Behavioral Neuroscience Notes

PSYC 360

Start

January 21, 2025

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End

May 14, 2025

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CHAPTER 7

PSYCHOPHARMACOLOGY

7.1 Overview – Unit 3

- Neurotransmitters and Neuromodulators
  - Psychopharmacology
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  - Pain

7.1.1 Psychopharmacology in Detail

- The scientific study of the effects of drugs on the nervous system and behavior.
- Psychopharmacology is the study of how drugs affect the mind and behavior.
  - Psychotherapeutic drugs
  - Better understanding of how things normally work.

Principles of Drug Action

- *Selective Action* – Drugs are selective in their action on the nervous system.
  - *Sites of Action* – The location at which a drug interacts with the body to produce its effects.
  - Side effects are often due to the drug acting on sites other than the intended target.
    - Thus, side effects are relative to what our preferred site of action is.
  - *Example*: Opioids primarily affect the opioid receptor system.
- Drugs don't CREATE effects, they *modulate* ongoing cellular activity.
  - That is, they affect behavior by affecting neural transmission in some way.
  - *Agonist* – A drug that mimics or enhances the **effects of a neurotransmitter**.
    - Facilitates post synaptic effects.
    - *Example*: Morphine mimics endorphins, which are natural painkillers.
  - *Antagonist* – A drug that blocks or inhibits the effects of a neurotransmitter.
    - Inhibits post synaptic effects.
    - *Example*: Naloxone blocks the effects of opioids, reversing their effects.
  - Agonistic effects can become antagonistic if the drug is taken in excess.
    - *Example*: I make a neuron fire a neurotransmitter, but I also block the reuptake of that neurotransmitter.

Basic Process

- *Precursor* – A substance from which another substance is formed. AKA, the ingredients used to make a neurotransmitter.
- $$\text{Precursor} \xrightarrow{\text{Synthetic Enzyme}} \text{NT} \xrightarrow{\text{Metabolic Enzyme}} \text{Inactive Metabolite}$$
  - *Synthesis* – The process of creating a neurotransmitter from its precursors.
  - Sometimes, we break down the precursor to build the neurotransmitter.

7.1.2 Other Ways of Agonist and Antagonist

- Block Ca^{2+} channels from opening (antagonist)
- *Mimetic* – Mimics the action of a neurotransmitter.
  - *Direct Agonist* – Binds to the same receptor as the neurotransmitter and mimics its effects.
  - *Indirect Agonist* – Binds to a different site on the receptor and enhances the effects of the neurotransmitter.
- Blocking agent
  - Competitive
    - *Direct Antagonist* – Binds to the same receptor as the neurotransmitter and blocks its effects.
  - Non-competitive
    - *Indirect Antagonist* – Binds to a different site on the receptor and blocks the effects of the neurotransmitter.
  - *Inverse Agonist* – Binds to the same receptor as the neurotransmitter and produces the opposite effect.
- *Depolarizing* or *Desensitizing Agent* – A drug that causes the AP to stay in a depolarized state; refusing to let the neuron go through another AP, and it stays in the absolute refractory period. (Antagonist)
- Interfere with vesicles (leaky or transporter proteins). (Antagonist)
- Interfere with docking proteins. (Antagonist)
- Selectively deactivate autoreceptors. (Agonist)
- Selectively activate autoreceptors. (Antagonist)

7.2 What Do These Chemicals Between Neurons Do?

- Transmit information.
  - Glutamate
  - GABA
  - Glycine
- Modulate information.
  - Every other neurotransmitter.

7.3 Classes of Neurotransmitters (Revisited from Lab)

- Amino Acids
  - Glutamate, GABA, Glycine
    - *Glutamate* – Synthesized from precursor glutamine by an enzyme called *glutaminase*. It is the most common excitatory neurotransmitter in the brain.
      - Related closely with the *NMDA* receptor, which is a type of glutamate receptor that is important for synaptic plasticity and memory formation.
      - One drug that binds to this site, *Phencyclidine (PCP)* (direct antagonist), is a drug that blocks the NMDA receptor and causes hallucinations and dissociation. Another drug that is thought to bind here, *Ketamine* (direct antagonist), is a dissociative anesthetic that is used in surgery and is also being studied as a treatment for depression.
      - **Reuptake and Deactivation**
        - Reuptake is done by the *excitatory amino acid transporters (EAATs)*. These are important because it reduces the change of excitotoxicity, which is believed to be involved in damage to the brain in stroke and amyotrophic later sclerosis (ALS, Lou Gehrig's disease).
    - *GABA* – Synthesized from precursor glutamate by an enzyme called *glutamic acid decarboxylase (GAD)*. It is the most common inhibitory neurotransmitter in the brain.
- *Amines* (monoamines) – Derived from amino acids
  - Catecholamines
    - Contain catechol and derived from the amino acid tyrosine.
    - *Tyrosine* – Precursor for the catecholamines.
    - Dopamine (DA), Norepinephrine (NE), Epinephrine (Adrenaline)
    - Dopaminergic, Adrenergic, and Noradrenergic systems.
  - *Indolamines*

- *Serotonin* (5-HT)
- *Melatonin*

- Peptides (AKA: Neuropeptides)
  - Endogenous Opioids
- Acetylcholine (ACh)
- Lipids
  - *Anadamide* (Sanskrit for "bliss") – Endogenous cannabinoid.
  - These appear to be synthesized on demand; produced and released as needed and not stored in synaptic vesicles.
  - Anadamide is deactivated by the enzyme *fatty acid amide hydrolase (FAAH)*.
- **Two Other Classes**
  - Nucleosides
    - Adenosine
  - Soluble Gases
    - *Nitric Oxide (NO)* – Required for an erection.

7.4 Acetylcholine (ACh)

- First neurotransmitter discovered.
  - Otto von Loewy – Discovered ACh in 1921.
    - This guy took a frog heart and put it in saline. Then, he took simulated the parasympathetic part of the vagus nerve, and saw that the heart slowed down.
    - He then took the saline and put it in a different frog heart, and saw that the heart slowed down again.
    - "Vagusstoff" (ACh) – The chemical that was released from the vagus nerve that slowed the heart down.
    - Cholinergic – Referring to ACh.
- ***Some* Functions**
  - **Function in the ANS:**
    - Sympathetic
      - Spinal nerve leaves the cord and synapses in the paravertebral ganglion (ACh)
      - Then makes neuromuscular junction with smooth muscles and glands (NE)
        - *Neuromusclar Junction* – The synapse between a motor neuron and a muscle fiber.

