcher alter this rate?
- What makes the cell response decrease?

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Single Cell Recording.

- Limitations.
- Cause and Effect.

- Invasive.

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Single Cell Recording

- Did it solve the mysteries of Brain function as predicted?

- Aggregate behaviour of neurons might be worth more than the sum of the parts.
  - Firing patterns of groups rather than each individual.
- Led to advances in single cell recording.

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Lesions.

- Prominent in Animal Studies.
- Brain is composed of many distinct structures – distinct regions.
- Study how removing one or more of these structures might alter behaviour.
  - If a neural structure contributes to a task then performing lesions to render the structure dysfunctional should impair the performance of the task.

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Lesions.

- Illegal to perform Lesions on Human – can observe natural occurring lesions.
- Animal researchers not constrained.
- Been used extensively.

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Lesion research.

- Has helped in gaining an understanding on the role brain regions plays on actions and behaviour.

- Pharmacological Lesions?
  - Drugs producing temporary amnesia (Nissen et al, 1993).

- Limitations.

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Limitations.

- Does it only eliminate the contributions of the lesioned area?
- Will altered behaviour, alter the operation of intact structures?
- Compensatory Strategy?
- Plasticity of the Brain?

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Compensatory Strategy

- Taub and Berman (1968) – Monkey Lesion experiment.
  - 1st lesion – deprived sensory feedback to one arm.
    - Hypothesis – Monkeys wouldn't use the limb.
    - Results – Hypothesis accepted.
  - 2nd lesion – deprived sensory feedback to other arm.
    - Hypothesis – Monkeys wouldn't use either limb.
    - Results – Hypothesis rejected – Monkeys could use BOTH!.

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Ethics and Animal Research.

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Observing Humans with Neurological Disorders.

- Tumors
- Degenerative Disorders
  - Parkinson’s Disease,
  - Alzheimer's
- Infectious Disorders
  - Aids Dementia
- Trauma
- Epilepsies.

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Studies in Neuroscience

- Typically design experiments that have at least two tasks.
- Best experiments are those in which two tasks are similar but differ in requiring one hypothetical mental operations.
- E.g. Knowledge (Gazzaniga et al, 2009).
  - President Kennedy's death…. People can remember WHERE they were when they heard the news for the first.
  - Familiarity (initial experience) vs acquired memory etc.
    - How can we measure if these are two separate aspects of memory?

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How could we research this?

- Explore patients with memory disorders.

- E.g. Temporal Lobe Lesions (Temporal Lobe is associated with Familiarity) compared to a control group.
- Aspect 1 – All participants (both groups) see a series of abstract drawings and asked then to put them in the sequential order…..

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Example – Place the following objects in the order displayed

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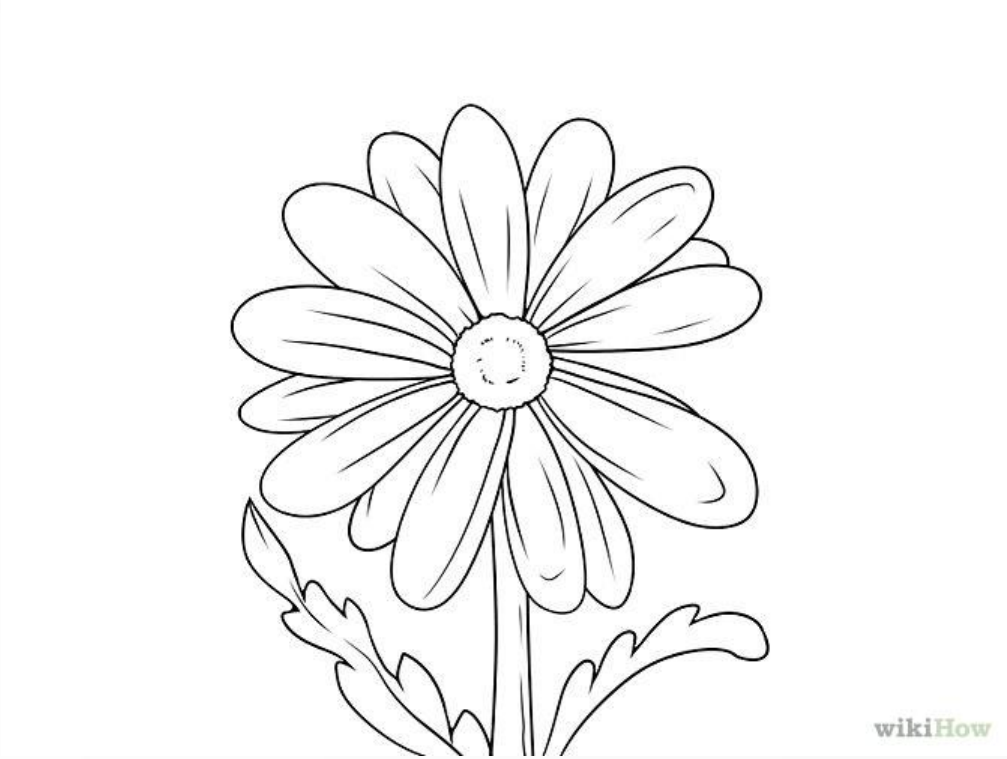

