Week 1: Transcranial Magnetic Stimulation

Neurological Basis of Psychological Function and Dysfunction via two approaches:

1) Top-down approach: starts with a description of psychological functions, then tries to explain these functions in terms of their biological substrates via a range of techniques such as TMS, EEG, fMRI, and modern molecular genetic techniques
2) Bottom-up approach: starts with a description of neurons, neural architecture, and transmitters, then links this up to explain behaviour and abnormal behaviour

Transcranial Magnetic Stimulation (TMS) – a "non-invasive" technique to create virtual cortical "lesions" (tissue damage to the brain)

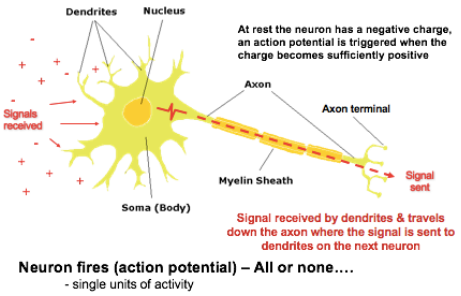
- Studies on patients with real lesions have informed cognitive science for a long time as they allow studying what patients can't do anymore
    - e.g. Phineas Gage (1823-1860), American railroad construction worker who suffered a serious injury by an iron rod piercing his head and frontal cortex → led to severe changes in his personality
- Temporary and reversible, localised lesions (at a far smaller scale) could allow for better understanding the function of specific brain regions
  ~ TMS can mimic and function like a lesion, but can be gone/reversible
    - e.g. H.M. → removed most part of his hippocampus, parahippocampal gyrus, and amygdala led to severe anterograde amnesia (cannot form new memories)
    - Lesions in *Broca* and *Wernicke* areas have been linked to impairments of speech production and language comprehension, respectively
    - Recovery and brain plasticity might compensate for lesions over time → patients might become quite "special" over time
- TMS can be applied externally, using a coil placed 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 current causes neurons to fire randomly increasing the level of neural noise, thereby masking the neurons that are firing correctly
    - 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 "phosphines" (visual sensations that "appear" as dots, but are a result of stimulating the occipital pole cortex)
    - Magnusson & Stevens (1911) developed the first "head coil" covering the entire head
    - Barker, Jalinous, & Freestone (1985) developed the current TMS technique, which had the great advantage of not being painful
- Can be modified such that it creates a fast sequence of pulses ("repetitive", or rTMS)
    - To create a magnetic field strong enough for stimulation, very fast loading times (~100-200 μs) and short durations (<1 ms) are required
    - Different coils have been used, but the common one is the 'figure-eight' coil
        - Generates a magnetic field in the opposite direction → generating offset current loops that also circulate in opposite directions
        - A more focal area of the cortex is stimulated as compared to the round coil
            - Advantage: researcher has a very clear idea what part of the cortex was affected

Different ways that TMS can be used in research:

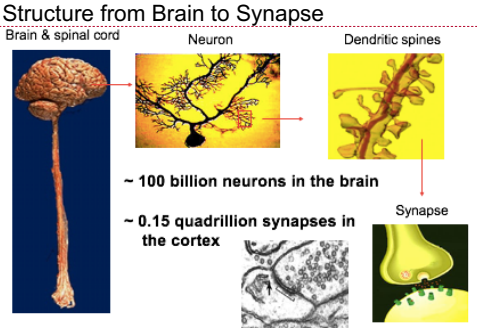
1) The injection of "*neural noise*" approach: using *single-pulse TMS* to disrupt cognitive processing

Week 9.1: Basic Introduction to Psychopharmacology

Signaling in the Brain: Neuron



Structure from Brain to Synapse



Receptors

- Neurons have a cell "membrane" that acts like a wall preventing things from entering or leaving the neuron
- The cell wall has two layers with the fatty inside of each layer sticking together like a sandwich
- Because of the fatty inside layer, fluids and other chemicals like neurotransmitters are not able to pass through
- Receptors located on the outside of the cell membrane allow the released neurotransmitters to influence the post-synaptic neuron
- Two types of receptors:
    - Ion Channels → act like a "gate" for ions
        - When a neurotransmitter binds to the receptor outside the neuron, this causes the gate to open and ions (positively and negatively charged molecules), can flow through
        - *Channels are normally "selective" and only allow one or a few types of ions to pass through when they are open* (e.g. a calcium ion channel)
    - G-Protein coupled → work through second messengers
        - When the neurotransmitter binds to the receptor it activates a "second messenger system" that can either *open a channel or cause other things to change within the cell* (e.g. DNA being transcribed and new proteins being made)

