IV. TRANSFERING AND PROCESSING INFORMATION

- Info must be moved from 1 cell to another.

- The body must decide what to do with the info, and send out a command.

A) THE SYNAPSE: INFO TRANSFER

- Word means “clasp” or “join”.

- Function: information transfer

- 2 types of classifications:

1. Classified based on what is connected:

   GOOD NEWS: they all work the same!

   (i) INTERNEURONAL: between neurons.

   * Gives us a PRESYNAPTIC and POSTSYNAPTIC neuron.

   * AXODENDRITIC: between axon of one neuron & dendrite of another; most common type.

   * NOTE the variations: can be axoaxonic and axosomatic.

   (ii) NEUROMUSCULAR & NEUROGLANDULAR - named after the effector organ (Muscle or gland).

2. Classified based on how info is transferred:

   (i) CHEMICAL SYNAPSE - most common.

   *controlled by a NEUROTRANSMITTER.

   *characteristics: activity of post-synaptic membrane can be modulated (vary the strength of the signal).
   You can increase activity (EXCITE), lessen activity (INHIBIT), or one input can counteract another input.

   * Parts:

   (a) Knob-like AXONAL TERMINAL or SYNAPTIC END BULB of the presynaptic neuron.

   End Bulb contains vesicles with neurotransmitter.

   (b) RECEPTOR REGION on membrane of post-synaptic neuron or effector cell, with receptor proteins that react to neurotransmitter.

   Modulation: See next section on inhibitory versus excitatory synapses.

   (c) SYNAPTIC CLEFT: fluid filled space between pre- and post-synaptic neurons.
- Function = permit **UNIDIRECTIONAL COMMUNICATION** between neurons ONLY! Info can only go in one direction!
  - *impulses are not directly transmitted!*

- Step-by-step for an excitatory synapse:

  1. AP on pre-synaptic axon causes voltage-gated Ca++ channels to open in presynaptic axonal terminal; Ca++ floods in from extracellular fluid.

  2. Ca++ ions cause vesicles w/ neurotransmitter to be released via **EXOCYTOSIS**.

  3. Neurotransmitter diffuses across cleft

  4. NT binds to postsynaptic receptor on LGCs.

  5. Sodium and Potassium ion channels in postsynaptic membrane open.

  6. Na+ floods into cell, and potassium diffuses out, and depolarizes the membrane

  7. If the depolarization is strong enough, this causes an AP on the postsynaptic membrane (see description of **THE SPIKE** outlined in an earlier section).

- An **ESTERASE** then deactivates the NT, preventing the continued entry of Na+ and eventual destruction of the cell via lysis.
  - * This turns off the depolarization, and therefore stops the AP.

- Difference for an inhibitory synapse: only potassium channels are opened. This hyperpolarizes the membrane.

(ii) **ELECTRICAL SYNAPSE**: less common of the 2 types.

  * **BRIDGE JUNCTIONS**: similar to gap junctions of other body cells.

  Protein channels interconnect the membranes of neurons, coordinating their activity.

  AP on 1st membrane brings Na+ in, which diffuses through the channels and depolarizes the other cell. Potassium moves out.

  * Characteristic: no control; if one neuron fires, they all fire! Also, communication can go both ways!

  ** Only seen in neurons controlling “Stereotyped Actions” (jerk movements of the eye, hormone release by pituitary gland, etc.).
B) **STRENGTH OF STIMULUS**: since all APS are of identical strength, how do we get info concerning weak stimulus vs. strong stimulus?

- 2 ways of communicating "strength of stimulus":

1. Wave summation (Temporal summation) = frequency
   - Nervous system interprets FREQUENCY of stimulation, not strength of stimulation. If I increase the pressure on your skin harder, APs become more frequent, not stronger!
   
   Lots of NT in the cleft!

2. Recruitment = increased number of receptors, and therefore sensory neurons activated.
   
   A larger area of skin is pushed upon by the larger stimulus. Pushing on a bigger area of your skin sets off more receptors.