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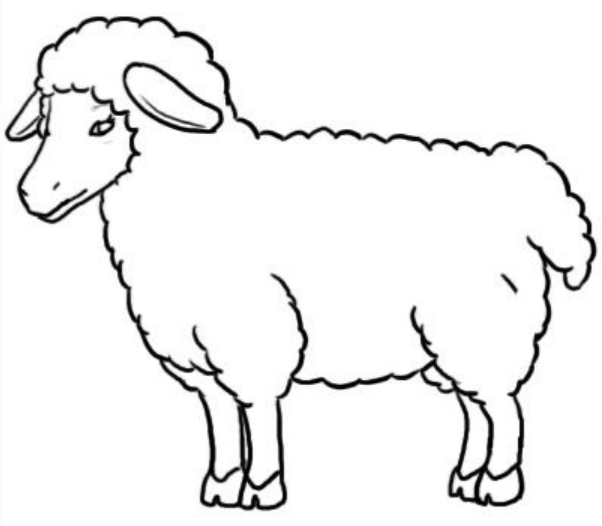

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Answer

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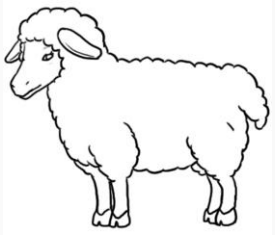
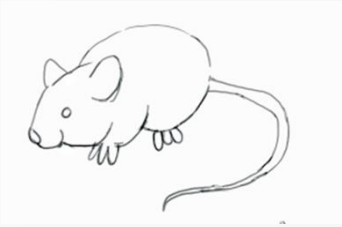
Answer

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- This measure recency memory and a test of temporal order. The ability to remember something when it is learned.

- But what about familiarity.

- Aspect 2 of the study…… All participants are now shown pairs of pictures and asked how many of each pair was seen in the first aspect.

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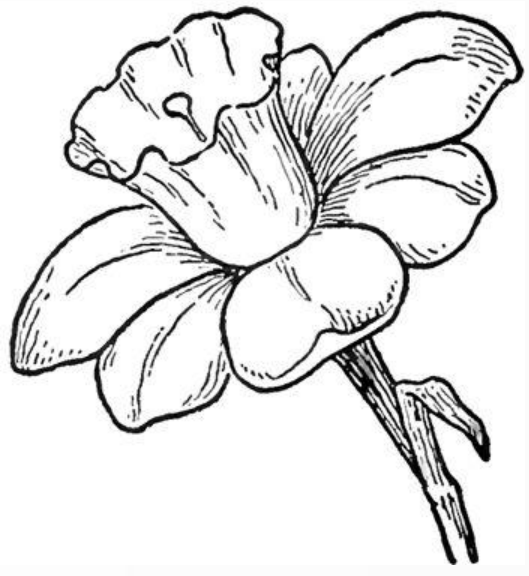

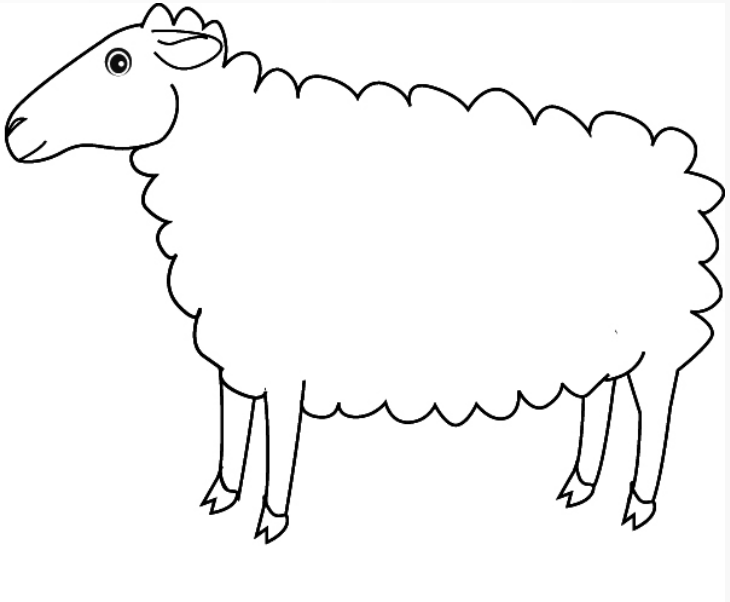

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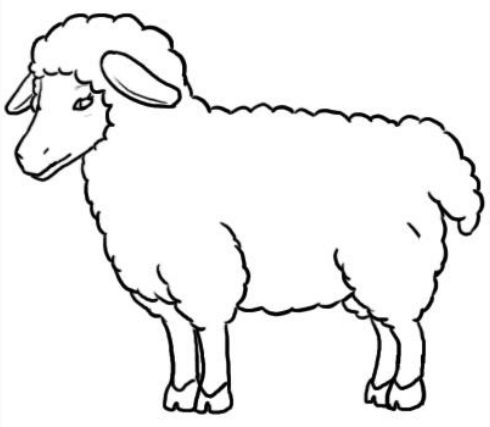

