Week 1 – Methods in Biological Psychology:

→ We rarely get the chance to measure the activity of neurons *directly* in humans. Therefore, we rely on techniques that measure neural activity 'indirectly' via **non-invasive methods** – meaning that we do not open the skull or interfere with brain function.

→ One class of neuroimaging methods detects **frequencies in neural signals** (i.e. the rate of change of the signal over time) (measured in Hertz). Biological signals never contain just one frequency (as in artificial signals). Complex signals can be decomposed into frequency components – each with a particular frequency (e.g. 1 Hz, 2 Hz, 3 Hz etc.) The **amplitude** describes *how much* the signal goes up and down, whilst **phase** describes *when* it goes up and down.

***Correlational* Methods that measure fast-changing electrical activity from outside the scalp are:**

→ Magnetoencephalography (MEG): measures electrical activity through the magnetic fields produced by the electrical activity of neurons.

→ Electroencephalography (EEG): measures small voltage fluctuations picked up by sensitive scalp electrodes.

→ Hemodynamics: the changes at the cell membrane leading up to the generation of AP's and neurotransmitter release at the synapse all require energy. For this, oxygenated blood is transported to 'active' brain regions, because oxygen is used there to produce the necessary energy. Changes in brain activity are closely linked to changes in oxygenated blood flow in those areas, and so we can use this to map brain functions in humans. This is useful if we can't measure neural activity directly from neural activity

- Functional near-infrared spectroscopy (fNIRS): is an optical imaging technique that uses light to study blood oxygenation through the skull.
- **Positron emission tomography (PET):** can measure the distribution of specific molecules in the blood (by radioactive labelling – therefore we don't want to use this often due to the radioactivity).
- **Functional magnetic resonance imaging (fMRI):** measures local changes in blood-oxygenation with high spatial resolution.

→ These methods rely on *correlation (as opposed to causality)* to study functions of the brain.

→ **Neuronal clustering:** Neurons with similar 'interests' (i.e. those that serve similar functions) tend to cluster together. This clustering happens at the level of small 'columns', but also in larger 'areas' which serve roughly the same functions.

→ **Brain Imaging trade-offs:** In terms of imaging methods, we have to ***trade-off*** between methods that have a high spatial resolution (e.g. fMRI which produces very vivid images) versus methods that have a high temporal (time) resolution (e.g. EEG) (fMRI has poor temporal resolution as images take a long time to produce).

→ **Causal methods: '**causal' methods rely on *direct* stimulation of the brain in order to study the effects this might have, and therefore which regions of the brain are responsible for what. The most commonly used causal method is Transcranial Magnetic Stimulation (TMS).

Transcranial Magnetic Stimulation (TMS):

→ **TMS** is a relatively 'non-invasive' technique used to create 'vertical cortical lesions'.
→ These temporary, reversible & localized lesions allow for a better understanding of specific brain regions (e.g. we observe the effects of temporarily inactivating one part of the brain).
→ TMS can be applied externally, using a coil places on the scalp that produces a rapidly changing magnetic field to induce electrical currents in the brain. These currents can depolarise neurons in a small, circumscribed area of cortex.
→ TMS-induced currents cause neurons to fire randomly, acting as 'neural noise' – thereby masking the neurons that are firing correctly. This neural noise can disrupt cognitive processing.
→ In order to create the current pulse (which is required to generate a magnetic field), a capacitator is charged and then suddenly discharged (very fast loading times (~100-200 µs) and short discharge durations (<1 ms) are required).
→ This process can be modified such that it creates a fast sequence of pulses instead of a single pulse (called repetitive TMS/rTMS).
→ Different coils have been used, but the most common one is the 'figure eight' coil. The **figure-eight coil** generates magnetic fields generating offset current loops that circulate in opposite directions, allowing for high precision in the stimulation (a more focal area of the cortex is stimulated using the figure-eight coil compared to the round coil – usually 3-4mm radius is stimulated, but up to 1mm radius is possible). The advantage of this higher precision is that the researcher knows which part of the cortex was affected.

Real lesions:

→ Studies on patients with **real lesions** have informed cognitive science for a long time as they allow us to study what patients can't do anymore. For example, *Phineas Gage*: a railroad construction worker who suffered a serious injury by an iron rod piercing his head and frontal cortex – leading to severe changes in his personality. Lesions can tell us a lot about the functions of a specific brain region.

Why don't we just rely on patients with natural lesions?

→ Removing most parts of the hippocampus, parahippocampal gyrus and amygdala led to severe anterograde amnesia in patient H.M.
→ In the same way, Lesions in Broca and Wernicke areas have been linked to impairments of speech production and language comprehension.
→ There wouldn't be enough of these patients to study all cognitive functions.
→ Lesions in single, specialized areas are rare.
→ Recovery and brain plasticity might compensate for lesions over time – patients might become quiet 'special/weird' over time.

History of TMS:

- → *Fritsch & Hitzig (1870)* were the first to electrically stimulate the cortex of animals.
- → *D'Arsonval (1896)* discovered that the magnetic stimulation of the visual cortex can elicit "**phosphenes**" (seeing light without light actually entering the eye).
- → *Magnusson & Stevens (1911)* developed the first "head coil" covering the entire head – that could stimulate the brain from the outside.
- → *Barker, Jalinous & Freestone (1985)* developed the current TMS technique, which had the advantage of not being painful.

