Brain & Behaviour Review for Mid-Term #1
Introduction & History

Why Study Brain & Behaviour?

- Many behavioral disorders can be explained and possibly cured by understanding the brain
- The brain is the most complex living organ on Earth and is found in many different groups of animals
- How the brain produces both behavior and human consciousness is a major unanswered scientific question

What is Behaviour?

- Irenäus Eibl-Eibesfeldt:
  - "Behavior consists of patterns in time."
  - Examples – Movements, vocalizations, thinking
- Can be:
  - **Relatively Fixed (Innate) Behaviors** – Dependent on heredity
  - **Relatively Flexible Behaviors** – Dependent on learning

Hippocrates Father of modern medical ethics. First to describe effects of head injuries **4 humours: (excess of) Black bile** = depressive, **Yellow bile** = mood swings, **Phlegm =** 'sluggish', **Sanguine (blood)** = optimistic; tendency for mania

Aristotle **Mentalism:** An explanation of behavior as a function of the nonmaterial mind. **Psyche:** Synonym for mind; an entity once proposed to be the source of human behavior

Galen Correctly identified 7 of 12 cranial nerves

Renaissance (``Re-Birth``) DaVinci laid the foundations for anatomical drawings

Rene Descartes **Dualism:** Mind and brain are separate **"I think therefore I am cogito Ergo-sum"**

Luigi Galvani Demonstrated that nerves conduct electricity. *Studied the sciatic nerve in a frogs leg*

1800's localization of function: hypothetically the control of each kind of behaviour by a different specific brain area

Franz Gall **Phrenology:** Mental and moral faculties determined by shape of skull

Pierre Flourens Advocate of experimental ablation: remove part of brain and observe which behaviours remain**. Falsely believed we only use 10-20% of our brain**

Paul Broca Observed stroke patient who had lost ability to speak **Patient "Tan".** Concluded area important for speech production: Broca's Aphasia

William James Modern approach to biological psychology**.** Concepts of consciousness and human experience described as properties of the nervous system

Wilder Penfield Neurosurgeon procedure to treat intractable epilepsy. Stimulated brain with electrical probes to observe their responses. Mapped out 'homunculus'

Donald O. Hebb Father of modern behavioural neuroscience **. Hebb Rule:** "What fires together, wires together."

Eric Kandel Nobel Prize (2000) for research in nerve transduction: Molecular mechanisms underlying learning and memory **Sea Slug**

Evolution & the Brain

Mentalism is the view that behaviour is a product of an intangible entity called the mind (psyche); the brain has little importance

Dualism is the idea that the immaterial mind acts through the material brain to produce language and rational behaviour; brain alone responsible for "lower" behaviours that are common to other species

Materialism Behavior can be fully explained by the workings of the nervous system, without explanatory recourse to an immaterial mind. Supported evolutionary theories of Alfred Wallace and Charles Darwin

New species evolve: 1) Fossil records; 2) Structural similarities; 3) Programs of selective breeding

Natural Selection: Variations in traits that increase fitness will increase the probability of that species' survival

Sexual selection: Each sex has anatomical and behavioral features that favor reproductive success **e.g., peacock feathers**

Common Ancestor: A forebearer from which two or more lineages or family groups arise Example: Humans and apes are thought to share a common ancestor

Taxonomy: Branch of biology concerned with naming and classifying species. Groups organisms with common characteristics. Useful for helping us trace the evolution of brain cells and the brain

Cladogram ("branch") Display groups of related organisms as branches on a tree. Branch order represents how the groups are related evolutionarily, as well as the traits that distinguish them. Read from left to right; the most recently evolved organism or trait is located farthest to the right

Jerison (1973), Principle of Proper Mass: Species exhibiting more complex behaviors will possess relatively larger brains. Jerison developed an index of brain size to allow comparisons among different species. Used body size to predict brain size

Encephalization Quotient (EQ) Measure of brain size obtained from the ratio of actual brain size to the expected brain size for an animal of a particular body size. H. sapiens have the largest EQ