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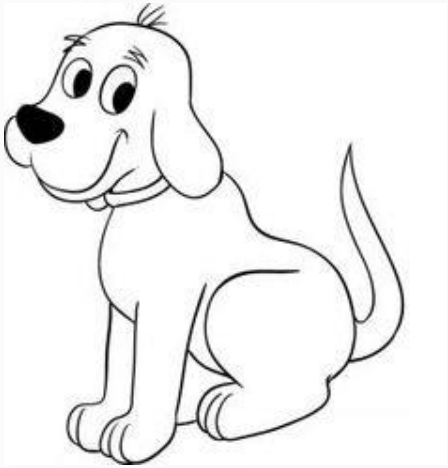

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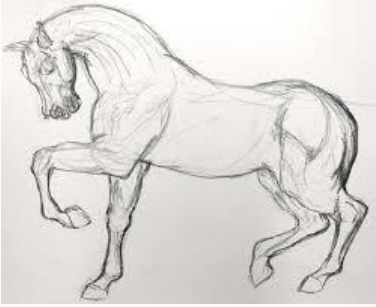

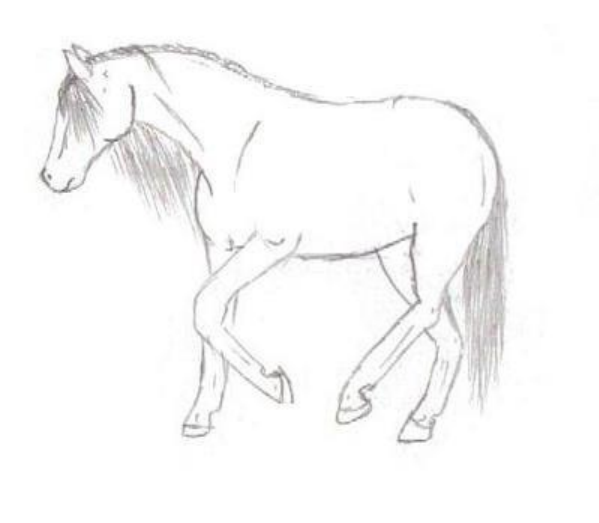

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Single Dissociation

- If your hypothesis was supported and that the group with the temporal lobe lesion performed significantly worse in task 2, but there were no significant differences in task one – then this is an example of a **SINGLE DISSOCIATION**

- **Single Dissociation =** Two groups (usually one of these being a control group) tested on two tasks but difference is only noted in one of the tasks (Gazzaniga et al, 2009).

- Many many studies in this field.
  - How do we know that participants with Broca's aphasia have intact comprehension.
    - Comparison with healthy controls.

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Issues with Single Dissociation Studies

- Two tasks assumed to be equally sensitive to differences between controls and experimental group…..
- But is that always the case?
- Think of the test you have just done – was aspect 1 too easy for us to deduct that people with temporal lobe damage would have no issues with recency memory?

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Gazzaniga et al's (2009) – Example.

- Two 6 cylinder cars – 1 = perfect condition, 2nd = only running on 5 cylinders.

- Tested on two conditions.
  - 1) – City driving.
    - 30 mph, lots of roundabouts, lots of stopping, top gear = third gear.
  - 2) – Motorway driving.
    - 70 mph, straight line, fifth gear.

- Results = No significant difference in condition 1… but car 1 outperforms car 2 in condition 2.
  - Is that because differences between the cars is ONLY when they are going 70mph.
  - Or is it because condition 1 was so restrictive that you couldn't see and difference, but if cars were going 50 mph then you would find a difference.

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Double Dissociations

- Helps to avoid these problems.
- 3 groups are compared to each other.
- In our example…..
  - Compare groups with frontal lobe damage, temporal lobe damage and control.
  - Frontal Lobe damage = hypothesised to do poorly in Aspect 1.
  - Temporal Lobe damage = hypothesised to do poorly in Aspect 2.
  - Control = No impairment on either task.

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(a) Single dissociation

Group	Tasks (% correct)	
	Recency memory	Familiarity memory
Temporal lobe damage	90	70
Controls	90	95

(b) Double dissociation

Group	Tasks (% correct)	
	Recency memory	Familiarity memory
Temporal lobe	90	70
Frontal lobe	60	95
Controls	90	95

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What other issues might there be in relation to biological psychology / neuroscience research.

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Individual Differences!!!!!

- As we have learned (and we will continue to learn) – the brain is a complex organ which can be very flexible and individualised when dealing with trauma recovery and disease.
- For example – Alzheimer's disease - symptoms, neurological deficits and impairments will vary from person to person.
- Looking at existing trauma's will never have the type of control that performing lesions with animals can have (Gazzaniga et al, 2009).
- Caramazza (1992) – supported the notion of more individual case studies in relation to cognitive neuroscience.
  - But this also has major issues.

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- As an example – single case studies of stroke patients.

