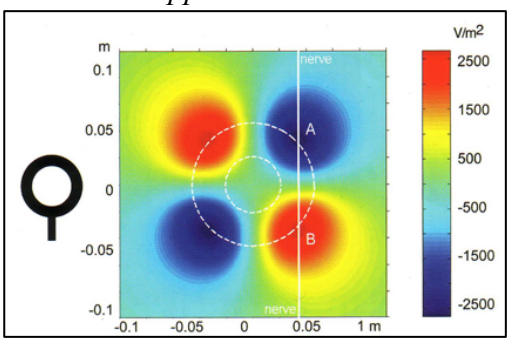
Week 1 – Transcranial Magnetic Stimulation (TMS)

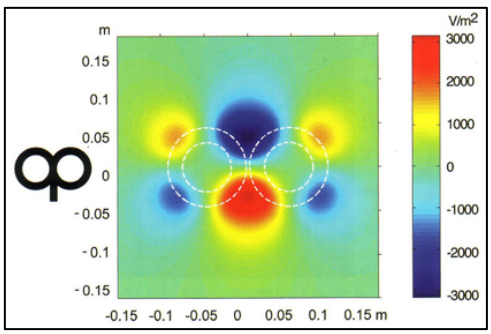
- What is TMS? An overview regarding how it works and what it does
- Using TMS for Biological Psychology research
    - The injection of "neural noise" approach using single-pulse TMS (Amassian et al., 1989; Amassian et al., 1993)
    - The "virtual lesion" approach using repetitive TMS
    - The "probing excitability" approach using single-pulse TMS (Eisenegger et al., 2007; Bode et al., 2007)
    - Probing information transfer using the "paired-pulse approach" (Fitzgerald et al., 2001; Pascual-Leone & Walsh, 2001)
- Clinical applications

- Timeline:
    - Fritsch & Hitzig (1870): first to electrically stimulate the cortex of animals
    - D'Arsonval (1896): discovered that magnetic stimulation of visual cortex can elicit 'phosphenes'
    - Magnusson & Stevens (1911): developed the first 'head coil', covering the entire head
    - Barker, Jalinous & Freestone (1985): developed the current TMS technique (brain stimulation is localised at a particular area), but used a plain circular coil

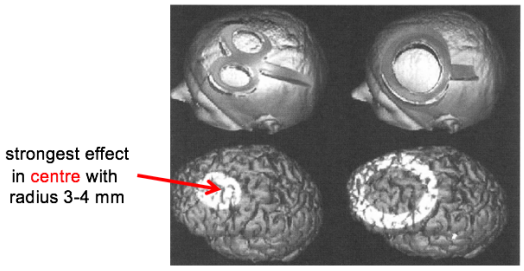
TMS: non-invasive technique to create *temporary and localised* 'lesions', allowing for better understanding of specific brain region functioning

- Can be applied externally with a coil on the scalp, which produces a rapidly changing magnetic field, inducing electrical currents in the brain
- The currents depolarise neurons in a localised area (random neuronal firing), hence increasing *neural noise* and masks neurons that are firing correctly
- This process can also be modified to use a fast sequence of pulses (*repetitive TMS* – rTMS)
- Fast loading times (~100–200μs) and short durations (<1ms) are required to create a strong enough magnetic field for stimulation
- Most commonly use the 'figure-eight' coil:
    - Two magnetic fields generated in *opposite directions*, generating offset current loops that also circulate in *opposite* directions





    - This creates a more focal area of stimulation compared to a round coil

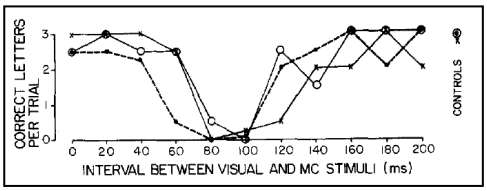


Research using TMS

Injection of 'neural noise' approach: using single-pulse TMS to disrupt cognitive processing

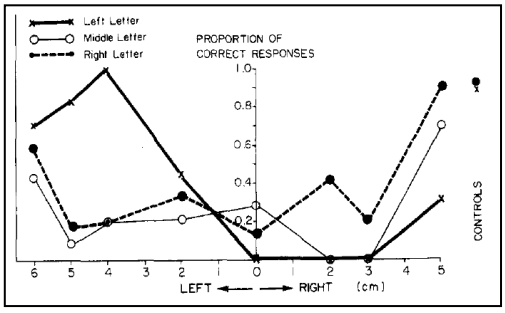
- If a pulse to a specific brain region *disrupts* cognitive function, this demonstrates a causal involvement of brain region in this particular process
- To test causality, inject 'neural noise' at a specific location at a specific point in time, impairing normal functioning (brain region does NOT stop working altogether)
- Can be used to understand the timing of cognitive functions (the time it takes for brain to receive specific information in a particular brain region and process information)
- TMS is the only method for testing causality, other neuro-imaging techniques rely on correlations