        - *Paravertebral Ganglion* – A ganglion located next to the spinal cord.
        - Except sweat glands (ACh)
      - *Sympathetic Chain* – A chain of ganglia that runs parallel to the spinal cord. This is the reason for when you get anxious, ALL of your body gets anxious.
    - Parasympathetic
      - Spinal nerve leaves the cord and synapse in the parasympathetic ganglion (ACh)
      - Then makes neuromuscular junction with smooth muscles and glands (ACh)
    - The only NT in the parasympathetic branch.
    - NT of the preganglionic sympathetic branch.
  - **Function in the Somatic NS**
    - Excites the neuromusclar junction (ACh)
    - So, ACh is important for getting motor messages out to all kinds of muscles and glands.
  - **Function in the CNS**
    - ACh is important in:
      - Learning and alertness (*Basal Forebrain*)—activates the cortex and facilitates learning.
        - *Nucleus Basalis* – Projects to the cortex
        - *Medial Septal Nucleus* and *Nucleus of Diagonal Band* – Projects to the hippocampus through the fornix.
      - Memory (*medial septal nucleus*)—modulate the hippocampus
      - REM sleep generation (*Pedunculopontine nucleus (PPT)* and *Laterodorsal Tegmental Nucleus (LDT)*)—projects to the pons and thalamus.
      - Reward system.
- **Synthesis and Metabolism**
- **Drugs and Disorders**

7.4.1 ACh Synthesis and Metabolism

- **Synthesis**
  - In a nutshell: A breakdown of lipids leads to Choline, which is the precursor for ACh. Acetate is the anion in vinegar (Acetic acid). Then, this is combined with Acetate to make ACh.
  - In more detail:
    - CoA attaches to an acetate ion (*Acetylcoenzyme A (acetyl-CoA)*).

- Then, *choline acetyltransferase (ChAT)* transfers the acetate from the acetyl-CoA to the choline molecule.
- Mnemonic: **ChAT**: From right to left: Transfers acetate to choline.

- **Metabolism**
  - ACh is broken down by the enzyme *acetylcholinesterase (AChE)* into acetate and choline. Nice and simple!
  - The choline is taken back up by active transport and reused, and the acetate is broken down and eliminated.

7.4.2 Two Types of Cholinergic Receptors

- Nicotinic Receptors
  - Agonist at low doses, but antagonist at high doses.
  - Iontropic.
  - Found at the Neuromusclar Function in the PNS.
  - *Curare* (direct antagonist) – A drug that blocks nicotinic receptors, causing paralysis.
    - Competitive blocking agent
    - Paralysis, surgery
- Muscarinic Receptors
  - Comes from a hallucinogenic mushroom (Amanita muscaria).
    - **Don't confuse with Serotonin's Mescaline: Cactus; nor Psilocybin: Mushroom.**
  - Vikings (probably took this drug before raiding) and Koryaks (Nordic people who used this mushroom in religious practices).
  - Metabotropic receptors.
  - Predominates in the CNS (although, both types are found in the CNS).
  - *Atropine* (direct antagonist) – A drug that blocks muscarinic receptors, causing pupil dilation and increased heart rate.
    - Competitive blocking agent
    - Belladonna alkaloids (deadly nightshade)

7.5 MORE Drugs and Toxins Affecting ACh

- *Botulinum Toxin* – A waste product of *Clostridium botulinum*, which are bacteria who grows without oxygen.

- Interferes with Ca^{2+} influx channels, preventing the release of ACh.
- Because Botox causes paralysis, it can interfere with emotional *expression* because it paralyzes muscles like the orbicularis oculi.
- Additionally, since we know that expression influences experience, when we paralyze these muscles, then the emotional *experience* is also negatively affected.
- **Does Botox Decrease Emotional Experiences?**
  - Population: Women who want wrinkles gone.
  - One IV: two levels: Botox or restylane (dermal filler).
  - Method: Everyone had wrinkle reduction. AND, Everyone watches some emotion evoking movies.
  - Results: Botox group had less emotional experience than the restylane group.
  - **Is this a good thing?**
    - Another study takes a sample of depressed people and gives them either Botox or a placebo.
    - Results: 15% of placebo had a decrease in depression, while 52% of the Botox group had a decrease in depression.
- Botox can also be used to treat migraines, cerebral palsy, and hyperhidrosis (excessive sweating).

- *Black Widow Spider Venom* – A neurotoxin that causes the release of ACh at the neuromuscular junction, causing continual release of ACh and paralysis.
- *Cobra and Krait Venom* – A neurotoxin that blocks the binding of ACh to nicotinic receptors, causing paralysis.
- *AchE Blockers* – Comes into contact with the enzyme that breaks down ACh, causing an increase in ACh in the synaptic cleft.
  - Irreversible
    - Insecticides (Parathion)
    - Nerve gas: DFP (Diisopropylfluorophosphate (don't need to know the whole name)) and Sarin.
      - Readily crosses the blood-brain barrier so PNS and CNS are affected.
      - Antidote?
        - *Atropine* – A drug that blocks muscarinic receptors, preventing the effects of excess ACh.
        - *Pralidoxime* – A drug that reactivates AChE, allowing it to break down ACh again.
  - Reversible
    - *Neostgmine* (**Prostigmin**) and *Physostigmine* (**Antilirum**) – Drugs that inhibit AChE, increasing the amount of ACh in the synaptic cleft.
      - Doesn't cross the blood-brain barrier, so it only affects the PNS.

- Used to treat *myasthenia gravis* (a disease that causes muscle weakness and fatigue).
  - Autoimmune disease that attacks nicotinic receptors at the neuromuscular junction.
- *Donepezil* (**Aricept**) and *rivastigmine* (**Exelon**) – These drugs do the same thing as the above drugs, but they cross the blood-brain barrier and are used to treat Alzheimer's disease and Parkinson's disease (only the cognitive part).

7.6 New Drug for Schizophrenia

- We'll talk about dopamine drugs later in this unit.
- This new drug now:
  - *Xanomelne and trospium chloride* (**Cobenfy**) – A drug that blocks the muscarinic receptors in the CNS, but not in the PNS.
  - Dopamine but also Ach!

7.7 Catecholamines

- Dopamine (DA)
- Norepinephrine (NE)
- Epinephrine (Adrenaline)

7.7.1 Dopamine (DA)

- Synthesis and Metabolism
- Function
- Drugs and Disorders

Dopamine Synthesis

- Tyrosine was first discovered from cheese (tyrosine = cheese).
  - Tyrosine is the precursor for DA, NE, and Epi.
  - *Tyrosine Hydroxylase* – The rate-limiting enzyme in the synthesis of catecholamines.
    - Converts tyrosine to L-DOPA.
    - L-DOPA is the precursor for DA, NE, and Epi.
  - L-DOPA is converted to DA by the enzyme *DOPA decarboxylase*.

Dopamine Metabolism

- DA is broken down by the enzyme *Monoamine Oxidase (MAO)* into *Dihydroxyphenylacetric acid (DOPAC)*.
- Then, *Catechol-O-methyltransferase (COMT)* converts DOPAC into *Homovanillic acid (HVA)*.
- Also, starting from DA, we can use COMT to convert it to 3-methoxytyramine (3-MT), then with MAO, we can convert it to HVA.