- Strokes will usually cover a wide area and will affect the structure of several regions, potentially even bilaterally (across both hemispheres)

- Therefore, through observing multiple people with similar deficits we might find impairment areas of overlap and can make deductions from this.
  - But as we will see throughout the lectures, both case studies and group studies have its place in cognitive neuroscience research.

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Neuroimaging Techniques.

- Structural Imaging.
  - CT scan.
  - MRI scan.

- Functional Imaging.
  - EEG
  - MEG
  - FMRI
  - PET
    - Can also be structural
  - SPECT
    - Can also be structural.
  - TMS?

- Single Cell Recording.

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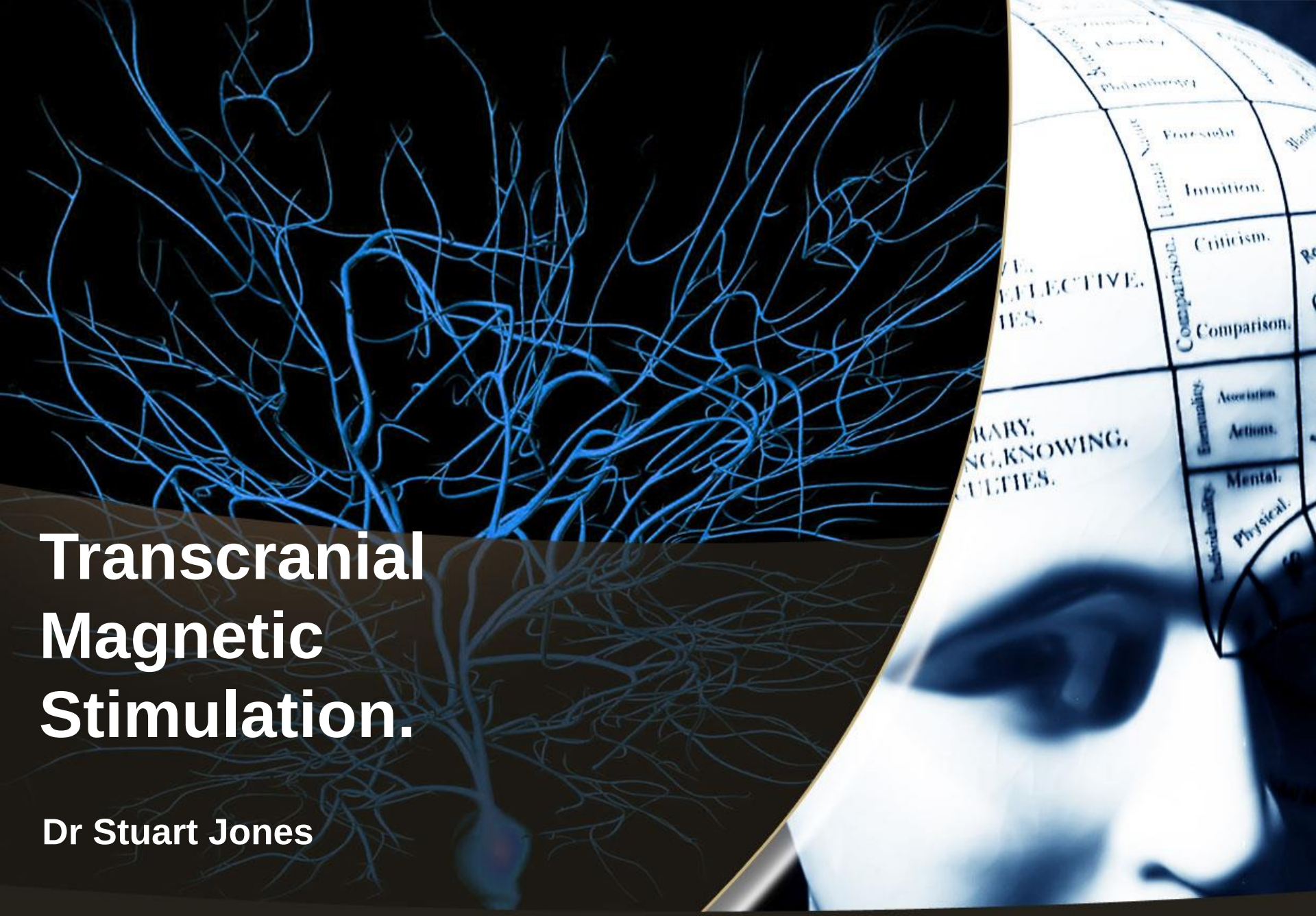

Transcranial Magnetic Stimulation.