- **Amassian et al. (1989)**: investigated the effects of letter perception with varying time intervals between visual stimuli and time of stimulation
    - Participants presented with 3 alphabetical letters under difficult viewing conditions
    - Was found that a critical period (40-120ms) affected detection performance



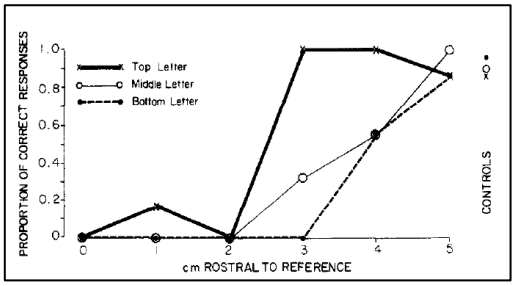
This time period represents when visual cortex processes the information. TMS causes random neural firing, therefore masks stimulus during this time.

    - When shifting the stimulation site from left to right (letters displayed horizontally), perception of letters in the contra-lateral visual field was predominantly impaired



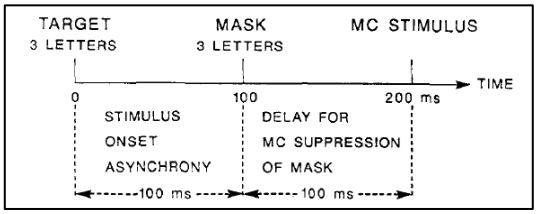
Suggests that the *left* visual cortex processes the *right* side of the visual field.

    - When moving stimulation from top to bottom at midline (letters displayed vertically), stimulation above reference line suppressed letters at the bottom

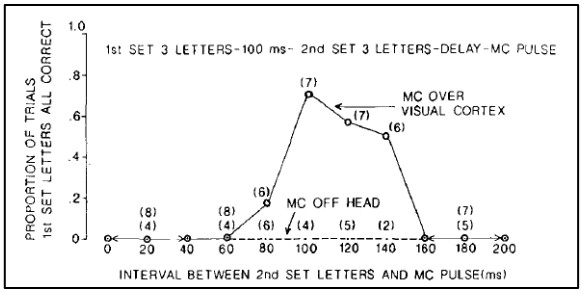


Stimulating below the centre was not possible since bone (inion) was in the way

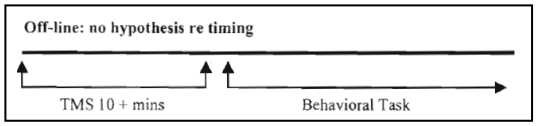
- **Amassian et al. (1993)**: investigated whether a visual mask can be masked, ie. 'un-masking' the stimulus
    - Usually, backwards 'masks' are presented after the stimulus, used to disrupt the visual processing of the target
    - Since TMS can be used to disrupt processing of stimuli, it could therefore also disrupt processing of the mask



- Without TMS, at 100ms between target and mask, detection rate of target was 0.37, but with TMS following the mask, detection rate increased to 0.9
- 'Unmasking' occurred between 60–140ms after the mask was exposed



The 'virtual lesion' approach: using repetitive TMS to interrupt/enhance cognitive processing

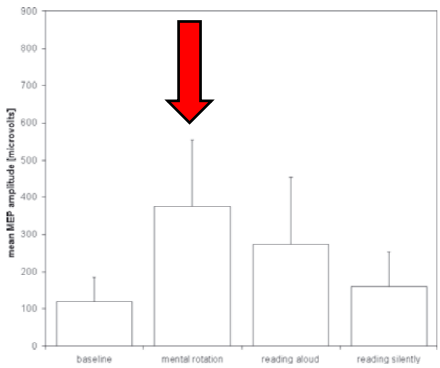


- Inhibit cognitive functions for a longer period of time using rTMS: individuals are often inaccurate/slower, NEVER total breakdown in ability
- Can then be measured whether (and for how long) specific cognitive task is impaired, compared to task performance without TMS
- There are two brain regions where we see immediate effects of TMS: motor cortex (hand twitch) and visual cortex
- To determine stimulation strength (people have various thicknesses in skulls, etc.), first determine a *motor* threshold (the weakest current that results in limb movement)

Probing excitability approach: using single-pulse TMS to test the responsiveness of brain region

- Eg. if the motor cortex is required for a cognitive task, it should already be activated when single-pulse TMS is delivered – measure how strongly the motor cortex reacts to this additional TMS pulse
  - If brain region of the brain *is* activated, additional TMS pulse would result in a larger effect (eg. large twitch) compared to if the motor cortex was *not* activated (eg. small twitch)
- The excitability of the primary motor cortex can be measured by recording the electrical activity of muscles – 'motor evoked potentials' (MEPs), using electrodes placed on skin – electromyogram (EMG),
  - In the hand the muscle is the Musculus abductor pollicis brevis (APB)
- Can measure MEPs for each stimulation, and compare average MEPs between experimental conditions