Why the Hominid Brain Enlarged 1)the primate lifestyle, 2)changes in hominid physiology, 3)Neoteny ("juvenilization"): juvenile stages of predecessors become the adult features of descendants

> **1. The Primate Lifestyle** The foraging behavior of primates is more complex than other animals. Finding fruit is more difficult than eating grass or other vegetation on the ground. Need good sensory, spatial, and memory skills. Fruit eaters have larger brains
>
> **2. Changes in Hominid Physiology** Radiator Hypothesis (Falk, 1990) The more active the brain is, the more heat it generates. Homo species' skulls had more widely dispersed blood flow, which allowed for increased brain size. Increases blood circulation → improved brain cooling → enabled size of hominid brains to increase
>
> **3. Neoteny ("juvenilization"): juvenile stages of predecessors become the adult features of descendants**. Rate of maturation is slowed. Allows more brain cells to be produced. Adults retain some infant characteristics. Newly evolved species resemble the young of their common ancestors

Evolutionary Approach: Make brain-behavior comparisons between different species

How Does the Nervous System Function?

The Brain's Surface Features

Meninges: Three layers of protective tissue

- **Dura mater:** "hard mother"; tough outer layer of fibrous tissue
- **Arachnoid layer:**"like a spider's web"; thin sheet of delicate connective tissue
- **Pia mater:** "soft mother"; moderately tough inner layer that clings to the brain's surface

Cerebrospinal Fluid (CSF) Sodium chloride and other salts. Fills the ventricles and circulates around the brain and spinal cord in the subarachnoid space (located between the arachnoid layer and the pia mater)**. Meningitis** Infection of the meninges and CSF

The Brain's Surface Features

Cerebrum Major structure of the forebrain, consisting of two virtually identical hemispheres (left and right). Most recently evolved brain structure in humans
Cerebellum: "Little brain" Involved in the coordination of motor and possibly other mental processes
Brainstem Central structures of the brain, including the hindbrain, midbrain, thalamus, and hypothalamus, responsible for most unconscious behavior
Gyrus (pl. gyri) A small protrusion or bump formed by the folding of the cerebral corte
Sulcus (pl. sulci) A groove in brain matter, usually found in the neocortex or cerebellum
Fissure A very deep sulcus

Nucleus (pl. nuclei) A group of cells forming a cluster that can be identified with special stains to form a functional grouping
Nerve Large collection of axons coursing together outside the central nervous system
Tract Large collection of axons coursing together within the central nervous system
The Corpus Callosum Fiber system connecting the two cerebral hemispheres

The Brain's Internal Features – Macro View

Gray Matter Areas of the nervous system predominately composed of cell bodies and blood vessels
White Matter- Areas of the nervous system rich in fat-sheathed

Two Main Types of Brain Cells

- **Neurons** Carry out the brain's major functions**.** Approximately 80 billion
- **Glial cells** Aid and modulate neurons' activities**.** Approximately 100 billion

The Central Nervous System: Three Major Components: Spinal Cord, Brainstem, Forebrain

The Spinal Cord - Controls most body movements**.** Can act independently of the brain**.** Spinal reflex: Automatic movement**.** Hard to prevent (brain cannot inhibit)

The Brainstem – Begins where spinal cord enters the skull. Produces movement and creates a sensory world.
Three regions: Hindbrain, Midbrain, Diencephalon

Hindbrain Evolutionarily the oldest part of the brain
Contains:

- **Cerebellum** Controls complex movements and has a role in a variety of cognitive functions. Size of cerebellum increases with the physical speed and dexterity of a species
- **Reticular Formation** Netlike mixture of neurons (gray matter) and nerve fibers (white matter). Stimulates the forebrain: Regulation of sleep-wake behavior and behavioral arousal
- **Pons ("bridge")** Connects cerebellum to the rest of the brain. Controls important movements of the body
- **Medulla** Rostral tip of spinal cord. Vital functions: Control of breathing and heart rate, Control of movement