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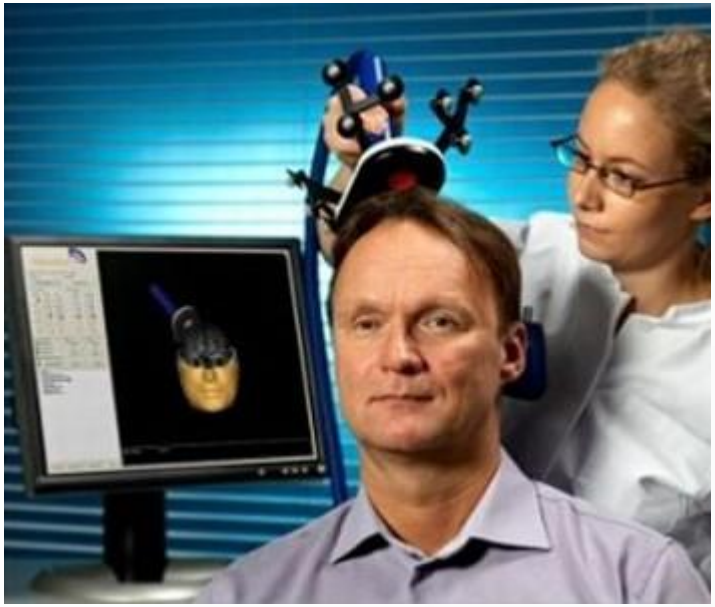
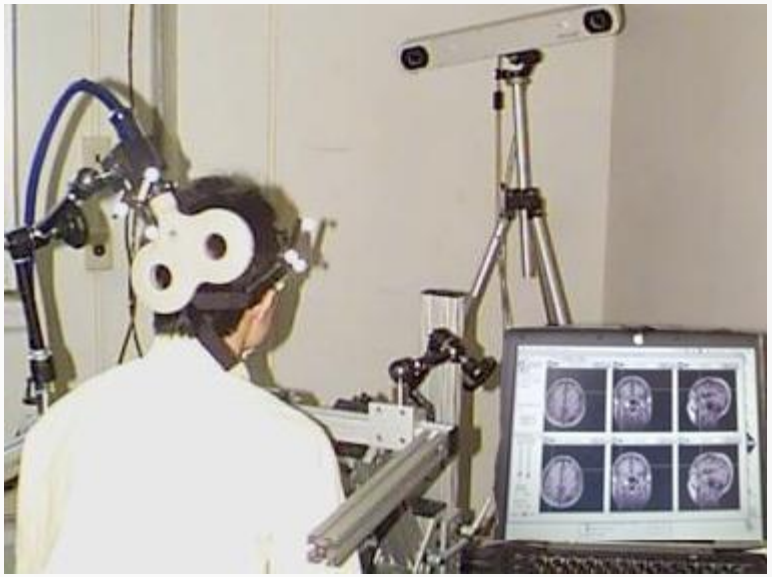
Transcranial Magnetic Stimulation (TMS).





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What is TMS?

- Nervous system can be manipulated by Magnetic Fields.
- TMS uses electromagnetic induction to induce weak electrical currents using a rapidly changing magnetic field.
- Most common = Figure of 8 shaped.

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TMS

- TMS has a very high level of spatial resolution, so it is possible to pinpoint very specific areas of cortex for stimulation.

- The coil is placed on the scalp.
- Induces an electrical field in the underlying cortex.
- Stimulate Neuronal activity and change the excitation and organisation of neuronal firing in the stimulated region (O’Shea and Walsh, 2007).

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TMS

- First demonstrated in 1985 (Baker et al).
- Widely used in studies that stimulate peripheral nerves and brain tissues.
  - Human Development.
  - Motor Control.
  - Movement Disorders.
  - Vision.
  - Autonomic Functions.
  - Language
  - Memory

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TMS Video Clips.

- http://www.youtube.com/watch?v=XJtNPqCj-iA
- http://www.youtube.com/watch?v=FMR_T0mM7Pc&feature=related
- http://www.youtube.com/watch?v=B2m_4ppcF4o

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TNS as a treatment for Depression.

- Series of Studies have highlighted that TMS can significantly reduce Depression.
- TMS more appropriate for “non-psychotic” depression (George et al, 1999).
- TMS effective for patients who have not responded to antidepressants (Fitzgerald et al, 2003).
- Limitations of TMS use as a treatment for depression?

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Limitations of TMS.

- Can mostly only do the Superficial Cortex.
- Question marks still about how focused it is? Does it stimulate other areas nearby.
- Whilst non-invasive, can be uncomfortable.
- Side effects?

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Limitations

- Currently TMS can only (we think!!) stimulate superficial areas of the cortex – outler layers.
- Remember back to previous lectures – where are the emotion / mood centres of the brain.
- Limbic system – DEEP within the temporal lobe.

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Limitations

- Remember back to previous lectures – Anti depressants are thought to influence the areas of the brain influenced by mood.

- School of thought that the Placebo effect plays a significant role on the impact of TMS and Depression.

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However

- Isn’t there a certain placebo effect involved with anti-depressants?
- Also, remember your previous lectures.
  - The neural **pathways** and connections are essential for our behaviour.
  - Not just solely the limbic system involved in depression, but CBT highlights the role of cognition (frontal lobe).
  - **Does TMS cover more than just superficial cortex?**

