The Nervous System
Functional Neuroanatomy and How Neurons Communicate

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The Nervous System

In response to data collected from the environment, the Nervous System, coordinates the functioning of all the major organs of the body to help maintain overall homeostasis.
Substance abuse impairs nervous system function and target organs become adversely affected – homeostasis becomes compromised.

The Nervous System coordinates the functioning of major body organs.
Parts of the Nervous System

- The nervous system is comprised of two parts: the **Peripheral Nervous System** and the **Central Nervous System**.

  The **Peripheral Nervous System** includes the body’s sense receptors, muscles and glands.

  The **Central Nervous System** comprises the brain and the spinal cord.
As you know, the target organ for psychoactive drugs is the brain.

The brain contains over 100 billion nerve cells, called neurons, that communicate with each other in an electrochemical manner.
The Nervous System

The smallest unit of communication within the nervous system is the neuron.

All behavior is contingent upon the effectiveness of one neuron communicating to other neurons.
Using powerful microscopes, we can see the tiny structures of individual neurons and how they connect with other cells.
#### Types of Neurons

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory Neurons</td>
<td>carry messages to the brain about sensations</td>
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<tr>
<td>Motor Neurons</td>
<td>carry messages from the brain to the muscles and glands</td>
</tr>
<tr>
<td>Intraneurons</td>
<td>are connecting neurons between the sensory and motor neurons</td>
</tr>
</tbody>
</table>

Communication between neurons occurs in the synaptic gaps with chemicals called *neurotransmitters*.
A neural neighborhood

Each neuron synapses with approximately 1,000 other neurons making for about 100 trillion synapses that regulate balance (homeostasis).
A neural complex within a microscopic area of brain tissue
While neurons differ in size and shape, their functional anatomy is the same.
Schwann cells and myelination
Degeneration of mylenation
Neural Communication
Synaptic Transmission
Neurons signal each other in an electrochemical way.
Electron Microscopic Slide of a Single Synapse

- **Synaptic cleft**
- **Presynaptic vesicles**
- **Presynaptic membrane**
- **Postsynaptic membrane**
Neural Communication

Electrochemical process

- **Postsynaptic potential** alters the **membrane potential**
  - EPSP (excitation)
  - IPSP (inhibition)

- Under certain conditions, membrane potential will reach threshold and result in an **Action Potential**

- The action potential, in turn, results in transmitter release at the axon endings
Neurotransmission and the Nerve Impulse

The Nerve Impulse: An Electrochemical Event
Neurotransmission
Characteristics of neurotransmitters

• 2 General effects:
  – EPSP
  – IPSP

• Specific effects depend on receptor activated

• Molecular structure is mimicked by psychoactive drugs
Neurotransmitter Criteria

• Synthesized in a neuron
• Present in axon terminal & released in response to stimulation
• When applied exogenously, get a biological effect
• There is some mechanism for removing them from its site of action (synaptic cleft)
Types of Neurotransmitters

2 main NS signaling substances:

• Small molecule transmitters
  – Amines
    • Acetylcholine: ACh
    • Biogenic amines (monoamines) Catecholamines (DA and NE), Indolamine - Serotonin (5-HT)
  – Amino Acids: Glycine, Glutamate, GABA

• Neuroactive peptides
  – Endorphins, Substance-P, enkephalins

• (Soluble Gases: Nitric Oxide)
Peptide Ntx

(a) Amino acid NT: Glutamate, GABA

(b) Amine NT: Acetylcholine, Norepinephrine

(c) Peptide NT: Arg, Pro, Lys, Pro, Gin, Gin, Phe, Phe, Gly, Leu, Met

Substance P
Review of 7 Primary Neurotransmitters Studied In Behavioral Health
# 7 Neurotransmitters Studied In Behavioral Health

<table>
<thead>
<tr>
<th>Precursor</th>
<th>NTX</th>
<th>Function</th>
<th>Pathology</th>
<th>Drugs</th>
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<tbody>
<tr>
<td>Tyrosine</td>
<td>Dopamine (DA)</td>
<td>Movement, mood, motivation and pleasure</td>
<td>Depression, Schizophrenia, Parkinson's</td>
<td>Antidepressants, Antipsychotics, stimulants, drugs of abuse</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>Norepinephrine (NE)</td>
<td>Mood, alertness, attention, concentration, mental energy</td>
<td>Depression, schizophrenia, ADD</td>
<td>Same as above, beta-blockers</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>Serotonin (5-HT)</td>
<td>Appetite, mood, sex, sleep</td>
<td>Depression, Schizophrenia, appetitive disorders, (bulimia), and OCD</td>
<td>SSRIs, Wellbutrin, Atypical (newer) antipsychotics</td>
</tr>
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<tr>
<td>Glutamic Acid Decarboxylase</td>
<td>Gamma Amino Butyric Acid (GABA)</td>
<td>neural inhibition, restful, tranquil, (an endogenous valium)</td>
<td>Seizure, anxiety disorders, sleep disorders, stress syndromes</td>
<td>Alcohol, CNS depressant drugs</td>
</tr>
<tr>
<td>Choline and Co-enzyme A</td>
<td>Acetylcholine</td>
<td>Movement, memory and mood</td>
<td>Movement disorders, memory impairment, Alzheimer’s, depression</td>
<td>Nicotine, atropine, cannabinoids, depressants</td>
</tr>
<tr>
<td>peptides</td>
<td>Endorphins</td>
<td>Analgesia, blood pressure, mood stress control,</td>
<td>Depression, pain syndromes, blood pressure problems</td>
<td>Morphine-based drugs (opioids)</td>
</tr>
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<td>neural excitation</td>
<td>Seizure, anxiety disorders, withdrawal syndromes</td>
<td>stimulants</td>
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In the 1990s, research focused on how neurotransmitters affected behavior.