   - Of course, both wave summation & recruitment are occurring at the same time.

C) **OTHER TYPES OF POTENTIALS** - Terminology

1. **GENERATOR POTENTIALS** - a stimulus that occurs in an area that **LACKS** voltage-gated channels; therefore, an AP cannot occur.
   
   * But...it might generate one.
   
   * Examples: this happens on the body & dendrites of neurons, assuring that an AP only can occur on the axon.

2. **GRADED POTENTIALS** - a subthreshold stimulus ("below threshold") that won’t open voltage-gated channels, even though they are there.

   * Cause a small depolarization as Na+ flows in (not shown). They can become stronger as the stimulus gets stronger. Until they reach threshold!

   * If this happens with chemically-gated channels at a synapse, it is called a RECEPTOR POTENTIAL.
* If the stimulus is neurotransmitter released by another cell, this is called the POST-SYNAPTIC POTENTIAL (“after the synapse”).

(i) **EXCITATORY SYNAPSES & EPSPs** (Excitatory Post-Synaptic Potentials)

* Effect of the neurotransmitter is to open both Na+ AND K+ channels **simultaneously**. Axons then generate an AP.

(ii) **INHIBITORY SYNAPSES & IPSPs** (Inhibitory Post-Synaptic Potentials)

* Neurotransmitter binding to receptor protein **REDUCES** the neuron’s ability to cause an AP on the postsynaptic neuronal axon.

* E.G.: The NT doesn’t affect Na+ permeability; just K+ permeability.

* One input can counteract another.

D) **SYNAPTIC INTEGRATION and PROCESSING**: How does the NS tie in all the info coming in from several neurons?

* RECALL: Neurotransmitter causes a kind of graded potential called a postsynaptic potential, which has a certain frequency of APs according to the AMOUNT of neurotransmitter present (which is determined by freq. of APS on presynaptic neuron).

ALSO RECALL: I also said that sometimes the neurotransmitter excites, sometimes it inhibits.

- Most neurons receive both excitatory & inhibitory input from THOUSANDS Of neurons = lots of INTEGRATION.

* **FACILITATION**: most neurons are kept NEAR threshold by continuous input from thousands of neurons. If the NS wants the neuron to fire, it just increases the frequency of a few Excitatory neurons. Want to dampen the neuron, increase the frequency of a few inhibitory neurons.

* **PRESYNAPTIC INHIBITION**: release of excitatory neurotransmitter is reduced by activity of another neuron. In other words, 2 presynaptic neurons synapse with each other!
- PROCESSING - how do we respond to a stimulus?

Through what pathway does a stimulus cause a response? How do we get 1 stimulus to give more than one response?

(if you want to see how many muscular and vocal responses can be produced from one stimulus, bang your shin on a table corner in the middle of the night!)

1. Circuits & Pools

How the neurons are connected to form a feedback loop.

Simplified:

(i) Divergent (diverging circuit): One stimulus leads to multiple outputs.

(ii) Convergent: Multiple stimuli lead to a single output.

(iii) Reverberating: One stimulus leads to continued output, that may be amplified.

2. Types of Processing - pathway to a response

(i) SERIAL PROCESSING - input along a single path to a specific destination (will see in more detail later with reflex arcs).

Serial Processing gives speed. Only a few synapses in the CNS.

E.G.: SIMPLE REFLEX ARCH:

(ii) PARALLEL PROCESSING - input is segregated (“split”) into several pathways. Lots of divergence.

Slower, but one input can bring about many responses and effects, including emotional response, long-term memory, learning, etc.

- Because of parallel processing, some sensory info (such as, say, smelling a pie) can bring back so many memories & responses.

(salivation, childhood memories, begin digestive processes, feelings of “pleasure”, sexual arousal, etc.).
E) NEUROTRANSMITTERS (NT)

- Whether or not a chemical acts as a NT depends on its ability to bind to a ligand-gated channel

* If the tissue doesn't have a channel to bind to, no effect!

* So, different NTs affect different parts of the nervous system, depending on where the correct channels are.