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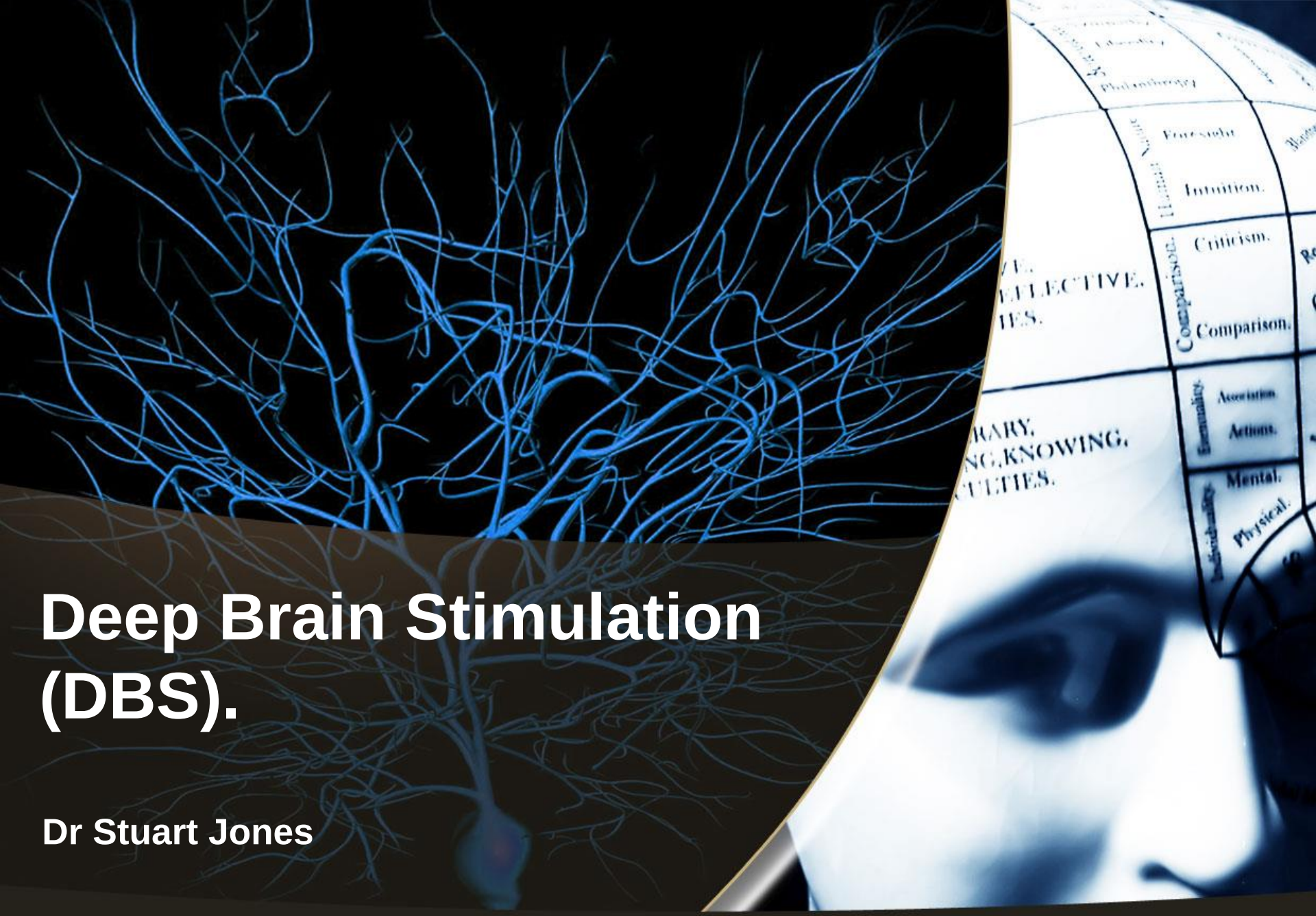

Deep Brain Stimulation (DBS).

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Deep Brain Stimulation

- Ever since Fritsch & Hitzig's (1870) first demonstrated the electrical excitability of the motor cortex, electrical stimulation of the brain has played a major role in investigations of brain function.

- Remembering back to the work of Wilder Penfield and homunculus – 1930s

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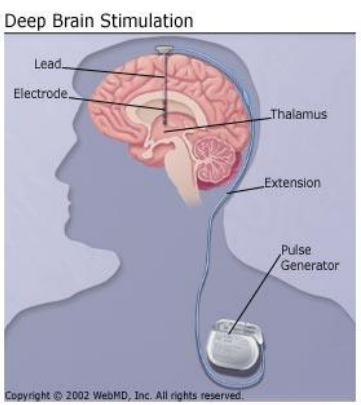
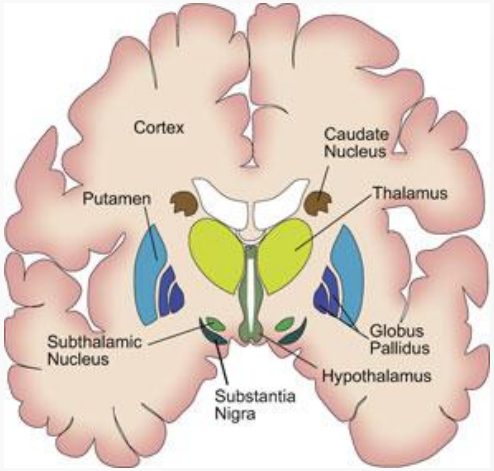
What is Deep Brain Stimulation

- Surgical procedure used to treat neurological disorders associated with issues involving deeper structures of the brain.



