NEUROTRANSMITTERS NTs (Handout, Learn 1st)
Revised 7/2/12

- Are chemical LIGANDS released into synaptic clefts to bind with specific receptors to alter membrane permeability and thereby alter membrane potential. Result may be an EPSP or an IPSP.

- Are the CHEMICAL “LANGUAGES” of neuronal communication. Neurons “talk” to each other and to effectors via the release of NTs.

- About 50 different chemicals are known or suspected to be NTs. Some neurons release only one kind of NT, but most make 2 or more NT.

- MOST NTs ARE AA BASED (proteins) and synthesized by the neurons themselves in their synaptic knobs or in the cell body and transported to synaptic knobs.

- Sleep, comas, consciousness, unconsciousness, joy, anger, depression, motor impulses to skeletal muscle for mobility, etc. are all due to NTs.

- The effect of any NT could be depolarization (to create an EPSP) or hyperpolarization (to create an IPSP). It is the receptors present at the cleft that determine the response. Therefore, the same NT may have a stimulating effect in one part of the brain and an inhibitory effect in another. Any given synapse will, however, always be either excitatory or inhibitory.

- Effects of NTs on postsynaptic membranes are very short-lived due to:
  1. decomposition by enzymes
     e.g. acetylcholine -- decomposed by ACETYLCHOLINESTERASE
     e.g. NE and Serotonin -- decomposed by MONOAMINE OXIDASE (MAO)
  2. reuptake back into synaptic knob for reuse
  3. diffusion away from the cleft

   The benefit of the effects being short-lived is that it provides a greater degree of control.

- Understanding the basics of NTs and chemical synapses enables us to understand the effects of many drugs and meds.
  See handout: “Generic Effects of Drugs and Medications”
  See handout: “Neurotransmitter Hall of Fame”
  Know clinical examples of NTs.
EFFECTS OF DRUGS/MEDICATIONS (handout) (Learn 2\textsuperscript{nd})

1. **MIMICS A NT OR HORMONE...** they bind to the same receptor sites yielding the same effect.

   - The drug **NICOTINE** mimics the neurotransmitter ACh in the brain.
   - The drug **VALIUM** produces a sedating effect by mimicking a naturally sedating NT called GABA.
   - The drug **PITOCIN** mimics the natural hormone **OXYTOCIN** thereby inducing labor contractions associated with childbirth.
   - The drugs **MORPHINE**, **DEMEROL**, and **HEROIN** all relieve pain by mimicking your own naturally occurring pain blocking NTs called **ENDORPHINS** and **ENKEPHALINS**.
   - The drug **DOPAMINE** in the PNS mimics norepinephrine (NE) causing vasoconstriction thereby \( \uparrow \) BP.

2. **BLOCKS RECEPTOR SITES...** they bind to the receptor sites of an NT but do NOT produce the same effect thus preventing the NT from having its effect.

   - The drug **BENADRYL** (an antihistamine) blocks \( H_1 \) and \( H_2 \) receptor sites for histamine.
   - The drug **PROCARDIA**, a “calcium channel blocker,” inhibits smooth muscle contraction resulting in dilation of coronary and peripheral arteries thereby \( \downarrow \) BP.
   - The drug **INDERAL**, a “BETA BLOCKER,” blocks beta receptors for NE at the heart thereby \( \downarrow \) HR and \( \downarrow \) strength of contraction thereby \( \downarrow \) high BP.
   - **Curare** blocks ACH receptor sites causing temporary paralysis.
   - The drug **VERAPAMIL**, a “calcium channel blocker” helps suppress certain cardiac dysrhythmias.

3. \( \uparrow \) or \( \downarrow \) THE AMOUNT OF NT RELEASED

   - **AMPHETAMINES** increase the release of NE and dopamine. **COCAINE** blocks the reuptake of both NE & dopamine. The surplus of these “feel good” NTs in the CNS is what provides the “rush” users become addicted to.
   - Botulinus toxin (botulism) blocks release of ACH at neuromuscular junctions.

4. \( \uparrow \) or \( \downarrow \) THE RATE OF REMOVAL OF A NT FROM THE CLEFT... thereby lessening or prolonging the effect of the NT

   - The popular antidepressants Prozac & Paxil both inhibit the reuptake of the NT **SEROTONIN** which is a “feel good” NT of the CNS. The “feel good” effects of your own serotonin are thereby prolonged.

5. \( \uparrow \) or \( \downarrow \) MEMBRANE PERMEABILITY to Na\(^+\), K\(^+\), Ca\(^{++}\), Cl\(^-\) thereby shifting the polarity of neuronal membranes either closer to or farther from threshold. Thus, when NT is released the neurons are thereby made either more likely or less likely to “fire.”