DA Function

- **Movement/Motor systems**
  - *Nigrostriatal System* – Starts in the substantia nigra and ends in the striatum (caudate nucleus and putamen).
  - Here's the route: We start at the striatum, which then sends an inhibitory GABA signal to the substantia nigra, who sends a reciprocal inhibitory DOPA signal back to the striatum nerve that sends an inhibitory GABA signal to the globus pallidus. Then, the globus pallidus excites the thalamus, who then excites the primary motor cortex, who then excites movement.
    - Note that if the inhibitory signal to the substantia nigra is limited, then the signal that the striatum sends to the globus pallidus is much stronger, which leads to a weaker signal to the thalamus, and thus to movements.
  - Parkinson's Disease symptoms:
    - Weakness,
    - Tremor at rest,
    - Muscle rigidity,
    - Problems with balance,
    - Abnormal gait,
    - Trouble learning
  - Treatment
    - *Reserpine* (**Raudixin**) for ↓ **BP** (Not in use anymore because it caused Parkinson's-like symptoms)
      - 1960's
        - Blocks monoamine transporters
          - Developed Parkinson's symptoms
          - Can't fill vesicles and DA is lowered
      - Then, discovered Substantia Nigra was pale.
    - L-DOPA can be a direct treatment for Parkinson's as well.
    - *MPTP* – Neurotoxin for DA cells in the Nigrostriatal System (which is not endogenous).

- **History of MPTP – or why you shouldn't use illicit drugs**
  - 1982 – young California heroin users
  - Had used what they THOUGHT was synthetic heroin
    - *MPPP* – Opioid analgesic drug
      - Not used clinically
      - Illegally manufactured for recreational drug use
    - INSTEAD it was MPTP (oh no!)
      - They instantly developed Parkinson's-like symptoms
      - Bad for them, but good for us because we can study it.
        - Led to animal model development and possible treatment ideas.
  - We don't know why Parkinson's patient's cells are dying, but maybe something similar.
  - MPTP is converted to the chemical *MPP+* by the enzyme MAO (which is what breaks down DA), which is what damaged the cells.
    - Question: Could MAO-I improve Parkinson's?
    - Yes!
    - *Deprenyl*, also called *selegiline* (**Eldepryl**, **Jumex**) – A drug that inhibits MAO, can slow down progression of the disease.
- New treatment
  - Molecule keeps proteins from misfolding
  - *Lewy Bodies* – Misfolded proteins that are found in the brains of people with Parkinson's.
    - These are toxic to DA cells
- *Huntington's Chorea* – A genetic disorder that leads to uncontrolled movements and cognitive decline.
  - Too little GABA from the Striatum to the Substantia Nigra causes an increase in dopamine back to the Striatum which, in turn, lessens the signal to the Globus Palidus, which increases overall movements.
  - *Tetrabenazine* (**Xenazine**) – Drug that inhibits the DA vesicle transporters.
  - *Pallidotomy* – A surgery that affects the Globus Pallidus to inhibit movement.
- *Choreoathetotic Movements* – too much movement
  - *Athetosis* – Slow continually writing movements
  - *Choreic* (to dance) – Rapid, purposeless, involvuntary movements

- **Behavioral Arousal and Attention**
  - Narcolepsy
    - *Methylphenidate* (**Ritalin**) – A drug that increases DA and NE in the brain, used to treat ADHD, but can also be used for narcolepsy.

- *Hypocretine* – A neuropeptide that is involved in the regulation of sleep and wakefulness.
  - Created by the lateral hypothalamus.
  - Hypocretine: *Hypo* for *hypo*thalamus, *cretine* for *secretin* (a hormone).
  - *Orexin* – Another name for hypocretine; makes you want to eat.
- From hypocretine, researchers developed an antagonist for the orexin receptor, which is used to treat insomnia. This drug is called *Suvorexant* (**Belsomra**).
- **Treatment**
  - *TAK-994* – OX2R (Orexin-2 receptor) Agonist
  - *Hcrt-1* – Intranasal hypocretine-1 (orexin-1) agonist
  - Hypocretine Cell Transplant
  - Gene Therapy: *introduce* preprohypocretin gene into the brain to make more hypocretine.
  - Opiates (exogenous) can increase the number of hypocretin-producing cells in the brain.
  - Indirect role for opiate agonists in treating narcolepsy.

- ADHD
  - Uses Methylphenidate for selective attention.
- *Mesocortical System*
  - From ventral tegmental nucleus to prefrontal cortex, limbic CORTEX, hippocampus, all frontal lobes, and association areas of parietal and temporal lobes in primates.
  - Short-term memories, planning, and problem-solving are all associated with this system.

- **Reinforcement and Reward**
  - *Mesolimbic System (MLS)* – Responsible for reward and reinforcement.
    - From vental tegmental nucleus to limbic system
      - Amygdala, hippocampus, and nucleus accumbens.
      - Opioids cause the release of dopamine at the nucleus accumbens, which is the pleasure center of the brain.
  - James Olds & Peter Milner (1954)
    - They asked: "Does electrical stimulation of the reticular formation facilitate learning?"
    - James Olds visits a conference and listens to Neal Miller, who says electrical stimulation is aversive, so it should be avoided.
    - One lone rat was put in a box with a lever, and when the rat pressed the lever, it would get a shock to the reticular formation. He ended up pressing the level 700 times per hour.

- More studies of this
  - Skinner box
    - Rats press 2000 times per hour for a shock to the MLS.
    - Monkeys press 8000 times per hour for a shock to the MLS.
    - Starving animals will choose the MLS over food 80% of the time.
    - They also press the button for these conditions too:
      - Thirsty,
      - Getting shocked (at their feet),
      - Mother instincts.
- Delgado (1969) – For people who were getting their brain stimulated for seizures, this researcher also asked them about what they thought of the stimulation. They all thought that it was pleasurable.

Part II

Behavioral Neuroscience Lab Notes

CHAPTER 8

LAB 2: PSYCHOPHYSIOLOGY

We're starting with three studies:

1. **Study 1:** Blinking:
    - Three levels of blinking:
        - Reflexive blinking. Ex: When a puff of air is directed at the eye.
        - Voluntary blinking. Ex: When you're asked to blink.
        - Endogenous blinking. Meaning: "originating from or due to internal causes."
    - *Endogenous blinking* is the focus of this study.
        - Endogenous blinks occur during reading or speaking and reflect changes of attention and changes in thought processes. The more attention required by a visual task; the fewer endogenous blinks occur.
        - More attention required is associated with fewer endogenous blinks. Especially for visual tasks.
        - **The harder the tasks → the fewer the blinks.**
        - Even when a task is not visual, there is a decrease in endogenous blink rate (EBR) during a difficult task followed by flurry of blinks when task is over.
        - **But wait!**
            - EBR has been shown to increase when a cognitive secondary task is performed concurrently, and the cognitive task does not involve visual attention.
        - **WHY?**
            - EB is a dopaminergic activity.
            - Dopamine plays a big role in selective attention.
    - Through this study, we learned that endogenous blinking (DV) is affected by cognitive load (IV)
2. **Study 2:** Cartoon Judgement:
    - Group 1 and 2 membership.
    - Follow group instructions then rate the 3 cartoons that follow on scale from 1-10.
        - 1 is NOT funny
        - 10 is VERY funny
        - Answers (Lips = Pen in lips; Teeth = Pen in teeth):