- Most well known use of DBS is for the movement disorder Parkinson's Disease (Perlmutter and Mink, 2006).

- Parkinson's Disease = Disorder of the Basal Ganglia.
  - Particularly - globus pallidus and subthalamic nucleas.



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- Important to Note that DBS is not a Neuroimaging Technique – but is considered a Neurosurgical procedure.

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Deep Brain Stimulation

- DBS uses a surgically implanted, battery-operated neurostimulator to deliver electrical stimulation to targeted areas in the deeper within brain.
  - Similar to a heart pacemaker.
- Before the procedure, a neurosurgeon uses magnetic resonance imaging (MRI) or computed tomography (CT) scanning to identify and locate the exact target within the brain where electrical nerve signals generate the symptoms (Perlmutter and Mink, 2006).

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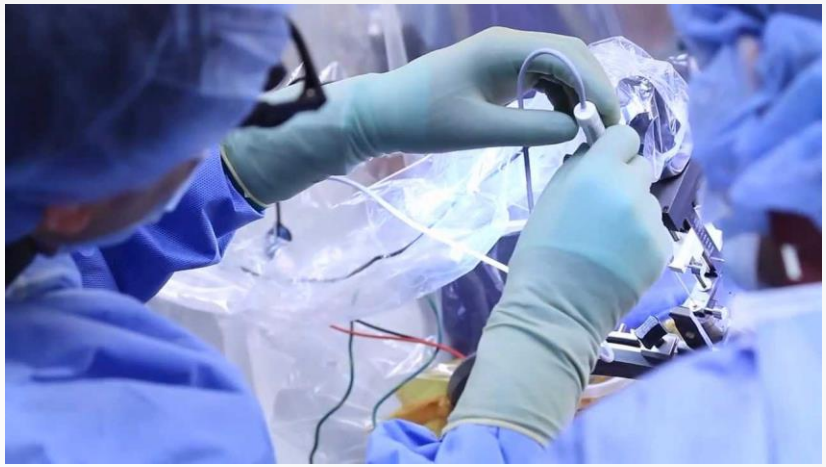
Deep Brain Stimulation

- Due to the invasive and risky nature of this procedure, DBS is only used in relation to clinical / medical procedures and usually very much as a last resort if other treatments have not work.
  - Parkinson Disease (e.g. Anderson et al 2005).
  - Chronic Pain (e.g. Young & Brechner T, 1998 – Cancer pain)
  - Tourrettes Syndrome (e.g. Diederich et al.2005)
    - Tourrettes Syndome Association – Results promising but far too early to make a clear statement.
  - Major Depression (e.g. Schlaepfer et al, 2013).
  - Epilsepsy (e.g. Boon et al, 2007).



- https://www.youtube.com/watch?v=abHuHFt_izI
- https://www.youtube.com/watch?v=q7_7bwHmG4M

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How effective is DBS…

- Much of the research is in its relative infancy and while there are promising findings, there must still be some cautions (Gazzaniga et al, 2009).

- Why DBS works is still a bit of a mystery (Gazzaniga et al, 2009).

- Hutchinson et al (2004) – HYPOTHESISES that in relation to Parkinsons disease – stimulation restores a periodic pacemaker to the cortex…
  - Movement is timed to fluctuating electrical boosts in cortical excitability
    - DBS enhances these boosts.

