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LECTURE 1: Introduction to The Integrated Brain

The Nervous System

- Central Nervous System: Comprises the brain and spinal cord
- Peripheral Nervous System: Collection of nerves that exist outside of the brain and spinal cord (can be sensory, mix nerves, etc)
- Neurons (in nervous system): Comprises of cell bodies, axon, and dendrites. Communicate with each other via electrical signals "action potentials" are transmitted along the axons
- Synapses (where the neurons meet): Chemical signals "neurotransmitter" transmitted between neurons. The neurotransmitter pass through other neurons through the synapses (it's like a gap between the neurons)

Neurotransmitter/Neuromodulators

- All neuron in the CNS, PNS, and ENS (enteric nervous system) communicate through chemical signals (neurotransmitters and neuromodulators)
    - Neuromodulator is slower acting
- Without these chemical signals, the action of one neuron would not influence other neurons (no brain intergration and no useful brain function)
- These chemicals modulate neural activity and a range of other functions (exp: synapses plasticity – building new synapses or altering old ones – increase neuron communication)
- **Neurotransmission:** either excitatory or inhibitory and very quick and precise, point-point communication
- **Neuromodulator:** slower, alter subsequent responsiveness of neurons
- NOTE: These two terms are interchangable
- CNS: 100 billion neurons
- Neutrotransmitter originate in small cluster of neurons (nuclei) deep within the brain but released through out the CNS
    - Norepinhephrine: Locus Coereleus
        - Important in terms of increasing or controlling arousal or allerting
        - Evolved in increasing attentional and waking function
        - Very strong interaction with amygdala and midbrain, prefrontal cortical regions
    - Histamine: Posterior Hypothalamus
        - Allergy
    - Cholinergic (Ach): Pontine and basal forebrain
        - Important for allerting an attentional function
        - Implicated with ADHD
    - Dopamine: Ventral tegmental area, substantia nigra area (both in midbrain)
        - More localized to subcortical regions
        - Involved in reward functions as well as motor
        - Involved with schizophrenia
    - Seretonin (5-HT): several "Raphe" nuclei
        - Relating with depression

Hormones

- Signaling molecules **produced by glands** and **transported through the blood** to regulate physiology and behaviours
- Glands: pineal, hypothalamus, pituitary, thyroid, parathyroids, thymus, adrnals, pancreases, ovary, testes

Neurotransmitter vs Hormones

- Neurotransmitter = nervous system and transmit between neurons, and very fast
- Hormones = endocrine system and transmit throughout blood, and slower
- Hormones also directly modulate neurotransmitter levels and function

Blood Brain Barrier

- Exist within 600km of blood vessels in the CNS
- Barrier prevent many substance from passing between the blood and brain
- Many drugs and natural chemicals or foreign infections can't pass through (some small amount still can)
- Mutiple other avenues for controlled passage between blood and nervous system exist

Peripheral Nervous System

- Nerves and glanglia outside of the brain and spinal cord
- Receives sensory information about body position and pain and temperature
- Transmit signal to the glands, send messages from brain to control muscles and movement

Enteric Nervous System

- Part of the PNS
- Termed as the second brain
- Contains 100 millions neurons
- Has its own relfexes and senses and can act independently of the brain (only part of PNS that can do this)
- Nearly every neurotransmitter found in the brain can also found in the guts
    - 95% seretonin is found in the gut
- Bacteria in the gut can trigger certain cells to synthesisze seretonin → increase muscle action and gut motility
- ENS doesn't only help with digestion. 90% of connections between brain and gut go from the **gut to brain**
- Play major role in emotions and stress (why you feel "butterfly" in your stomach) → gut is link to emotion (brain)
- Gut increasingly found to play a role in clinical depression
- Not involve in conciousness, can't make decisions or philosophy
- Relating to: anxiety, pain, autism, MS, CVDs, depression, obesity

Brain Gut Interactions

- Still unclear, however there are 3 areas being examined

    - 1) Peripheral seretonin: State of gut microbe related to how much seretonin is released thus linked to depression?
    - 2) Immune system: Intestinal microbiome can prompt immune cells to produce cytokines that affect neurophysiology
    - 3) Bacteria molecules: Microbes produce metabolite (butyrate) that can alter acitivities of cells in the blood brain barrier

<u>Gut microbiota-brain interactions</u>

- Microbiome: combined genetic material of the microbiota
- Microbiota: trillions of bacteria and other microorganigsm that live in the gut
- Adult microbiom contains more than 100 times more gene than human genome
- Microbiota impacts the brain, behavior and cognitive function
    - Shy mice become more adventorous after receiing a gut microbiota transplant from social/active mice
- Gut microbiota modulates development and **homeostasis** (important! Everything needs to be in balance) of the CNS through immune, circulatory and neural pathways. CNS impacts gut via neural endocrine response
- Range of possible interactions (different pathways and outcomes)
    - Microbiota dysbiosis: dominant of some bacteria or viruses (things are out of balance)
        - Risk factors: (Not guaranteed, but if involved chronically will enhance your risk of disease, or cause relapse)
            - If you have genotyp HLA-DR15, you are prone to get Microbiota Dysbiosis. But it doesn't mean you will get it for sure
            - Low sunlight exposure/low vitamin D
            - EBV+/Mononucleosis
            - Tobacco smoker
            - Obesity
            - Shift work with with unstable carcadian rhymth

<u>Sickness Behaviour</u>

- There are bidirectional links form brain to immune system and immune system to brain
- Activation of the immune system due to illness triggers a series of temporary behavioral, cognitive, and emotional changes including:
    - Fever
    - Increased sleep
    - Depressed mood
    - Hyperalgesia
    - Loss of interest in usual activities
    - Anorexia
    - Decrease social interaction
    - Impaired concentration
- Sickness behavior believed to be triggered by cytokines released by the body repsonse to infection and travel to the brain

- Cytokines: a group of small protein important in cell signaling. They are released by cells and influence behaviour of other cells
    - IL-6: Impact on depression
    - Too big to pass through blood brain barrier. Pass through the brain indirectly pr trigger new cytokines to be released within the brain
    - Experiment: volunteer injected with common cold and showed impaired performances
        - People with more severe illness had negative mood, fatigue, memory, attention
        - More accidents are found when employees are sick

Sickness Behaviour and Mental Health

- Sickness behavior is thought to be an organized strategy evolved to conserve energy and improve the fight against infections
- Excessive sickness behavior (and cytokines release) may lead to neuropsychiatric syndromes such as fatigue syndromes and major depression. Theory is based mainly on overlapping symptoms and is still speculative
- Cytokine release can also trigger "the stress response" and stress can be linked to changes in immune functions

Examples of our Intergrated brain

- Kissing: Transmitting sickness, but we do it because it allows the transfer of hormones like testosterone to passed on to directly increase arousal and show trust and connection

LECTURE 2: Stress and the Brain

Neuroscience and Society

- The brain and mind is an intergrated system including genes, neurons, individuals and society
- Certain genotype increase the risk of responsiveness to stress and the risk of actually having different repsonse to stress
- Stress deveop neurons on neuronal development as well as toxicity
    - Early model: stress toxicity model → neuronal death of the dendrites of neuron when there is chronic stress → reduce size and function of the hippocampus
- Stress has high level of **individuality**: People respond to stress differently
- **Societal** context can deliver chronic and constant level of stress which will affect the general society's mental health capabilities
- Some people have protective effect from stress if they have a warm and nuturing relationship in a stressful environment (environmental input can produce or protect from problems)

Conditions for stress

- Stress is a response to a perceived aversive or threatening situation