Groups	Pics 1	Pics 2	Pics 3	Average
Lips	3	3	4	$3\frac{1}{3}$
Teeth	4	4	3	$3\frac{2}{3}$
Stretch	4	5	6	5
J. Jacks	4	2	3	3

- **Facial Feedback Hypothesis**
  - Selective activation or inhibition of facial muscles has a strong impact on emotional responses to stimuli.
  - Zygomatic major muscle.
    - When we had the pen in our teeth, we were activating the zygomatic major muscle.
    - This muscle is responsible for smiling.
  - Our data supported this hypothesis with a probability of $p < 0.02$.
- **Arousal**
  - Increased heart rate in many emotions.
  - Heart rate and attraction
    - 1973 Dutton and Aron
      - Shaky high bridge vs. low stable bridge.
      - Woman on the other side who is asking questionnaire questions (faux DV).
      - She gave her phone number to the guys once they got done answering the questions.
      - The actual DV was the amount of phone calls she received and the sexual content in questionnaire answers.
      - The high bridge group had more sexual content in their messages.
    - 15 minutes of physical activity, then rate attractiveness of potential mates.

Psychophysiology: Behavioral, cognitive, emotional, and social events are all mirrored in physiological processes.

The idea is that we can get a peep into your psychology by looking at what your biology is doing.

Sleep: EEG (Electroencephalogram; measuring brain activity), EOG (Electrooculogram; measuring eye movement), EMG (Electromyography; measuring muscle movement), ERP (Event-Related Potential; measuring electrical activity in the brain in response to a stimulus).

When your brain is hooked up to the ERP and you are asked either task relevant-stimulus, important stimulus, or surprising stimulus, it will produce a higher p—300 amplitude compared to otherwise. Think about how this would be used for interrogating a suspect, for

example.

Then, there are n—350 amplitudes which are activated when we are asleep, and we hear our name, for example.

Notice the implications of this with sleeping: the more tired you are (or closer to falling asleep), the harder it will be to find the p—300 amplitude.

Omitted Stimulus Paradigm – Given a constant stimulus, this is the phenomena wherein there is a gap in the pattern. This will result in a higher p—300 amplitude.

Polygraph: Respiration, GSR (EDA), Blood flow, Blood pressure, and heart rate.

With a polygraph, we're looking at all the components of the peripheral nervous system. That is, when we're "looking at " a polygraph, we're not measuring lying, but all the physiological responses that are associated with lying.

EDA

- *Electrodermal Activity*
  - Old name: Galvanic Skin Response
  - Measuring sympathetic nervous system activity by detecting sweat gland activity by measuring the conductance of an electrical signal from one electrode to another.
  - More rapid conductance with more activity.
  - Particularly good for emotion.
  - Maybe attention.
  - This also is a good measure for the sympathetic nervous system because it is the only one that can enervate the sweat glands.

What if I Want to Know

- If you're lying
- Cognitive or emotional states when you're sleeping
- If you're attending to stimuli I'm presenting

Psychophysiology is different from Physiological Psychology. Note that Psychophysiology is where mind/behavior is the IV, and physiology is the DV. Similarly, Physiological Psychology uses the same IVs and DVs, but notice that we are manipulating the physiological psychology to measure psychology. Remember the independent variable is first (mnemonic).

Examples

- Present snake photo or not. Then measure effects on physiology that evidence fear.
- Presenting in-group and out-group photographs. Then measure effects on physiology that evidence prejudicial cognition.
- Drugs: Measure effects on psychology (behavior/aggression)
- Lesion: Measure effects on psychology (cognition/memory)
- Manipulate heart rate: (behavior/attractiveness ratings)
- Electrical Stim of Brain [tDCS (transcranial direct current stimulation)]: Measure effects on psychology (mood/emotion/depression)

EEG

- Activity in large groups of neurons.
- Difference in electrical activity at a reference point and site of interest.
- You get: Wavelike patterns.
- *International 10-20 system*.
  - Fz, Fp1, Fp2, F7, F8, F3, F4, T3, T4, Cz, C3, C4, T5, T6, Pz, P3, P4, O1, O2.
    - F = Frontal
    - T = Temporal
    - C = Central
    - P = Parietal
    - O = Occipital
    - Odd numbers = left hemisphere.
    - Even numbers = right hemisphere.
    - Z = Midline
- Researchers use *visual inspection* to look at the EEG data.
- Measurements
  - *Frequency* – $\frac{1}{\text{time}}$ (in Hz)
  - *Amplitude* – Height of wave (in μV)

Neurofeedback

- Learn to control your brain activity.
  - See the activity
  - Get reinforcement or punishment

- Make changes
- Even if you don't "know" what you're doing, you can still learn to control your brain activity.

NEW NOTES FOR 03/20/25

8.1 Physiological Psychology (Video Lab) Experiment

Research Question: *Do opioids play a role in social behavior?*

- Pros of videoing:
  - Minimizes the effect of the experimenter.
    - Called "reactivity"
  - Permanent data record
  - Double blind procedures
    - Observer bias/experimenter effect

8.1.1 Good Introductions

- *Rationale* – Why is this study important?
  -
- *Questions* – What are you trying to answer?
- *Hypothesis* – What do you think will happen?
- *Support for Hypotheses* – Why do you think this will happen?
-

8.2 Classes of Neurotransmitters

- Peptides (AKA: Neuropeptides)
  - Endogenous opioids

8.2.1 Peptides—Opioids

- *Peptides* – Short chain of amino acids.
- **Opioid vs. Opiates:**
  - *Opioid*: Endogenous (from inside the body).
  - *Opiate*: Exogenous (from outside the body) morphine, codeine, heroin, percodan (*levorphanol*), opium, OxyCotin, fentanyl, etc.
    - All agonists.
  - Richard Deyo, the guy whose data we're going to be using says opiates are the ones derived by plants.

8.2.2 Antagonists

- NARCAN (Naloxone) – Opioid antagonist.
  - Reverses opiate intoxication.
- Vivitrol (Naltrexone) – Opioid antagonist.
  - Blocks euphoric effects but may not work that well on addiction because doesn't get rid of cravings.

8.2.3 New NonOpioid Pain Relievers

- VX-548 (January 2024—Late stage trials)
  - Acute post-surgical pain.
  - No addiction risk.
- Blocks Na^+ channels in peripheral (not CNS) pain pathways.
- Better than placebo but not as good as hydrocodone + acetaminophen.

8.3 Opioid Receptors

- 3 Kinds:
  - *Mu* (μ) – Analgesia and euphoria.
  - *Delta* (δ) – Analgesia
  - *Kappa* (κ) – *Colocalized* with certain *catecholamines*, learning and memory, emotional control, stress response and analgesia.
    - *Colocalized* – When two or more neurotransmitters are released from the same neuron.