Ways in which TMS can be used in research:

1. Injection of neural noise (single-pulse TMS):

- → Uses single-pulse TMS to disrupt cognitive processing.
- → Informs us about the time-course of processing.
- → If a single TMS pulse to a specific region of the cortex disrupts a cognitive function, this is a powerful demonstration of its *causal* involvement in this function. Testing for causality is impossible using most other neuroimaging techniques, which usually rely on *correlations*.
- → One way of doing this is to interfere with the process of interest at exactly the time window during which the region is required (e.g. to delay movements or to disrupt visual processing). Regions do not stop working completely, but this 'neural noise' interferes with normal processing.

STUDY 1: Effects of TMS on Letter Perception:

Researchers used 3 alphabetical letters as stimuli presented under difficult viewing conditions using illuminated frames and backgrounds. Magnetic stimulation was applied 2cm above the inion over the visual cortex. Effects on letter perception were investigated when varying the interval between visual stimulation and the time point of TMS stimulation. **It was found that during a critical period (40 – 120 ms), TMS stimulation affected detection performance. It is during this critical period that visual information reaches the primary visual cortex.** There was close to no interference when the interval between visual stimuli and TMS stimulation (MC stimuli) was low, as visual information was yet to reach the primary visual cortex during this time. People are back to normal when stimulation occurs following a delay greater than ~160 ms, as by this time visual information has already reached the primary visual cortex and been processed (and therefore the neural noise will not interfere with any processing).

- → When shifting the stimulation site (MC site) from left to right, perception of the letters in the contra-lateral visual field was impaired.

- → When moving the TMS stimulation from top to bottom at midline, and letters were displayed vertically, stimulation above the reference line supressed letters at the bottom of the display. This demonstrates that there is a cortical map of vision. Stimulation below the centre was not possible – as the bone was in the way.

STUDY 2: Whether A Visual Mask Can Be Masked:
Researchers investigated whether a visual mask can itself be masked using single-pulse stimulation, thereby unmasking the stimulus. Backward masks are presented after the stimulus used to supress perception of the briefly presented visual stimulus. As TMS can be used to disrupt stimuli processing, it could potentially disrupt the processing of the mask and thereby prevent that the stimulus is supressed.

Without TMS, the detection rate was 0.9. Unmasking was found between 60 and 140 ms stimulation after the mask meaning stimulation affected detection performance**. This technique can inform us about the *time-course of processing*.**

2. 'Virtual lesion' using repetitive TMS:

→ Involves using repetitive TMS (rTMS) to disrupt or enhance cognitive processing. By using repetitive TMS, it is possible to inhibit cognitive processes in a region for a longer period of time. It can then be measured whether (and for how long) a specific cognitive task is impaired (usually slowing instead of a total loss of function). This is a *correlational* approach.

3. 'Probing excitability' using single-pulse TMS:

→ Used to localize functions of the brain by testing how responsive/excitable a structure of the brain is in response to a pulse. For example, if the motor cortex is required for a cognitive task, then it should already be activated (by virtue of an increase in motor evoked potentials/MEP's) when a single-pulse TMS is delivered. Here, the measure of interest is how strongly the motor cortex reacts to the pulse itself. If the motor cortex is already excitable due to its involvement in the cognitive task, then when it is stimulated with the single TMS pulse a higher MEP response will be recorded. This higher than baseline reading will signify that the motor cortex is involved in the cognitive task. This is a *correlational* approach.

→ The excitability of the primary motor cortex can be measured by recording 'motor evoked potentials' (MEPs) using the electromyogram (EMG) (which measures the electrical activity of muscles).

STUDY 1: Is the Primary Cortex (M1) Involved in The Mental Rotation of Objects?

→ Some neuroimaging studies (e.g. Eisenegger et al., 2007) found that stimulation of the primary motor cortex (M1) during mental rotation elicited stronger MEPs (and therefore greater motor cortex excitability) compared to baseline, reading aloud and reading silently. **This suggests that M1 is more excitable during mental rotation – it might already be activated, and hence involved in this cognitive process.**

STUDY 2 (Bode et al. 2007): Does the Involvement of M1 In Mental Rotation Depend on Strategy?

→ It's been suggested that some objects can be easily imagined as rotated by hand (tools) while others can't (building). Findings state that **MEPs were equally high** for mental rotation of all different stimuli, so the strategy does *not* play a role. The study cannot state whether M1 was only more excitable because of adjacent and interconnected regions were activated.

4.' Probing information transfer' using paired-pulse TMS:

- → Uses two pulses, delivered in quick succession, to examine how strongly the first pulse influences the second. The first pulse is usually sub-threshold, and the second supra-threshold.
- → Can be used to test for transfer between two regions, but also to test for the decay of induced activity within the same brain region.
- → For example, in Schizophrenia there is evidence that the cortical silence period (CSP) (a period of suppression of tonic motor activity) that follows descending excitatory activity is reduced. Researchers can produce the first excitatory stimulus using ESP, and then measure excitability by assessing the effect of a second pulse. Compared to the control, patients with Schizophrenia will show stronger responses to the second pulse – pointing to deficits in motor inhibition (i.e. the induced 'artificial' activity does not decay as quickly as it should) (Fitzgerald et al., 2003).

TMS as treatment for depression:

- → Usually, one hemisphere is stimulated over prefrontal cortex with the idea that depression is linked to an imbalance of prefrontal activity between hemispheres.
- → Mixed evidence for its effectiveness, typically used as a last resort.