(Brainstem) Midbrain

Tectum (roof of midbrain) Sensory processing (visual and auditory) . Produces orienting movements
Tegmentum (floor of midbrain) Eye and limb movements. Species-specific behaviors. Perception of pain

(Brainstem) Diencephalon

Hypothalamus: Hormone function. Through connections with the pituitary gland.
Feeding. Sexual behavior, Sleeping, Temperature regulation, Emotional behavior
Thalamus Gateway for channeling sensory information to the cortex
Primary role is sensory processing. Motor processing. Integrative functions

The Forebrain

Three Principle Structures
Neocortex: Regulates various mental activities
Basal Ganglia: Control of voluntary movement
Limbic System: Regulates emotions and behaviors that create and require memory

The Cortex

Neocortex ("new bark") 6 layers of gray matter. Creates and responds to a perceptual world
Limbic Cortex Evolutionarily older. 3 or 4 layers of gray matter. Controlling motivational states

The Cortical Lobes:

Frontal: Motor and executive functions
Occipital: Vision
Parietal: Tactile function
Temporal: Visual, auditory, and gustatory functions

The Basal Ganglia Collection of nuclei just below the white matter of the cortex**. 3 principal structures:** caudate nucleus, putamen, and globus pallidus**.** Controls voluntary movement**.** Related disorders Parkinson's disease and Tourette's syndrome

The Limbic System Group of structures between the neocortex and brain stem**. Principal structures:** amygdala, hippocampus, and cingulate cortex. **Regulation of :** Emotional and sexual behaviors, Memory,Spatial navigation

Term	Meaning with respect to the nervous system
Anterior	Located near or toward the front of the animal or the front of the head (see also *frontal* and *rostral*)
Caudal	Located near or toward the tail of the animal (see also *posterior*)
Coronal	Cut vertically from the crown of the head down; used in reference to the plane of a brain section that reveals a frontal view
Dorsal	On or toward the back of the animal or, in reference to human brain nuclei, located above; in reference to brain sections, a viewing orientation from above
Frontal	"Of the front" (see also *anterior* and *rostral*); in reference to brain sections, a viewing orientation from the front
Horizontal	Cut along the horizon; used in reference to the plane of a brain section that reveals a dorsal view
Inferior	Located below (see also *ventral*)
Lateral	Toward the side of the body or brain
Medial	Toward the middle, specifically the body's midline; in reference to brain sections, a side view of the central structures
Posterior	Located near or toward the tail of the animal (see also *caudal*)
Rostral	"Toward the beak" of the animal; located toward the front (see also *anterior* and *frontal*)
Sagittal	Cut lengthways from front to back of the skull; used in reference to the plane of a brain section that reveals a view into the brain from the side
Superior	Located above (see also *dorsal*)
Ventral	On or toward the belly or the side of the animal where the belly is located; in reference to brain nuclei, located below (see also *inferior*)

The Somatic Nervous System: Transmitting Information

The SNS is monitored and controlled by the CNS

The cranial nerves by the brain

The spinal nerves by the spinal cord segments

The Spinal Nerves

Connections of the Somatic Nervous System

Dorsal fibers are afferent: they carry information from the body's sensory receptors

Ventral fibers are efferent: they carry information from the spinal cord to the muscles

Law of Bell and Magendie: The general principle that sensory fibers are located dorsally and motor fibers are located ventrally

Dermatome Area of the skin supplied with afferent nerve fibers by a single spinal-cord dorsal root

The Autonomic Nervous System: Balancing Internal Functions

Two divisions working in opposition

Sympathetic System Arouses the body for action. Mediates the "fight or flight" response

Parasympathetic System Opposite of sympathetic: prepares the body to "rest and digest"**.** Reverses the "fight or flight" responses

What Are the Units of Nervous System Function? Cells of the Nervous System. Internal Structure of a Cell. Genes, Cells, and Behavior

Neurons: The Basis of Information Processing

Three Basic Subdivisions

Dendrites Gather information from other neurons

Cell Body or Soma Core region; contains the nucleus. Integrates the information

Axon Carries information to be passed on to other cells

Basic Structure and Function

Dendritic Spines Protrusion from a dendrite that greatly increases its surface area and is the usual point of contact with axons of other cells