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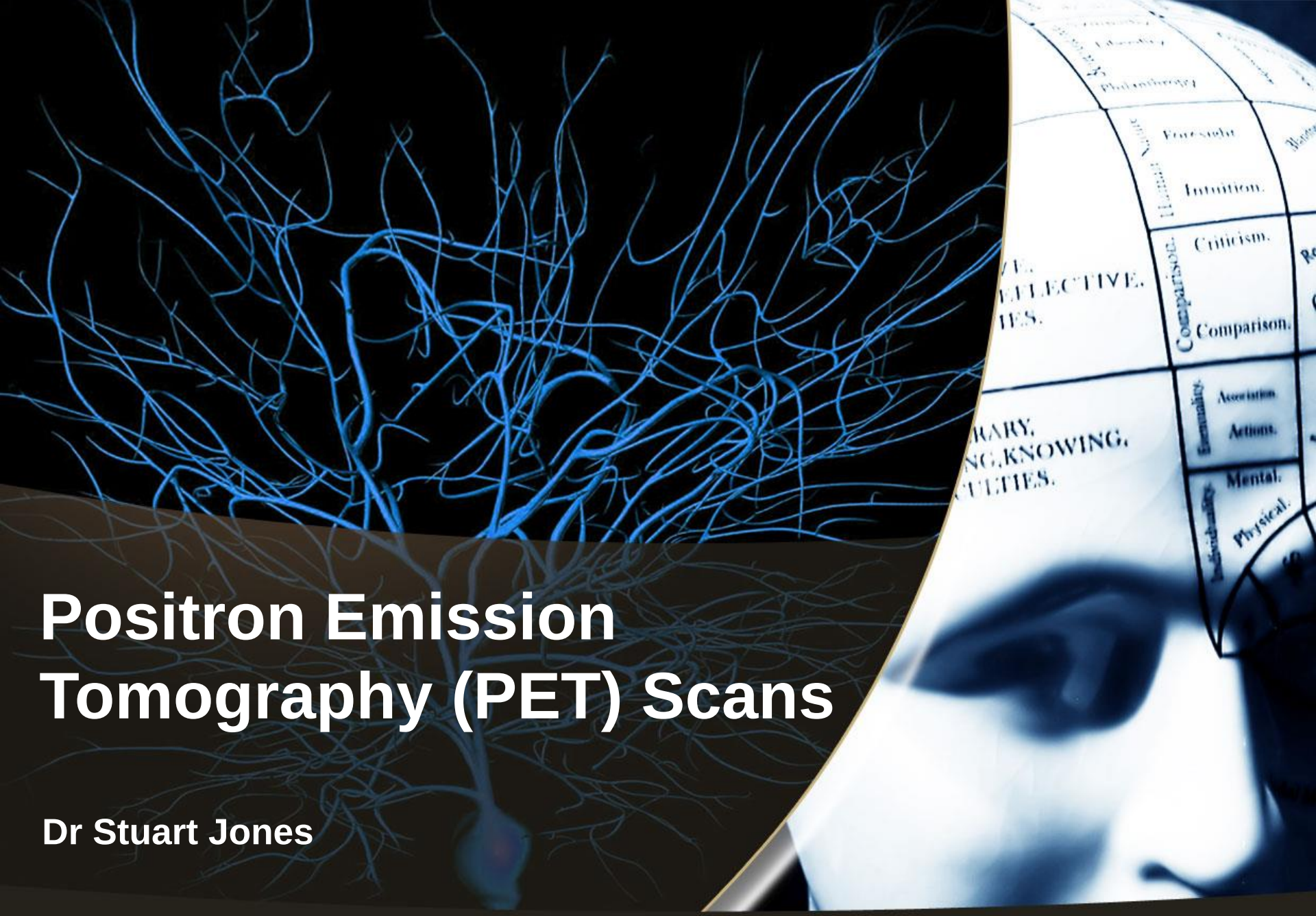

Positron Emission Tomography (PET) Scans

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You tube clips.

- Pet Scan.
- http://www.youtube.com/watch?v=QZQq7chGoO4
- http://www.youtube.com/watch?v=5hHiUleg1IA&feature=related

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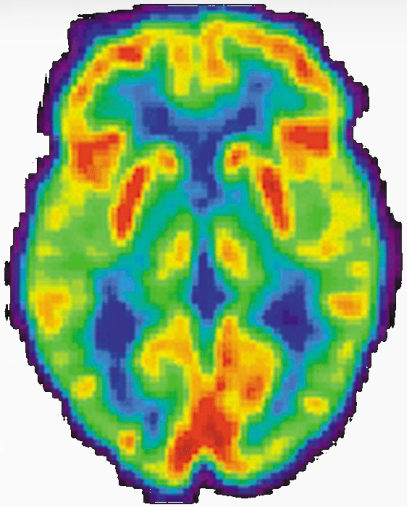
Positron Emission Tomography (PET).

- A highly specialized imaging technique that uses short-lived radioactive substances to produce **three-dimensional coloured images** of those substances functioning within the body



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PET scans

- Neurons use glucose as their principle source of energy.

- Small amount of a radioactive tracer compound can be mixed with glucose so that each molecule has small quantities of radioactivity (label).

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Pet Scans.

- A short-lived radioactive tracer is injected into the living subject.
- Pet scan is essentially highly sensitive detector of radioactivity.
- Active neurons require more glucose – therefore under these conditions will be most radioactive.

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Pet Scan.

- Measures the amount of radioactivity – send information to a computer.
- Draws a cross-sectional picture of the brain.
- Emission (sending out of) of positive charge particles called positrons.

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Pet Scan

- Positron - An elementary particle having the same mass and magnitude of charge as an electron but exhibiting a positive charge; a positive electron
  - Electron = Subatomic particle with a negatively electric charge.

- Emission – The sending out of.

- Tomography – Technique used for getting 3D images.

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Pet scan.

- Uses in Research.
- Schizophrenia (e.g. Andersen, 1988).
- Posner (1993) – Music, Maths, Speaking.

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Limitations.

- Need cyclotrons – and these are not cheap!
- Need to inject radioactive molecules.
- **Indirect measurement of neuronal activity.**
- Are activated areas essential for the task?
- Similar techniques (e.g. FMRI) appear to have better spatial and temporal resolution.

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False Positive results.

- Issue with PET scans.
- Type 1 error or False Positive
- Error of rejecting a true null hypothesis.
- Cancer diagnosis when it was really an inflammation.

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Next Weeks Lecture….

- Continue to discuss different Neuroimaging and Neurofunctional technqiues that are used to Neuroscience / Cognitive Neuroscience.

- Start to compare and contrast the differences and look at them with a critical eye.

- Please read the journals on the various techniques discussed in todays lecture. There are some excellent reviews of the methods discussed.

  – Discussion in Class Next Week.

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