Now, the new research places a greater biobehavioral focus on Receptor Sites!
Brain tissue made of billions of neural matrixes

Neurons communicate (signal) through synapses

SUDs cause structural and functional changes

Neural communication is an electro-chemical dynamic
To produce an effect:
1. A drug must bind to and interact with receptors (located on cell membranes)
2. Receptors are usually located on the surface of neurons
3. Drug-receptor binding leads to a change in the functional properties of the neuron

Receptor sites are key to the psychoactive effects a drug has on behavior
Receptors for Drug Action

Receptor: a large molecule (usually a protein) present on the surface of or within a cell.

Neurotransmitters or ligands: biologically active, naturally occurring endogenous compounds produce their effects by binding to receptors.

EXAMPLE

• Serotonin (5-HT) is a neurotransmitter that binds to more than 25 different serotonin receptor proteins

• Each receptor has a small difference in amino acid composition. They have been named as 5-HT1, 5-HT2, 5-HT2a, etc.

• A given drug can bind to one or multiple receptors.
Binding of a Drug to a receptor Results In:

1. **Agonist** action (A) – a drug that binds to a receptor site normally occupied by the neurotransmitter can initiate a cellular response similar or identical to that produced by the neurotransmitter itself. Called a **direct binding agonist** drug.

2. **Agonist** action (B) – a drug that binds to a site near the receptor-site binding site normally occupied by the neurotransmitter can facilitate neurotransmitter binding. Called an **indirect binding agonist** drug.
Binding of a Drug to a receptor Results In:

3. **Antagonist action** – a drug that binds to a receptor site normally occupied by the endogenous neurotransmitter but

* does not initiate a neurotransmitter-like action; and,

* blocks access of the neurotransmitter to its binding site, inhibiting the normal physiologic effect of the neurotransmitter.

4. **Partial agonist/antagonist** – a drug that partially binds and partially blocks (i.e. buprenorphine) receptor sites.
**Agonists and Antagonists**

**Agonists**
Drugs that occupy receptors and activate them.

**Antagonists**
Drugs that occupy receptors but do not activate them. Antagonists block receptor activation by agonists.

**Agonist alone**
- Full activation

**Agonist + antagonist**
- Less activation

**Antagonist alone**
- No activation
A critical concept in behavioral pharmacology is related to a drug’s . . .

Mechanism of Action
Psychoactive drugs work by effecting the way neurons communicate to other cells in the brain and nervous system.
Drug Mechanism of Action

Presynaptic membrane

Neurotransmitter release

Binding at receptor site

Reuptake

Enzyme degradation

Postsynaptic membrane
Drug Mechanism of Action: How They Work

1. Increased production and release of neurotransmitters
2. Reuptake Blocked
3. Degradation Inhibited
4. Receptor sites Blocked
Dopamine and its receptor sites within the MCLP play a critical role in the behaviors of motivation, pleasure and reward.
Dopamine D-2 (DR-D2) receptors play an important role in motivation, pleasure and mood.
Treatment of substance use disorders can produce changes in brain dopamine to near-normal functioning

**AND**

Treatment teaches clients the skills necessary to compensate for dopamine receptor site deficits.

Treatment helps patients learn and apply *dopamine-enhancing* lifestyles.
Key points:

1. Drug use triggers changes in brain chemistry producing changes in behavior (physically, mentally, emotionally)

2. Among other things, drugs with abuse potential target the brain’s reward circuitry and activate dopamine systems.

3. With prolonged use, drugs deplete targeted neurotransmitters causing a lasting deficiency syndrome that is both functional and structural.

4. The brain compensates for drug-induced changes in a number of ways through neuroadaptation (i.e. tolerance, withdrawal, upregulation, etc.)

5. Substance use disorders are expressed in different ways through various subtypes.
Neurobiological Processes at Synapse:

1. Depolarization
2. Ca²⁺ Influx
3. CaM II
4. Priming
5. Fusion
6. Release
7. Diffusion
8. Enzymatic Degradation
9. Receptor Binding
10. Conductance Change

Secondary processes:
- A. Biosynthesis
- B. Storage
- C. Transport
- 8.a. Transmitter Uptake
- 8.b. Membrane recycling
Neurotransmitters, such as dopamine and acetylcholine, are chemicals that carry signals from neuron to neuron across gaps called synapses. A sending neuron synthesizes neurotransmitter molecules and bundles them into packages; when the neuron becomes electrically excited, it releases the neurotransmitter molecules into the synapse. Once in the synapse, each molecule may:

- Dock on a receptor on the receiving neuron, initiating a cellular response (binding);
- Re-enter the sending neuron via a molecular conduit called the transporter (re-uptake);
- Encounter a metabolizing or degrading enzyme that destroys it (enzymatic degradation).

Drugs of abuse produce psychoactive effects by disrupting the normal balance of neurotransmitter release, signaling, recovery, and metabolism. Genetic variation in receptors, transporters, or enzymes can limit or exacerbate these effects and thereby affect susceptibility to substance use disorders.
Assignment for next week:

Describe the Synapse illustration we just diagramed to someone you know.

NOTE: It’s not that important if the person you are explaining the illustration to understands what you are talking about. It is important that you feel comfortable describing the neurobiological events at synapse.