Axon Hillockd Juncture of soma and axon where the action potential begins

Axon Collaterals Branch of an axon

Teleodendria End branches of an axon

Terminal button Knob at the tip of an axon that conveys information to other neurons; also called an end foot

Synapse Gap between one neuron and another neuron**.** Usually between an end foot of the axon of one neuron and a dendritic spine of another neuron

Different Types of Neurons

Sensory Neurons Bring information to the central nervous system

Interneurons Associate sensory and motor activity within the central nervous system

Motor Neurons Send signals from the brain and spinal cord to muscles

Five Types of Glial Cells

Ependymal Cells Small, ovoid; found in the walls of the ventricles. Make and secrete cerebrospinal fluid (CSF)

Hydrocephalus Build-up of pressure in the brain and swelling of the head caused if the flow of CSF is blocked. Can result in retardation

Astrocyte. Star shaped, symmetrical**.** Structural support for neurons**.** Transports substances between neurons and capillaries**.** But also protects the brain: Blood-brain barrier**.** Scar tissue formation**.** Enhance brain activity by providing fuel to active brain regions

Microglia Originate in the blood as offshoot of immune system **Phagocytosis:** scavenge debris (e.g., dead cells)

Oligodendroglia Cell Glial cell in the central nervous system that myelinates axons **Myelin** Glial coating that surrounds axons

Schwann Cell Glial cell in the peripheral nervous system that myelinates axons
Multiple Sclerosis (MS) Nervous system disorder that results from the loss of myelin around axons

Damage to Cells
Paralysis Loss of sensation and movement due to nervous system injury
Central Nervous System Repair does not take place, regrowth may even be inhibited
Peripheral Nervous System Microglia and Schwann cells help repair neurons

Genes, Cells, and Behavior
Genomics: Field of study directed toward understanding how genes produce proteins
Proteomics: Field of study directed at understanding what all the proteins do!

Chromosomes and Genes
Autosomes: Pairs 1-22
Sex chromosomes: Pair 23
Allele Alternate form of a gene; a gene pair contains two alleles
Homozygous Having two identical alleles for a trait
Heterozygous Having two different alleles for the same trait
Wildtype Refers to a normal (most common in a population) phenotype or genotype
Mutation Alteration of an allele that yields a different version of that allele
Genotype The full set of all the genes that an organism possesses
Phenotype The appearance of an organism that results from the interaction of genes with one another and with the environment

Dominant and Recessive Alleles
Dominant Allele The member of the gene pair that is routinely expressed
Recessive Allele The member of the gene pair that is routinely unexpressed
Complete Dominance Only the dominant allele's trait is expressed in the phenotype
Incomplete Dominance The phenotypic expression of the dominant allele's trait is only partial
Codominance The traits of both alleles of a gene pair are expressed completely in the phenotype

Tay-Sachs Disease Inherited birth defect caused by the loss of genes that encode the enzyme necessary for breaking down certain fatty substances**.** Appears 4-6 months after birth and results in retardation, physical changes, and death by about age 5**.**Caused by recessive allele

Huntington's Chorea Autosomal disorder that results in motor and cognitive disturbances. Caused by an increase in the number of CAG (cytosine-adenine-guanine) repeats on chromosome 4

Chromosome Abnormalities Genetic disorders involve aberrations in part of a chromosome (or the entire chromosome) rather than a single defective allele
Down Syndrome Chromosomal abnormality resulting in mental retardation and other abnormalities, usually caused by an extra copy of chromosome 21 (trisomy)

Genetic Engineering Adding or removing genes from a genome, or modification of a gene
Selective breeding Maintaining spontaneous mutations. Directly manipulating genetic expression
Cloning Producing an offspring that is nearly genetically identical with another animal

Approaches (2)
Chimeric Animals Have genes from two different species
Transgenic animals A gene is added to the genome and is passed along and expressed in subsequent generations
Knockout Technology Method used to inactivate a gene so that it is not expressed**.** Potential application to human genetic disorders