   - The pain medication **LIDOCAINE** \( \downarrow \) mem. perm. to sodium by preventing the opening of voltage-gated sodium channels.
## NEUROTRANSMITTER HALL OF FAME (handout) (learn 3rd)

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<tr>
<th>Neurotransmitter</th>
<th>Effect</th>
<th>Clinical Examples</th>
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| Acetylcholine (ACH) | Excitatory or Inhibitory depending on receptors. Always excitatory at skeletal muscle. | - Reduced levels of ACH in some brain areas noted in Alzheimer’s patients.  
- Nicotine mimics ACH in the brain triggering the release of excitatory hormones such as epinephrine and norepinephrine as well as dopamine.  
- Effects of ACH at skeletal muscle are prolonged by organophosphate insecticides (Malathion) and nerve gas which inhibit AChase resulting in tetanic muscle spasms and neural “frying.”  
- Release of ACH at skeletal muscle is inhibited by botulinus toxin.  
- ACH receptors at skeletal muscle can be blocked by curare.  
- Reduction in # of ACH receptors at skeletal muscle in myasthenia gravis. |
| Norepinephrine (NE) | Excitatory or Inhibitory depending on receptors. | - NE is released in greater amounts in your brain helping to create those “warm fuzzy” feelings associated with affection, romance, love, etc. Infants who receive lots of affection show more rapid and extensive brain development.  
- Amphetamines increase the release and/or block the reuptake of NE and dopamine resulting in overstimulation of the cortex. This is the “rush” users get addicted to.  
- Tricyclic antidepressants and cocaine (Elavil & others) inhibit reuptake of NE and serotonin from synaptic clefts thereby prolonging their effects.  
- NE is released in greater amounts in your brain when you have a positive “can do” attitude. This causes the release of more nerve growth factor to help with learning and/or recovery from stroke. People with positive attitudes recover faster and more completely.  
- NE is released in greater amounts during the “fight or flight” response thereby increasing the # of neurons responding to sensory input. You perceive this as “heightened awareness.”  
- MAO inhibitors prolong the effects of NE and serotonin by inhibiting the action of the enzyme monoamine oxidase (MAO). |
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<th>Generally</th>
<th>Effects</th>
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| Endorphins and Enkephalins | Inhibitory | - Your own natural opiates... “your body's own morphine.”
| | | - Inhibit the sensation of pain by:
| | | 1. preventing the release of substance P or
| | | 2. inhibiting ascending pain messages at the hypothalamus or thalamus or enhancing the release of dopamine at frontal cortex.
| | | - Narcotic pain killers such as morphine, Demerol, heroin, and methadone mimic endorphins & enkephalins. They bind to and activate the same receptor sites.
| Substance P | Excitatory | - The “Pain NT.”
| | | - Released in the spinal cord at the ends of afferent (sensory) neurons carrying pain impulses to the CNS.
| | | - Endorphins, enkephalins, morphine, heroin, etc. may reduce pain by inhibiting the release of Substance P thereby reducing the # of impulses reaching the cerebral cortex.
| Serotonin | Inhibitory | - Involved with mood, anxiety, appetite, nausea, migraine headaches, sleep induction, memory and learning.
| | | - Depending upon location in brain the effect may be calming & soothing OR stimulating and “mood elevating” similar to the “feel good” NTs.
| | | - Helps regulate the amount of information getting through the thalamus to the frontal cortex.
| | | - Deficiencies of serotonin lead to anxiety and depression.
| | | - Serotonin also helps you to be cautious and careful and use reasonable judgment. Drinking alcohol decreases serotonin levels causing you to have poor judgment, act irrationally, start fights, act stupid, drive dangerously, etc.
| | | - Chocolate elevates serotonin levels.
| | | - Reuptake is inhibited by antidepressant/antianxiety drugs such as Prozac and Paxil which are Serotonin Specific Reuptake Inhibitors (SSRI). Effects of serotonin are thereby prolonged.
| | | - Levels of serotonin are often elevated in schizophrenia causing delusions, euphoria, & hallucinations.
| | | - Activity is blocked by LSD
| | | - Activity is enhanced by ecstasy (MDMA)
| Dopamine | Generally Excitatory in cerebral cortex  
Inhibitory in the substantia nigra of the midbrain | • Dopamine is released (along with NE) in greater amounts when you have those “warm fuzzy” feelings associated with affection, romance, love, etc.  
• Endorphins cause levels of dopamine to increase thereby “smothering” the brain with pleasurable sensations rather than painful sensations.  
• **L-dopa and amphetamines** increase the release  
• Reuptake is blocked by cocaine and NE resulting in overstimulation of the cerebral cortex. This is the “rush” users get addicted to.  
• Dopamine neurotransmission is increased in cases of **schizophrenia**.  
• Dopamine deficiencies are present in **Parkinson’s disease**. Treatment is L-dopa to stimulate the synthesis of dopamine. |
| --- | --- | --- |
| Glutamate | Generally Excitatory | • Important in learning and memory  
• The “Stroke NT.” During a stroke, oxygen deprived neurons release large amounts of glutamate causing postsynaptic neurons to release nitric oxide (NO) which damages nearby cells. |