Atypical Visual Development in Infants at Risk for Autism Spectrum Disorders (ASD)

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Lecture 2:

Neurotransmitters and Drugs

Osher Series

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Today’s Lecture Outline

1) Neurotransmitter (NT) Types

2) Reminder about Neural Communication

3) A Day in the Life of a NT

4) Synapses & Drugs
MAJOR NEUROTRANSMITTER (NT) TYPES

**Acetylcholine (Ach)**
- Acetate (met)
- Choline (diet)

**Monoamines**

**Indoleamines:**
- **Serotonin**
  - From Tryptophan in diet

**Catecholamines**
- **Dopamine (DA)**
- **Nor-** (NE) **Epinephrine**
- **Epinephrine (EPI)**

**Amino Acids**
- **GABA**
- **Glutamate**

**Peptides**
- Endorphins
- Substance P
Overview of Events:
1) Electrical signal starts in the *presynaptic* neuron and travels down the axon to the presynaptic terminals.
2) Causes release of *neuromodulator* into the *synapse*
3) *Neuromodulator* binds to *receptors* ($R$) on *postsynaptic* neuron’s dendrites
4) Triggers an *electrical signal* in postsynaptic neuron, and so on…..
A Day in the Life of a Neurotransmitter (NT)
The neurotransmitter needs to GO AWAY!
6) The NT needs to go away!

a) NT is *re-absorbed* by the presynaptic terminals, i.e., *recycled*
   e.g., Monoamines

b) NT is altered (in the synapse) to be *inactive*
   
   i) broken down by **enzymes**
      e.g., Acetylcholinesterase (ACh):
      ACh -> acetate + choline
      choline reabsorbed and added to acetate
   
   ii) converted to an *inactive* state by **enzymes**
      e.g., MAO (monoamine oxidase),
      converts Monoamines to inactive state
      - drugs that inhibit MAO are used for depression

c) Release of more NT is inhibited by activation of
   *presynaptic AUTO-receptors*

d) NOTE: NT will *float away* eventually (relevant to drugs that inhibit re-absorption)
MAJOR RECEPTOR TYPES (named for which NT binds to it)

But note: receptors are sometimes named for Drug they bind to (no standard rule…….)

**Acetylcholine (Ach) Receptor:**
- ~4 Nicotinic Receptor Types (Ionotropic, fast acting)
- ~5 Muscarinic Receptor Types (Metabotropic, slow acting)
(of course bind Ach too)

**In PNS: at Neural-Muscular Junction**
- Nicotinic (skeletal muscle, e.g., bicep, diaphragm)
- Muscarinic (smooth muscle, e.g., uterus)

**In CNS: Both Nicotinic and Muscarinic Exist**

**Norepinephrine (NE):** 2 receptor types
- Alpha Receptors
- Beta Receptors

**Dopamine (DA):** ~5 Receptors

**Serotonin (5-HT):** ~14 Receptors
How Drugs Affect Neurons

**Agonist:** mimics or increases the effect of a neurotransmitter system

**Antagonist:** blocks or decreases the effect of a neurotransmitter system

5 ways to be an **AGONIST:**

1) Drug Stimulates Receptor: Mimics NT
   - e.g., Nicotine attaches to *Nicotinic Ach* receptor
     (and has roughly same effect)
   - e.g., XANAX (Benzodiazepine) attaches to *GABA* receptor
     (GABA is INHIBITORY)

2) Drug stimulates release of more NT
   - e.g., Amphetamines -> NE
     -> DA

3) Drug blocks re-absorption of NT at the synapse
   - e.g., Amphetamines & Cocaine (& Ritalin)
     Cocaine blocks the re-absorption of DA
     “Crashing” (depletion, because NT “floats away”)

4) Drug inhibits re-absorption of NT at the synapse
   - e.g., Amphetamines & Cocaine (& Ritalin)
     Ritalin blocks the re-absorption of NE

5) Drug inhibits re-absorption of NT at the synapse
   - e.g., Amphetamines & Cocaine (& Ritalin)
     Amphetamines blocks the re-absorption of DA
4) Drug acts as a precursor for the NT
e.g., L-DOPA synthesizes to DA (Parkinson’s)

5) Drug inactivates enzyme that breaks down NT:
e.g., Physostigmine inhibits Acetylcholinesterase
Iproniazid inhibits Monoamine Oxidase
5 ways to be an **ANTAGONIST:**

1) Drug blocks receptor  
   e.g., **Curare** attaches to *Acetylcholine (Ach) receptor*,  
   and keeps Ach from binding to receptor -> **muscle paralysis**

2) Drug inhibits NT release  
   e.g., *Clostridium botulinum* (bacteria) releases **botulin toxin** ->  
   inhibits *release* of Ach -> **muscle paralysis** (called “botulism”)

3) Drug inactivates synthetic enzyme  
   e.g., **AMPT** blocks enzyme that converts *tyrosine* -> **DOPA**

4) Drug makes the synaptic vesicles “leaky”  
   e.g., **reserpine**: *monoamine* vesicles

5) Drug stimulates autoreceptors  
   e.g., **Clonidine**: *NE autoreceptors*
**Recreational Drugs**
*(not always clear if they are Agonists or Antagonists)*

**Hallucinogenic Drugs (LSD, PCP, mescaline, X)**

*Serotonin system. Agonist??*
- Creates hallucinations, dream-like state
- Raphe nuclei in brainstem (sleep and dreams)

**Other Serotonin-Related (Agonist) Drugs**

- **PROZAC** (depression) -> prevents re-absorption
- **St. John’s Wort** for Depression (more natural?)
  - Social phobias, schizo, bulimia, autism

**Opiates (Heroin, Morphine, Methadone)**

- Endorphin receptor **AGONISTS**
- Used as “pain-killers” (more later in course)
- Produce “euphoria”
Marijuana (THC and other cannabinoids, from Cannabis plant) acts on cannabinoid receptors (numerous in the brain especially in HIPPOCAMPUS). Agonist? dissolve in body FATS intensified sensory experience, time slows down used clinically for pain, nausea, glaucoma, migraines

“Overdosing”: shutting down the medullary respiratory center Barbiturates and Opiates -> Yes Marijuana -> NO

Ondine’s Curse