Neurophysiology: Generation, Transmission, and Integration of Neural Signals

The Cell Membrane
Channel: Opening in a protein embedded in the cell membrane that allows the passage of ions
Gate: Protein embedded in a cell membrane that allows substances to pass only when open
Pump: Protein embedded in a cell membrane that actively transports a substance across the membrane

Giant Axon of the Squid Much larger in diameter than human axons**.** Humans: 1 to 20 micrometers. Squid: Up to 1 millimeter (1000 micrometers)**.** Easier on which to perform experiments**.** Used by Hodgkin and Huxley in the 1930s and 1940s

Equipment
Oscilloscope: A sensitive voltmeter to measure the very small and rapid changes in electrical currents that come from an axon
Microelectrode: Small electrode used to record electric potentials from living cells

Resting Membrane Potential The electrical charge across a cell membrane; the difference in electrical potential inside and outside the cell. -70 mv is the resting membrane potential
Ions: Atom that has gained or lost an electrical charge:
Anion: Negative Ion e.g., Chloride, or Cl- **Cation:** Positive Ion e.g., Potassium, or K+
Exists because positively and negatively charged ions are distributed unequally on two sides of the membrane

Factors Determining RMP
Diffusive Forces: Ions in random motion move down a concentration gradient.
Differential Permeability: Ions pass through ion channels
At rest, membrane totally resistant to passage of protein ions, extremely resistant to passage of Na+, and slightly resistant to passage of K+ and Cl- ions
Electrostatic Pressure: Like charges repel; opposite charges attract
Sodium-Potassium Pump: Protein found in membrane of all cells that exchanges 3 Na+ ions (pumped out) for 2 K+ ions (pumped in)
Counters Na+ leak

Post-Synaptic Potentials. Change in the resting membrane potential. Can occur anywhere in the neuron; where the axon terminals of the pre-synaptic neuron synapse onto the post-synaptic cell

(Common) Types of Synapses
Axo-dendritic: axon terminal synapses on a dendrite or dendritic spine
Axosomatic: Synapse onto cell body
Axo-axonic: between two axons, mediates presynaptic inhibition
Dendro-dendritic: between two dendrites; found primarily in olfactory bulb

Excitatory Post-Synaptic Potentials (EPSPs) Depolarizations – Decrease in membrane potential caused by excitatory messages; increases probability that the neuron will fire

Inhibitory Post-Synaptic Potentials (IPSPs) Hyperpolarizations Increase in membrane potential, caused by inhibitory messages; decreases probability that the neuron will fir

Pre- and Postsynaptic Inhibition
Post-synaptic B inhibits excitatory effects of A synapsing on C, by hyperpolarizing C.
Pre-synaptic B inhibits excitatory effects of A on C by partially depolarizing A.

Properties of PSPs
Graded Amplitudes are proportional to the intensity of the signal
Decremental As the potential spreads across the membrane, the size decays as a function of the square of the distance Rapid & Passive, cable properties

Interim Summary Inside of cell more negative than outside: **RMP**. Due to imbalance in ions, 4 factors that contribute. Neuron is polarized. Membrane can become more (hyper) or less (de) polarized **Post-synaptic potentials**. If the threshold of excitation is reached (~-50mv), leads to an action potential

The Action Potential A sudden reversal in the membrane potential (from negative to positive) caused by a brief increase in the permeability of the membrane to Na+, immediately followed by a transient increase in the permeability of the membrane to K+

The Ionic Basis of the Action Potential

1. Threshold of excitation reached; Na+ channels open and sodium starts to come into the cell
2. K+ channels open, begin to leave the cell (to try to regain membrane potential)
3. Na+ channels become refractory (no more sodium comes into the cell)
4. K+ continues to leave cell, causes membrane potential to return to resting levels
5. K+ channels close, Na+ channels reset

Integration of PSPs

Individual post-synaptic potentials have little effect on firing of post-synaptic neuron
Firing depends on the integration of inhibitory and excitatory signals reaching the axon hillock
Rich in voltage-sensitive ion channels
Neurons integrate signals over space (spatial) and over time (temporal):
SUMMATION Influx and efflux of ions is what is being summed

Spatial Summation Summing of potentials that come from different parts of the cell
Influenced by distance Closer to the axon hillock, the more likely it will generate an AP (if depolarizing current)
If overall sum (EPSPs and IPSPs) can depolarize the cell at the axon hillock → AP!