Receptor specificity

- *Receptors are very selective (lock and key)*
- Each receptor can generally only be *activated by one neurotransmitter* (or a drug that is designed to mimic that neurotransmitter)
- They also have a *very specific function/action*. When a neurotransmitter binds to the receptor this *will trigger the same event every time* (either opening a channel or triggering a second messenger event).
- Receptors are not simple "open-shut" gates. They have *complex structures and it is often a small change in their shape that will "open" a channel, or cause it to "do its thing"*

Neurotransmitters – Criteria for Defining Neurotransmitters

- Present in presynaptic terminals
- Released from presynaptic terminals after the neuron fires
- Existence of receptors on postsynaptic neurons

Comment [LY23]: Neurons communicate through neurotransmitter release at synapses

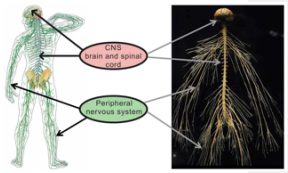
Comment [LY24]: Receptors either act as ion channels (gates) or they cause downstream effects within the neuron through a "second messenger"

The specificity of neurotransmitter effects is due to the different receptors having different functions in different parts of the neuron/brain

- Pupil dilation accompanies a switch during perceptual rivalry
- Pupil dilation can also be used as an index of cognitive decisions

- Theoretical Implications
  - *Noradrenalin and the LC likely play the same role in perceptual and cognitive decisions, as they are believed to play in behavior* (optimizing a balance between "exploitation"/ "stability" and "exploration"/ "flexibility")

Week 12.1: Acetylcholine: Attention, Memory, & Alzheimer's

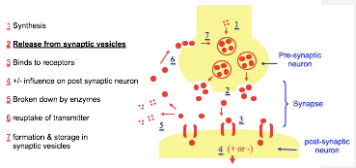


Acetylcholine (ACh)

- Central & Peripheral
  - Acetylcholine is a major neurotransmitter of the *Central Nervous System* (CNS) and *Peripheral Nervous System* (PNS)
- Synthesis
  - Acetylcholine is made from choline (derived from the breakdown of lipids) and acetate (sometimes called acetic acids)
- Receptors
  - Two types of ACh receptors
    - Ionotropic (ion channel) – stimulated by nicotine so is called Nicotinic Receptor
      - In the PNS – *muscle fibers* must be able to contract rapidly so they contain rapid, ionotropic *nicotine receptors*
    - Metabotropic (G-Protein coupled) – stimulated by muscarine (found in the poison mushroom *Amanita muscaria*) so is called the *Muscarinic receptor*.
      - In the CNS – both nicotinic and muscarinic receptors exist but muscarinic receptors predominate
- In the periphery
  - In PNS, ACh is the primary neurotransmitter that acts on nicotinic receptors at the neuromuscular junction
  - *ACh transmits signal from the motor neuron and causes muscle to contact → controlling muscular movement*

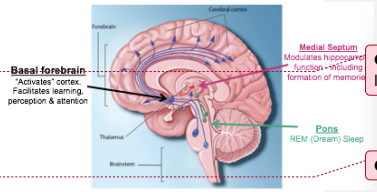
Comment [LY50]: Controls muscle contraction

ACh drugs in the periphery



- Botulinum toxin is produced by bacteria that grows in canned food (most acutely lethal toxin known). *Causes death by paralyzing respiratory muscles*
- Prevents the release of ACh
- *Botox is a very dilute solution of botulinum toxin injected directly into muscles*. Causes muscle weakening for 3-6 months
- Can be used cosmetically to relax facial muscles (reducing wrinkles)
- *Can treat spasticity* (muscle tightening) *in cerebral palsy* (non-specific brain damage)
- The venom of the black widow spider causes death by heart attack (very rarely)
- *Triggers/Stimulates* the release of ACh
- Together *botulinum toxin and Black Widow venom show that too much or too little both have catastrophic consequences. A balance is required*.

Acetylcholine in the Brain (CNS)



- Effects of ACh in brain are generally facilitatory (promoting neural firing)

Comment [LY51]: ACh in the brain is important for learning/memory & perception/attention

Alzheimer's Disease

Comment [LY52]: ACh function is impaired in AD