  - Drugs have certain effects based on whether or not they bind to the nervous system, and where they bind!

    Pain medications, anti-anxiety, anti-inflammatory, increase/decrease blood pressure and heart rate, etc.

    This also accounts for the side effects of many medications! Weight loss, sleeplessness, sleepiness, digestive and reproductive issues, etc.

- Some drugs/chemicals and toxins attach too strongly. This is the basis for "physiological addiction". More on this later.

- More than 50 chemical currently known.

- Most neurons make & use more than one!

- Some chemical classifications that you need to know:

  1. Amino acids:

     **Glutamate**

     Glutamate (glutamic acid) is used at the great majority of fast excitatory synapses in the brain and spinal cord. It is also used at most synapses that are "modifiable".

     Most common NT. Over 75% of all excitatory synapses in the brain. Important in memory.

     MSG - monosodium glutamate is a common salt of glutamic acid. Your taste for "glutamate" is called "Umami" (Japanese word for "Savory" or "delicious").

     **γ-aminobutyric acid (GABA)**

     GABA is used at the great majority inhibitory synapses in virtually every part of the brain.

     Found in all cells, usually inhibitory. Also inhibits muscles, giving us muscle tone.

     Many sedative/tranquilizing drugs act by enhancing the effects of GABA.

     Diazepam (Valium) the anti-anxiety medication, enhances its effects.

     It and Librium were the first completely "man-made" pharmacological molecules.
2. Monoamines and other biogenic amines:

- Especially potent in the emotional areas of the brain, as well as perceptions (how important are stimuli)

**Dopamine (DA)**

Many functions in the brain, including important roles in behavior and cognition, voluntary movement, motivation, important role in "reward-driven learning" and "gratification" (food and sexual), sleep, dreaming, mood, attention, working memory, and learning.

Too much dopamine seen in schizophrenia.

Too little production in one part of the brain leads to the rigidity of Parkinson’s disease.

**Norepinephrine** (noradrenaline; NE, epinephrine (adrenaline))

Important players in the "Sympathetic nervous response". Excitatory on some tissues, inhibitory on others. More info in the ANS section.

Epinephrine is also a hormone.

**Histamine**

Although histamine is small compared to other biological molecules (containing only 17 atoms), it plays an important role in the body. It is known to be involved in 23 different physiological functions.

Important in sleep functions (modulation). Some people get sleepy with antihistamines, others do not.

**Serotonin**

Regulate appetite, sleep, memory and learning, temperature, mood, behaviour, muscle contraction, and function of the cardiovascular system and endocrine system.

LSD is a similar molecule & mimics its effects.

It is speculated to have a role in depression.

Serotonin Re-uptake Inhibitors: Paxil, Prozac, Zoloft

* Too little serotonin may be the cause for many types of chronic depression.

PROZAC inhibits reabsorption of serotonin by synaptic knobs.

3. Peptides: Includes the Opioid peptides (a large family)

- Neurotransmitters that act within pain pathways and the emotional centers of the brain; some of them are analgesics and elicit pleasure or euphoria.
**Morphine** - It was first isolated in 1804 by Friedrich Sertürner. First distributed by him in 1817, and first commercially sold by Merck in 1827.

Most abundant opiate found in opium, the dried latex extracted by shallowly slicing the unripe seedpods of the *Papaver somniferum* poppy.

**Endorphins** ("endogenous morphine") - "Second Wind"

When a nerve impulse reaches the spinal cord, endorphins that prevent nerve cells from releasing more pain signals are released.

The term "endorphin rush" is used in popular speech to refer to feelings of exhilaration brought on by pain, danger, or other forms of stress, supposedly due to the influence of endorphins.

**Codeine and Hydrocodone**

4. Other NTs:

**Acetylcholine** (ACh)

Excitatory on skeletal muscle, inhibitory on cardiac muscle. Also acts as a NT in the brain.

1st to be ID’d

**Novel Messengers**: (don't fit a chemical category)

Nitric oxide

ATP and ADP

Some ions (like zinc), waste products, etc.