Temporal Summation Summing of potentials that arrive at the axon hillock at different times
Closer in time they arrive, the greater the summation and possibility of an AP. Cannot have EPSP + IPSP!
Single synapse

Conduction of Action Potentials

All-or-none law: An action potential either occurs or does not occur; once triggered, it is transmitted down to the end of the axon
Action potential always remains the same size, without growing or diminishing, but☜ Action potentials are conducted more slowly than post-synaptic potentials
Rate Law: Variable information is represented by the axon's rate of firing
Not the amplitude of the action potential that is important, but the number of times a neuron fires for a given time period

Refractory Periods

Absolute refractory period: 1-2 ms after an action potential, another AP cannot be generated, no matter what kind of input the neuron receives
Relative refractory period: Action potential can only be elicited by high levels of stimulation

Conduction in Unmyelinated Neurons

Once an AP has been generated at the axon hillock, it travels passively along the axonal membrane to the adjacent voltage-activated sodium channels → active
In response, Na+ channels open and another full-blown potential is generated
Continues down the length of the axon in 'waves' of depolarization
Refractory periods create a single, discrete impulse that travels only in one direction
Relatively slow

Conduction in Myelinated Axons

AP 'jumps' from node to node: Saltatory Conduction

Myelination resists flow of K+ ions

Faster, requires less energy

Larger and myelinatined axons conduct faster

Neuropharmacology – How Do Neurons Communicate and Adapt?

A Chemical Message

Otto Loewi (1921) Frog heart experiment**.** Demonstrated that the neurotransmitter acetylcholine (ACh) slows heart rate

AcetylcholineThe first neurotransmitter discovered in the PNS and CNS; activates skeletal muscles in the somatic nervous system and may excite or inhibit internal organs in the autonomic nervous system

What are Neurotransmitters?

Chemical released by a neuron onto a target with an excitatory or inhibitory effect

Outside the CNS, many of these chemicals circulate in the blood stream as hormones

Structure of Synapses

Presynaptic Membrane Membrane on the transmitter **-** output side of a synapse

Postsynaptic Membrane Membrane on the transmitter **-** input side of a synapse

Synaptic Cleft Gap that separates the presynaptic membrane from the postsynaptic membrane

A Chemical Message Structure of Synapses

Synaptic Vesicle Organelle consisting of a membrane structure that encloses a quantum of neurotransmitter

Storage granule Membranous compartment that holds several vesicles containing a neurotransmitter

Neurotransmission in Four Steps

Step 1: Synthesis and Storage

Step 2: Neurotransmitter Release

Step 3: Receptor-Site Activation

Step 4: Deactivation of the Neurotransmitter

Two Classes of Receptors

Ionotropic Receptor

Embedded membrane protein with two parts

A binding site for a neurotransmitter

A pore that regulates ion flow to directly and rapidly change membrane voltage

Limitation of Ionotropic receptors

Fast, direct, but does not allow for learning / plasticity

How do we get change in the nervous system?