- *Catecholamines* – Dopamine, norepinephrine, and epinephrine.

- [The process was] Discovered in early 1970s.
- Mid 1970s endogenous opioids were discovered.
  - *Endorphins* – Binds to mu receptors the most.
  - *Enkephalins* – Binds to delta receptors the most.
  - *Dynorphins* – Binds to kappa receptors the most.

8.4 Functions of Opioids

- Prevents diarrhea.
- Euphoria.
- Analgesia.
- Stress response, body temperature, emotions, feeding motivation, sexual behavior, learning (reinforcement), drowsiness.
- Social behavior?

8.4.1 Pain is Good

- Unpleasant sensory and emotional experience associated with actual or potential tissue damage.

Pain Pathway

- From face
  - Comes in via cranial nerve V (trigeminal nerve).
- From neck down
  - Cones in via a spinal nerve in one of 2 pathways:
    - Direct (fast pain pathway)
      - Sharp and well localized pain.
      - Immediate and brief.
      - *A-delta fibers* (myelinated) – Fast conducting fibers.
      - Mechanical (strong) and thermal (extreme temperature).
    - Indirect (slow pain pathway)
      - Slow pain.
      - Throbbing, aching and dull pain.

- Takes longer, but lingers.
- *C-fibers* (unmyelinated) – Slow conducting fibers.
- Chemical (inflammatory) pain.
- Receptors are sensitive to chemical simulation.
- *Prostaglandins* – Inactive until tissue damage occurs.
  - *Cyclooxygenase* (COX) – Enzyme that converts inactive prostaglandins to active prostaglandins.
- Pain arrives at the brain stem reticular formation (BSRF)
- After the BSRF:
  - Thalamus (Arousal)
  - Limbic system: Anterior Cingulate Cortex (ACC) (emotional)
  - Periaqueductal gray region (Opioids)
    - This is activated when there is too much pain.
    - For example, a person gets their finger cut off; instead of incapacitating the person, the periaqueductal gray region will activate and release opioids to help the person get away from whatever is causing the pain.
  - Frontal lobes (Association)
  - and others.

8.5 NSAIDs

- 2 Classes:
  - *Proprionic Acid Derivatives* – Ibuprofen, naproxen, ketoprofen.
  - *Salicylates* – Aspirin, diflunisal, salsalate.
- Block cyclooxygenase
- *COX-2 Inhibitors* – *celecoxib* (Celebrex), *rofecoxib* (Vioxx) (removed from market because heart attack and stroke).

8.6 Opioid Systems at Work?

- Acupuncture
- The placebo effect activates the opioid system.
- For example, if I were to give you a pill, and said it was going to relieve your pain, but it was actually just a sugar pill, you would still feel relief from the pain. However, if I gave you a pill, such as Nalaxone (which is an opioid antagonist), you would not feel relief from the pain.

New Notes for 04/03/25

8.7 Carefully Plan Some Hypotheses

- *Conceptual Hypothesis* – A statement of the expected relationship between the IV and DV.
- *Statistical Hypothesis* – A statement of the expected relationship between the IV and DV in statistical terms.
- Consider the example "Does technology use disrupt sleep quality."
  - Conceptual:
    - Null: TU (tech users) do NOT have lower sleep quality than NTU (non-tech users).
    - Alternative: TU have lower sleep quality than NTU.
  - Statistical:
    - Null: $\mu_{TU} \geq \mu_{NTU}$
    - Alternative: $\mu_{TU} < \mu_{NTU}$
  - For the test that we would use to test this hypothesis, we would use a paired t-test.
- Consider another example "Does too little vitamin D lead to depressed mood?"
  - Conceptual:
    - Null: Adequate VD (vitamin D) participants do NOT have lower mood than inadequate IVD (inadequate vitamin D) participants.
    - Alternative: Adequate VD participants have lower mood than IVD participants.
  - Alternative:
    - Null: $\mu_{VD} \leq \mu_{IVD}$
    - Alternative: $\mu_{VD} > \mu_{IVD}$
- For our question, "Does nalaxone increase play?" we need to be careful how we operationalize play.
- For rats, they play by:
  - Boxing, chasing, dorsal contact, PINNING, and social proximity. But these are not sufficient enough.

8.7.1 Nonspecific Effects

- The IV produces changes in the DV by acting on a system not directly related to the system in question.

- For example, I sleep deprive people and they have less sex. Thus, does sleep deprivation interfere with sex OR maybe, sleep deprivation reduces motivation and that leads to sex declines along with lots of other things indirectly.
- **Could the effect we see on play be due to something else?**
    - Level of behavior
        - Spontaneous activity
        - Crossing
    - Motivation
        - Exploratory behavior
        - Rearing
    - Fear of emotionality
        - If no food is available, grooming

8.7.2 Results

- IRR
    - For play and nonspecific effect (crossing)
    - Descriptive (includes graph)
- Play
    - Descriptive (includes graph)
    - Inferential
- Nonspecific effect
    - Descriptive (includes graph)
    - Inferential
- Play and nonspecific effect separately
- How can I show the relationship between rater 1 and rater 2's ratings?
    - Graph?
        - Scatterplot
    - Statistic?
        - Perason's Correlation coefficient (r)
    - Jamovi Variables?
        - Rater1_pins, Rater2_pins, Rater1_ns, Rater2_ns

Part III

Behavioral Neuroscience Practice Exams

3.1

Q3.1.1 Short Answer: What is psychopharmacology, and why do we study it?
Answer:

Q3.1.2 Multiple Choice: Which of the following is NOT a function of psychopharmacology?

(A) Study the effects of drugs on the nervous system

(B) Study the effects of drugs on behavior

(C) Study the effects of drugs on the immune system

(D) Study the effects of drugs on neurotransmitter systems

Q3.1.3 Fill in the Blank: The location at which a drug interacts with the body to produce its effects is called the _____.

Q3.1.4 Short Answer: What is the difference between an agonist and an antagonist?
Answer:

Q3.1.5 True or False: Drugs directly create effects in the body.
Answer:

Q3.1.6 Multiple Choice: Which of the following is an example of a drug that acts as an agonist?

(A) Naloxone (B) Morphine (C) Curare (D) Atropine

Q3.1.7 Short Answer: What is selective action?
Answer:

Q3.1.8 Multiple Choice: What is a precursor?

(A) A substance that inhibits neurotransmitter release

(B) A substance that enhances neurotransmitter release

(C) A substance from which another substance is formed

(D) A substance from which a neurotransmitter is broken down

Q3.1.9 **Short Answer:** What is an example of how an agonistic effect can become antagonistic?
Answer:

Q3.1.10 **Fill in the Blank:** The process of creating a neurotransmitter from its precursors is called _____.

Q3.1.11 **Fill in the Blanks:** A(n) _____ agonist binds to the same receptor as the neurotransmitter and _____ its effects, while a(n) _____ agonist binds to a different site on the receptor and _____ the effects of the neurotransmitter.