**DRUG ADDICTION**: Complicated term. Can refer to a physiological attachment to a chemical (nicotine, heroine) or an "emotionally-based" addiction (however, many people feel the "emotionally-based additions are strongly tied to dopamine release).

Substance dependence can be diagnosed with physiological dependence, evidence of tolerance or withdrawal, or without physiological dependence. Many of those that are physiologically dependence are chemicals that act as a neurotransmitter, attaching to channels in the NS.

At first, the person gets a "high". But they lose sensitivity, and soon must take the chemical in order to reach the same level as a non-addicted person (loss of high, but NS won't work without the chemical).

**Nicotine**: Physiological addiction. As nicotine enters the body, it is distributed quickly through the bloodstream and crosses the blood–brain barrier reaching the brain within 10–20 seconds after inhalation.

Nicotine increases the levels of several neurotransmitters – acting as a sort of "volume control". It is thought that increased levels of dopamine in the reward circuits of the brain are responsible for the apparent euphoria and relaxation, and addiction caused by nicotine consumption. Nicotine has a higher affinity for acetylcholine receptors in the brain than those in skeletal muscle, so the person must have nicotine in order to reach a normal state.
F) NEUROTRANSMITTER RECEPTORS

- 2 types:

1. CHANNEL-LINKED RECEPTORS - "immediate response" = fast-acting.

- What we saw in the "synapse" section of this chapter. NT attaches directly to them, causes conformational change, pore "opens".

   * if NT = excitatory (ACh, ATP), NT opens a cation channel, usually Na+.

   * if NT = inhibitory (GABA), NT opens anion (usually Cl-) or K+ channel = causes hyperpolarization.

2. G-PROTEIN LINKED RECEPTORS - indirect & slow, but longer-lasting.

- Do not directly open an ion channel; instead, usually act by controlling the production of a SECONDARY MESSENGER (cyclic AMP is the most common) inside the cell. The secondary messenger then opens an ion channel from the inside.

   * Some NTs, like dopamine receptors, work this way, but MANY hormones use this system. More detail in the Hormone section.
V. RELATED CLINICAL TERMS

- **NEUROPATHY** - usually refers to peripheral neuropathy - damage to nerves of the peripheral nervous system, which may be caused either by diseases or trauma to the nerve or the side effects of systemic illness.

- **NEUROTOXIN** - A toxin targeting the nervous system.

  Botulinum toxin is a protein and neurotoxin produced by the bacterium *Clostridium botulinum*. It stops exocytosis of vesicles with ACh.

  It is the most acutely toxic substance known, with an estimated human median lethal dose of 1.3–2.1 ng/kg (that's a NANOGRAM, or 1 billionth of a gram. 1 gram = .04 ounces!) intravenously or intramuscularly and 10–13 ng/kg when inhaled.

  BOTOX: drug that contains this toxin, injected to help with several diseases (not just cosmetic).

- **RETROGRADE AXONAL TRANSPORT** - some virus and toxins escape the immune system by hiding in the PNS or CNS (recall the blood-brain barrier). The hide in neuron bodies, for example. They can follow the neurons ("retrograde" means "against the flow").

  E.G.: polio, the various herpes, tetanus toxin, rabies.

  Occasionally, when the immune system has lowered its surveillance for the virus, they propel themselves along the axon to reach the cell body. This is why you can "feel a cold sore coming" a few days before eruption. The difference between the different herpes: which nerve’s ganglion do they usually congregate in (E.G.: *H. labalis* = trigeminal nerve).

- **MULTIPLE SCLEROSIS** - autoimmune disease of young adults. Immune system attacks and destroys myelin sheaths, causing short-circuiting of NS. Loss of control of muscles, visual problems, etc.

- **CNS Tumors**: as neurons do not undergo mitosis readily, “PRIMARY” tumors in nervous system are usually GLIAL. 90,000 deaths/year. “SECONDARY” tumors arise elsewhere and metastasize within the CNS.