Metabotropic / G-protein coupled Receptor

Embedded membrane protein with a binding site for a neurotransmitter but no pore

Indirectly produces changes in nearby ion channels or in cell's metabolic activity

Slow, longer-lasting effects

Linked to a G protein

A family of guanyl-nucleotide-binding proteins coupled to metabotropic receptors that, when activated, bind to other proteins

3 subunits (alpha, beta, gamma)

Alpha detaches when neurotransmitter binds; then binds to other proteins

Metabotropic Receptors (Cont'd)

- Two possible outcomes:
  - Alpha subunit binds to an ion channel; causes it to open
  - Alpha subunit binds to an enzyme, which activates a 2nd messenger
    - Bind to channel; alter ion flow
    - Cause proteins to be incorporated in to cell membrane (e.g,. New ion channels)
    - Instruct DNA to produce new proteins

Synaptic Transmission – Summary

Neuronal firing is a electro-chemical event

Neurotransmitter (chemical) binds to post-synaptic receptor

Causes change in local membrane potential (electrical)

Increase or decrease probability of cell firing

If action potential produced à leads to neurotransmitter release → re-start cycle

Varieties of Neurotransmitters

~50 different kinds have been identified

Some are inhibitory at one location and excitatory at another

More than one neurotransmitter may be active at a single synapse

No simple one-to-one relationship between a single neurotransmitter and a single behavior

Four Criteria for Identifying Neurotransmitters

The chemical must be synthesized in the neuron or otherwise be present in it

When the neuron is active, the chemical must be released and produce a response in a some target

The same response must be obtained when the chemical is experimentally placed on the target

A mechanism must exist for removing the chemical from its site of action after its work is done

Three Classes of Neurotransmitters

1. Small-molecule transmitters
2. Peptide transmitters
3. Transmitter gases

Acetylcholine Synthesis

Formed from choline and acetate **Enzymes:** Acetyl CoA & ChAT

Breakdown of acetylcholine **Enzyme:** Acetylcholinesterace (AChE)

Sequential Synthesis of Three Amines

Rate-Limiting Factor

Any enzyme that is in limited supply, thus restricting the pace at which a chemical can be synthesized

Amino Acid Transmitters

Glutamate: main excitatory transmitter

Receptors: NMDA, AMPA, kainate, and metabotropic glutamate receptor (slower)

Excitotoxicity: Neural injury such as stroke causes excess release of glutamate, toxic to neurons

GABA: main inhibitory transmitter

Synthesized from glutamate

Receptors: GABAA (fast, Cl-) and GABAB (slow), GABAC (fast; Cl-) **All inhibitory!**

GABA agonists are potent tranquilizers, e.g., Valium

1. Small-Molecule Transmitters

Class of quick-acting neurotransmitters

Synthesized from dietary nutrients and packaged ready for use in axon terminals

Amines: Dopamine (DA), Norepinephrine (NE), Epinephrine (EP), Serotonin (5-HT)

Amino Acids: Glutamate (Glu), Gamma-aminobutyric acid (GABA), Glycine (Gly)

2. Peptide Transmitters

Neuropeptide
A multifunctional chain of amino acids that act as a neurotransmitter
Synthesized from mRNA on instructions from the cell's DNA
Do not bind to ion channels; do not have direct effects on the voltage of the postsynaptic membrane
Examples: Opioids, insulin, corticosteroids

3. Transmitter Gases

Small molecules that diffuse through the cell membrane and stimulate second messenger production
Retrograde transmitter
Synthesized in cell, as needed
Examples: Nitric Oxide (NO) & Carbon Monoxide (CO)

Four Activating Systems in the Central Nervous System

Activating System

Neural pathways that coordinate brain activity through a single neurotransmitter
Cell bodies are located in a nucleus in the brainstem and their axons are distributed through a wide region of the brain

Four Systems Cholinergic, Dopaminergic, Noradrenergic, and Serotonergic

Learning Relatively permanent change in behavior that results from experience
Neuroplasticity The nervous system's potential for change that enhances its ability to adapt. Required for learning and memory

The Hebbian Synapse

Hebb Synapse "When the axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased."
Learning is mediated by structural changes in synapses

The Habituation Response

Habituation Learning behavior in which a response to a stimulus weakens with repeated stimulus presentations. ***Due to decreased Ca^{2+} influx***

The Sensitization Response

Sensitization Learning behavior in which the response to a stimulus strengthens with repeated presentations of that stimulus because the stimulus is novel or stronger than normal. ***Due to reduction in K^+ efflux → increased Ca^{2+} influx***