Q3.1.12 **Fill in the Blanks:** A(n) _____ antagonist binds to a different site on the receptor and _____ the effects of the neurotransmitter, while a(n) _____ antagonist binds to the same receptor as the neurotransmitter and _____ its effects.

Q3.1.13 **Multiple Choice:** Drugs that cause the action potential to stay in a depolarized state are called:

(A) Agonists
(B) Depolarizing agents
(C) Antagonists
(D) Inverse agonists

Q3.1.14 **Fill in the Blanks:** In the following diagram, label the specific enzyme for each arrow, and identify the outcome:

$$\text{Precursor} \xrightarrow{\text{\_\_\_\_\_ Enzyme}} \text{NT} \xrightarrow{\text{\_\_\_\_\_ Enzyme}} \text{\_\_\_\_\_}$$

Q3.1.15 **Long(-ish) Answer:** Describe the difference between a neurotransmitter and a neuromodulator.
Answer:

Q3.1.16 Matching: Match the following examples with them either being an antagonist or an agonist.

Choices

(a) *Curare*

(b) *Atropine*

(c) *Morphine*

(d) *Naloxone*

(e) *Botulinum Toxin*

(f) Interfering with docking proteins

(g) Blocking the reuptake of a neurotransmitter

(h) *Sarin*

(i) Interfering with vesicles

(j) Blocking receptors

(k) Black widow spider venom

(l) Cobra and krait venom

(m) Parathion

(n) DFP

(o) *Physostigmine*

(1) Direct antagonist ..... _____

(2) Indirect antagonist ..... _____

(3) Direct agonist ..... _____

(4) Indirect agonist ..... _____

3.2

Q3.2.1 Multiple Choice: Which of the following neurochemicals does NOT transmit information (according to our notes)?

(A) Dopamine (B) Glutamate (C) GABA (D) Glycine

Q3.2.2 Fill in the Blank: Peptides are short chains of _____.

Q3.2.3 Fill in the Blanks: The difference between opioids and opiates are that opioids are _____ and opiates are _____.

Q3.2.4 Short Answer: What is the pain pathway for the face? What about from the neck down? (Generally speaking.)
Answer:

Q3.2.5 Fill in the Blanks: The three types of opioid receptors are _____, _____, and _____.

Q3.2.6 Long Answer: What are each of the three opioid receptors responsible for, and what neurochemicals bind to each the most?
Answer:

Q3.2.7 Multiple Choice: Prostaglandins become active during

(A) Resting-and-Digesting (B) Crying

(C) Daydreaming (D) Bleeding

Q3.2.8 True or False: *Celecoxib* (**Celebrex**), a COX-2 Inhibitor, was removed from the market because it causes heart attacks and stroke.
Answer:

Q3.2.9 Fill in the Blank: *Cylooxygenase (COX)* is an enzyme that converts inactive _____ to its active state.

Q3.2.10 Long Answer: List the characteristics for the direct pain pathway and the indirect pain pathway.
Answer:

Q3.2.11 Fill in the Blanks: Pain arrives at the _____, then travels to the _____. Once there, it is processed by several brain regions. First, the _____ contributes to arousal. Then, the _____, particularly the anterior cingulate cortex (ACC), processes the emotional aspects of pain. When the pain is overwhelming, the _____ activates and releases endogenous opioids to reduce the sensation—this allows a person, for example, to escape danger despite a severe injury. Finally, the _____ and other areas help interpret and associate the pain with context.

Q3.2.12 Matching: Match the following drugs with their respective NSAID class.

Choices

(a) Ibuprofen

(b) Aspirin

(c) Diflunisal

(d) Naproxen

(e) Salsalate

(f) Ketoprofen

(1) Proprionic Acid Derivatives ..... _____

(2) Salicylates ..... _____

Q3.2.13 Long Answer: Some studies show that both the placebo effect and acupuncture can be blocked by Naloxone, an opioid antagonist. What does this suggest about the mechanism of acupuncture's pain-relieving effects? Does this prove that acupuncture is not entirely a placebo?
Answer:

Q3.2.14 Short Answer: What are some of the functions of opioids? (List the main effects and the side effects.)
Answer:

Q3.2.15 True or False: The term *colocalized* means two or more neurotransmitters are released from two separate neurons at the same time.
Answer:

Q3.2.16 Short Answer: What is the definition of pain? (DO NOT say this exam!!!!!!!!)
Answer:

3.3

Q3.3.1 True or False: The amines (monoamines) are derived from amino acids.
Answer:

Q3.3.2 Fill in the Blank: The two indolamines are _____ and _____.

Q3.3.3 Multiple Choice: What amino acid are indolamines derived from?

(A) Tryptophan (B) Tyrosine (C) Thymine (D) Phenylalanine

Q3.3.4 Fill in the Blank: The precursor to glutamate is _____, and the enzyme that synthesizes glutamate from it is _____.

Q3.3.5 Short Answer: What receptor does ketamine bind to, and what is its effect?
Answer:

Q3.3.6 Fill in the Blank: The enzyme _____ deactivates anandamide.

Q3.3.7 True or False: The most common excitatory neurotransmitter in the brain is GABA.
Answer:

Q3.3.8 Short Answer: What transporters are responsible for glutamate reuptake, and why is this process important?
Answer:

Q3.3.9 Multiple Choice: Which receptor is closely associated with glutamate and is important for synaptic plasticity and memory formation?

(A) GABA receptor (B) NMDA receptor
(C) Serotonin receptor (D) Dopamine receptor

Q3.3.10 Short Answer: What enzyme converts glutamate into GABA, and what type of neurotransmitter is GABA?
Answer:

Q3.3.11 Fill in the Blanks: The three catecholamine neurotransmitters are _____, _____, and _____.

Q3.3.12 Fill in the Blank: The drug _____ is a direct antagonist of the NMDA receptor and can cause hallucinations and dissociation.

Q3.3.13 Multiple Choice: What does DA, NE, and Adrenaline all contain, and what amino acid are they derived from?

(A) Catechol and are derived from tryptophan
(B) Catechol and are derived from tyrosine
(C) Indole and are derived from tryptophan
(D) Indole and are derived from tyrosine

Q3.3.14 Fill in the Blank: The enzyme _____ converts tyrosine into L-DOPA.

Q3.3.15 **Short Answer:** Explain how botox interferes with emotional expression.
Answer:

Q3.3.16 **Fill in the Blank:** The orbicularis oculi muscle influences _____.

Q3.3.17 **True or False:** Tyrosine is the precursor for serotonin.
Answer:

Q3.3.18 **Short Answer:** What are the names of the systems that use dopamine, norepinephrine, and epinephrine? *Answer:*

Q3.3.19 **Fill in the Blanks:** Melatonin is synthesized from _____ and is involved in regulating _____.