- **Eisenegger et al., (2007)**: is primary motor cortex (M1) involved in mental rotation of objects? Or involved in inner speech?
  - Stimulation of M1 during mental rotation elicited stronger MEPs compared to baseline, reading aloud, as well as reading silently – evidence M1 is more excitable during mental rotation, therefore already activated and may be involved in this cognitive process

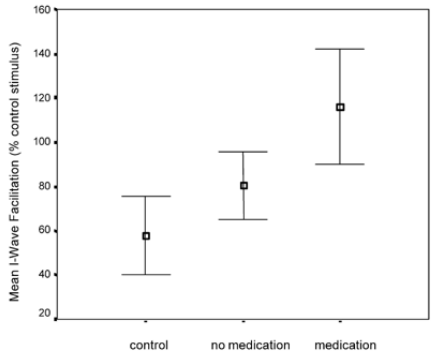


- **Bode et al., (2007)**: does M1 involvement in mental rotation depend on strategy? (eg. imagine physically rotating yourself versus imagining rotating due to external force)
  - Has been suggested that some objects may have been easier to rotate since you can imagine holding them.
  - Hypothesise that objects which cannot be held (eg. houses) should not activate M1 (therefore have lower MEPs), since you cannot physically move it with the hand

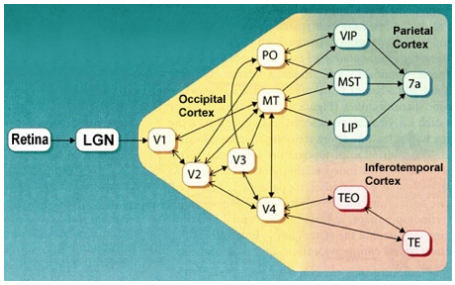
- Found that MEPs were equally high for mental rotation of all different stimuli, suggesting no role of strategy in mental rotation
- Limitation: study cannot conclude if M1 activation was due to adjacent brain regions being activated (spill-over effects)

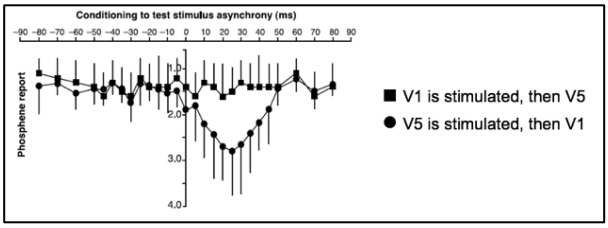
Probing information transfer using 'paired-pulse approach': two pulses delivered in brief succession to see how strongly the first pulse influences effect of the second

- **Fitzgerald et al., (2003)**: suggested that in Schizophrenia, there are abnormalities in inhibition of motor cortex – evidence that the *cortical silence* period (CSP; period of suppression of motor activity that follows excitatory activity) is reduced.
  - Those with Schizophrenia may have impaired motor activity suppression during CSP, hence resulting in a build-up of activation in motor cortex
  - First, stimulate left motor cortex with sub-threshold pulse (pulse below the strength where you can see an immediate effect), then give supra-threshold pulse (pulse that elicits a response), and measure MEPs – how strong are the MEPs elicited by the second pulse?
  - In healthy controls, the first pulse would normally be gone by the time the second pulse was elicited, so not a large difference would be expected. In Schizophrenics, since there is reduced suppression of motor activity, the second pulse should have a larger effect.
  - Results show that compared to control, schizophrenics with and without medication showed stronger responses to the second pulse – provides support for motor inhibition deficits



- **Pascual-Leone & Walsh (2001)**: testing whether feedback from secondary visual areas (eg. V5) to primary visual cortex (V1) is necessary to generate consciousness
  - The first pulse was administered at V1 (always subthreshold), resulted in no phosphene production with second pulse to V5/MT (always supra-threshold)
  - Study varied the timing between two stimulation pulses
  - When only V5 is stimulated, phosphenes are always present
  - When TMS was applied to V1 before V5, there was no effect on phosphenes for varying delays between the pulses (phosphenes always move)
  - When TMS was applied to V1 45ms *after* V5, less phosphenes were perceived, or phosphenes did not move – indicates that back-projections from V5 to V1 are required for awareness





Clinical applications of TMS

- Royal Australian & New Zealand College of Psychiatrists have endorsed TMS as a treatment option for depression, usually as a last resort
  - Usually, one hemisphere of prefrontal cortex is stimulated (thought that depression is linked to an imbalance of prefrontal cortex activity between their hemispheres)
  - If TMS pulse is relatively slow, TMS can enhance activity (eg. pulse can increase function in one hemisphere where there is less activity)
  - Mixed evidence for its effectiveness, but increasingly accepted as an option