Long-Term Potentiation and Associative Learning

Associative Learning Linkage of two or more unrelated stimuli to elicit a behavioral response
Long-term Potentiation (LTP)

In response to stimulation at a synapse, changed amplitude of an excitatory postsynaptic potential that lasts for hours to days or longer
Plays a part in associative learning
Occurs in hippocampus

A strong burst of electrical stimulation applied to the presynaptic neuron produces an increase in the amplitude of the EPSP in the postsynaptic neuron
First recorded in the hippocampus by Bliss and Lømø in 1973

Field Potential: EPSPs from many neurons; recorded with extracellular electrodes

Suggests

Physical change at the synapse
Change at the synapse might be related to everyday learning

Neurotransmission in Four Steps

Step 1: Synthesis and Storage

- Neurotransmitters are derived in two general ways:
  - Synthesized in the Axon Terminal
    - Building blocks from food are pumped into cell via transporters: protein molecules embedded within the cell membrane
  - Synthesized in the Cell Body
    - According to instructions contained in the DNA
    - Transported on microtubules to axon terminal

Step 2: Neurotransmitter Release

- At the terminal, the action potential opens voltage-sensitive calcium (Ca2+) channels
- Ca2+ enters the terminal and binds to the protein calmodulin forming a complex
- Complex causes some vesicles to empty their contents into the synapse, and others to get ready to empty their contents

Step 3: Receptor-Site Activation

- After being released, the neurotransmitter diffuses across the synapse and activates receptors on the postsynaptic membrane
- Transmitter-Activated Receptors
  - Protein embedded in the membrane of a cell that has a binding site for a specific neurotransmitter
  - Open up the receptor, allow passage of ions into OR out of the cell, depending on the receptor
- This is what leads to post-synaptic potentials!

Step 3: Receptor-Site Activation (2)

- Neurotransmitter may:
  - Depolarize the postsynaptic membrane causing excitatory action on the postsynaptic neuron
  - Hyperpolarize the postsynaptic membrane causing inhibitory action on the postsynaptic neuron
  - Initiate other chemical reactions that modulate either the excitatory or inhibitory effect, or influence other functions of the receiving neuron

Step 3: Receptor-Site Activation (3)

- Neurotransmitter may also interact with receptors on the presynaptic membrane
- Autoreceptors
  - "Self-receptor" on the presynaptic membrane that responds to the transmitter that the neuron releases
- In most cases, do not control ion channels or produce changes in membrane potential
- Instead, regulate internal processes
  - e.g., control synthesis and release of neurotransmitter

Step 4: Deactivation of the Neurotransmitter

- Accomplished in at least four ways:
  - Diffusion away from synaptic cleft
  - Degradation by enzymes in the synaptic cleft
  - Reuptake into the presynaptic neuron for subsequent re-use
  - Taken up by neighboring glial cells

Characteristics of Electrical Signals of Nerve Cells

Type of Signal	Signaling Role	Typical Duration (ms)	Amplitude	Character	Mode of Propagation	Ion Channel Opening	Channel Sensitive to
Action potential	Conduction along a neuron	1-2	Overshooting 100mV	All or none, digital	Actively propagated, regenerative	First Na then K, in different channels	Voltage depolarization
EPSP	Transmission between neurons	10-100	Depolarising from lea than 1 to more than 20 mV	Graded, analog	Local, passive spread	Na, K	Chemical neurotransmitter
IPSP	Transmission between neurons	10-100	Hyperpolarising from less than 1 to about 15 mV	Graded, analog	Local, passive spread	K, Cl	Chemical neurotransmitter

Differences between ionotropic and metabotropic receptors

Ionotropic	Metabotropic
• Fast • No long-term effects / does not allow for plasticity • Direct, allow ions to flow in and out of the cell • Not energy dependent • Has a pore • One outcome	• Indirect • Requires energy • Influences protein/gene expression • Has no pore • 2 possible outcomes / G-protein can attach to ion channel • Slow, long-term effects • Associated with learning • Affect the amplitude of the signal • 2nd messenger coupled system