Q3.3.20 **Short Answer:** What is another name for peptides in the context of neurotransmitters, and give an example.
Answer:

Q3.3.21 **Multiple Choice:** What is the name of the endogenous cannabinoid neurotransmitter whose name means "bliss" in Sanskrit?

(A) Anandamide
(B) Cannabidiol
(C) Tetrahydrocannabinol (THC)
(D) 2-Arachidonoylglycerol (2-AG)

Q3.3.22 **Short Answer:** How are lipid-based neurotransmitters synthesized and stored?
Answer:

Q3.3.23 **Fill in the Blank:** The gaseous neurotransmitter that is required for an erection is _____.

Q3.3.24 **Long Answer:** Describe the study that addressed the question, "Does Botox decrease emotional experience?" Describe the sample, the method, and the results
Answer:

Q3.3.25 **Short Answer:** Name one neurotransmitter that is a nucleoside. What is its function?
Answer:

Q3.3.26 **Fill in the Blanks:** Fill in the following spaces that describe the process of dopamine metabolism: DA is broken down by _____ into _____. Then, _____ converts it into _____.

Q3.3.27 Short Answer: What were the results of the study into depression that asks "Can Botox be used as a good thing?"
Answer:

3.4:

Q3.4.1 Short Answer: What does cholinergic mean?
Answer:

Q3.4.2 Short Answer: What are the four main functions of acetylcholine in the central nervous system?
Answer:

Q3.4.3 Multiple Choice: Who first discovered acetylcholine in 1921?

(A) Otto von Loewy
(B) James Olds
(C) Neal Miller
(D) Peter Milner

Q3.4.4 Fill in the Blanks: The following describes the experiment of the scientist that discovered acetylcholine.
He took a(n) _____, put it in _____, and stimulated the _____ part of the vagus nerve, which slowed it. When he put the solution into another _____, it also slowed down, showing a chemical (ACh) was released.

Q3.4.5 Fill in the Blanks: The _____ runs parallel to the spinal cord. This is why when you get anxious, _____ of your body responds at once.

Q3.4.6 Fill in the Blank: The original name given to acetylcholine by its discoverer was _____.

Q3.4.7 Short Answer: What are the two types of ACh receptors?
Answer:

Q3.4.8 True or False: Acetylcholine is the primary neurotransmitter used in the parasympathetic branch of the autonomic nervous system.
Answer:

Q3.4.9 Multiple Choice: Which of the following is NOT a function of ACh in the CNS?

(A) Learning and alertness
(B) Memory
(C) REM sleep generation
(D) Pain modulation

Q3.4.10 Fill in the Blanks The following describes the synthesis and metabolism process of acetylcholine.
_____ attaches to an acetate ion, of which is derived from _____. Then, _____ transfers the acetate from the first chemical to choline, which forms acetylcholine. When it is time to be broken down, ACh is broken down by _____ into acetate and _____. The acetate is then broken down and eliminated, while the latter chemical is taken back up by _____ and reused.

Q3.4.11 Multiple Choice: Which type of ACh receptor is ionotropic?

(A) Nicotinic receptors

(B) Muscarinic receptors

(C) Both nicotinic and muscarinic receptors

(D) Neither nicotinic nor muscarinic receptors

Q3.4.12 Short Answer: Explain what the sympathetic chain is, and identify where it is located.
Answer:

Q3.4.13 Fill in the Blank: The drug _____ is a direct antagonist of nicotinic receptors, causing paralysis.

Q3.4.14 True or False: Atropine blocks nicotinic receptors and is derived from the plant known as belladonna alkaloids (deadly nightshade).
Answer:

Q3.4.15 Short Answer: How does Botulinum Toxin interfere with acetylcholine function?
Answer:

Q3.4.16 Fill in the Blanks: Black widow spider venom causes _____ of ACh, while (cobra and) krait venom _____ ACh receptors.

Q3.4.17 Multiple Choice: Which of the following is a reversible AChE blocker used to treat myasthenia gravis?

(A) *Deprenyl* (**Eldepryl**)
(B) *Tetrabenazine* (**Xenazine**)
(C) *Physostigmine* (**Antilirium**)
(D) *Neostigmine* (**Prostigmin**)

Q3.4.18 True or False: *Xanomelne* (**Cobenfy**) crosses the blood-brain barrier and is used to treat the cognitive symptoms of Alzheimer's disease.
Answer:

Q3.4.19 **True or False:** Nicotinic receptors are antagonists at low does, but agonists at high doses.
Answer:

Q3.4.20 **Multiple Choice:** In the PNS, where are nicotinic receptors predominantly located?

(A) Brain and spinal cord
(B) Neuromuscular junctions
(C) Autonomic ganglia
(D) None of the above

Q3.4.21 **Fill in the Blanks:** The _____ is the synapse between a motor neuron and a muscle fiber, where ACh is released to stimulate muscle contraction. The _____ is part of the sympathetic nervous system, located near the spinal cord, where preganglionic neurons synapse with postganglionic neurons.

Q3.4.22 **Multiple Choice:** In the sympathetic nervous system, which neurotransmitter is used at the neuromuscular junction with smooth muscles and glands?

(A) Acetylcholine
(B) Norepinephrine
(C) Dopamine
(D) Serotonin

Q3.4.23 **Short Answer:** Compare the neurotransmitters used in the parasympathetic nervous system versus the sympathetic nervous system.
Answer:

Q3.4.24 **Multiple Choice:** Which of the following statements about acetylcholine in the autonomic nervous system is FALSE?

(A) ACh is the primary neurotransmitter in the parasympathetic branch
(B) ACh is used at preganglionic synapses in both sympathetic and parasympathetic branches
(C) ACh is used at postganglionic synapses to sweat glands in the sympathetic branch
(D) ACh is the primary neurotransmitter at the neuromuscular junction with smooth muscles in the sympathetic branch

Q3.4.25 **Fill in the Blank:** In the somatic nervous system, ACh _____ the neuromuscular junction.

Q3.4.26 **Multiple Choice:** Which structure in the basal forebrain that uses ACh is primarily responsible for activating the cortex and facilitating learning?

(A) Nucleus Basalis
(B) Medial Septal Nucleus
(C) Nucleus of Diagonal Band
(D) Pedunculopontine nucleus

Q3.4.27 **True or False:** The Medial Septal Nucleus, which uses ACh, primarily modulates the amygdala.
Answer:

Q3.4.28 **Fill in the Blanks:** For one of the four functions in the CNS, acetylcholine facilitates _____ _____ generation through the actions of the _____ and _____. These cholinergic structures project to the pons and thalamus, activating brain regions for this time period.

Q3.4.29 **Fill in the Blanks:** The _____ and _____ are structures that use acetylcholine and project to the hippocampus through the fornix. This is important for learning and memory.

Q3.4.30 **Multiple Choice:** Which of the following correctly describes the neurotransmitter pathway in the parasympathetic nervous system?

(A) ACh at preganglionic synapse, ACh at postganglionic synapse

(B) ACh at preganglionic synapse, NE at postganglionic synapse

(C) NE at preganglionic synapse, ACh at postganglionic synapse

(D) NE at preganglionic synapse, NE at postganglionic synapse

Q3.4.31 **Short Answer:** How did vikings and Koryaks engage with ACh?
Answer:

3.5:

Q3.5.1 **Fill in the Blanks:** The three catecholamines are _____, _____, and _____.

Q3.5.2 **Short Answer:** How does *deprenyl* (**Eldepryl**) (also called selegiline (**Jumex**)) work?
Answer:

Q3.5.3 **Multiple Choice:** What is the precursor for dopamine?

(A) Tyrosine (B) L-DOPA (C) Tryptophan (D) Choline

Q3.5.4 **Fill in the Blank:** The rate-limiting enzyme in the synthesis of catecholamines is _____.

Q3.5.5 **Short Answer:** Describe the pathway of dopamine synthesis from its amino acid precursor.
Answer:

Q3.5.6 **True or False:** The word "tyrosine" is derived from the word British variation of the word "tire" (spelled "tyre") for its circular shape.
Answer:

Q3.5.7 Multiple Choice: Which pathway is involved in movement and motor control?

(A) Nigrostriatal system
(B) Mesocortical system
(C) Mesolimbic system
(D) Tuberoinfundibular system

Q3.5.8 Fill in the Blanks: The following describes the nigrostriatal system for movement: We start at the _____, which then sends an inhibitory _____ signal to the _____, who sends a reciprocal inhibitory _____ signal back. Then, the first system sends an inhibitory _____ signal to the _____. Then, that system excites the _____, who then excites the _____, which causes voluntary movement.

Q3.5.9 Short Answer: List four symptoms of Parkinson's disease.
Answer:

Q3.5.10 Short Answer: What is a drug that was used to lower blood pressure, but gave Parkinson's-like symptoms as a side effect?
Answer:

Q3.5.11 Fill in the Blank: The misfolded proteins found in the brains of people with Parkinson's disease are called _____.

Q3.5.12 True or False: In Huntington's Chorea, there is too much GABA from the Striatum to the Substantia Nigra.
Answer:

Q3.5.13 Long Answer: Explain how the MPTP incident in 1982 contributed to our understanding of Parkinson's disease.
Answer:

Q3.5.14 Fill in the Blank: *Methylphenidate* (**Ritalin**) increases levels of _____ and _____ in the brain.

Q3.5.15 Multiple Choice: Which system is primarily responsible for reward and reinforcement?

(A) Nigrostriatal system
(B) Mesocortical system
(C) Mesolimbic system
(D) Tuberoinfundibular system

Q3.5.16 **Short Answer:** What neuropeptide, also called orexin, is involved in the regulation of sleep and wakefulness?
Answer:

Q3.5.17 **Multiple Choice:** What neurotoxin led to the development of an animal model for Parkinson's disease?

(A) MPTP (B) MPPP (C) MPP+ (D) MAO

Q3.5.18 **Fill in the Blank:** The drug _____ is an orexin receptor antagonist used to treat insomnia.

Q3.5.19 **True or False:** The mesocortical system is involved in short-term memory, planning, and problem-solving.
Answer:

Q3.5.20 **Multiple Choice:** Which researchers discovered that electrical stimulation of certain brain areas could be rewarding rather than aversive?

(A) Otto von Loewy
(B) James Olds and Peter Milner
(C) Neal Miller and Delgado
(D) Lateral hypothalamus researchers

Q3.5.21 **Short Answer:** What structure within the limbic system is considered the "pleasure center" of the brain?
Answer:

Q3.5.22 **Fill in the Blanks:** The following is a paragraph the describes dopamine synthesis: Tyrosine is converted to _____ by the enzyme _____. This converted form is then used to create dopamine by the enzyme _____.

Q3.5.23 **Multiple Choice:** Which of the following is NOT a function of dopamine in the CNS?

(A) Movement and motor control
(B) Reward and reinforcement
(C) Learning and memory
(D) Sleep-wake cycles and REM sleep

Q3.5.24 **Short Answer:** Describe the metabolism of dopamine.
Answer:

Q3.5.25 **Short Answer:** Define choreoathetotic movements.
Answer:

Q3.5.26 **Fill in the Blanks:** The term _____ refers to slow, continuous writhing movements, while _____ (from the Greek word for "dance") refers to rapid, purposeless, involuntary movements.

Q3.5.27 **True or False:** Both athetosis and choreic movements are characterized by too little movement.
Answer:

Q3.5.28 **Short Answer:** Where in the brain is hypocretin produced?
Answer:

Q3.5.29 **Multiple Choice:** Which drug is an orexin agonist and can be used to treat narcolepsy?

(A) *Suvorexant* (**Belsomra**)
(B) *Methylphenidate* (**Ritalin**)
(C) TAK-994
(D) Hypocretin

Q3.5.30 **Short Answer:** Explain the difference between athetosis and choreic movements.
Answer:

Q3.5.31 **Fill in the Blank:** _____ is a neuropeptide involved in the regulation of sleep and wakefulness that is also known as orexin.

Q3.5.32 **Short Answer:** What is the role of adenosine in the body?
Answer:

Q3.5.33 **True or False:** Nucleosides and neuropeptides are the same thing.
Answer:

Q3.5.34 **Multiple Choice:** Spinal nerves leave the spinal cord and synapses in the paravertebral ganglion. This action is part of the _____ system.

(A) Sympathetic
(B) Parasympathetic
(C) Somatic
(D) Central Nervous System (CNS)

Q3.5.35 **Short Answer:** What neurotransmitter was used in the previous problem?
Answer:

Basic Concepts

Selective Action Drugs are selective in their action on the nervous system.

Sites of Action The location at which a drug interacts with the body to produce its effects.

Drug Action Terminology

Agonist A drug that mimics or enhances the effects of a neurotransmitter.

Antagonist A drug that blocks or inhibits the effects of a neurotransmitter.

Precursor A substance from which another substance is formed. AKA, the ingredients used to make a neurotransmitter.

Synthesis The process of creating a neurotransmitter from its precursors.

Storage The neurotransmitter is stored in vesicles until it is needed.

Release The neurotransmitter is released into the synaptic cleft when an action potential arrives at the axon terminal.

Binding The neurotransmitter binds to receptors on the post-synaptic neuron, causing a change in the neuron's activity.

Inactivation The neurotransmitter is removed from the synaptic cleft by reuptake or enzymatic degradation.

Mimetic Mimics the action of a neurotransmitter.

Direct Agonist Binds to the same receptor as the neurotransmitter and mimics its effects.

Indirect Agonist Binds to a different site on the receptor and enhances the effects of the neurotransmitter.

Direct Antagonist Binds to the same receptor as the neurotransmitter and blocks its effects.

Indirect Antagonist Binds to a different site on the receptor and blocks the effects of the neurotransmitter.

Inverse Agonist Binds to the same receptor as the neurotransmitter and produces the opposite effect.

Depolarizing or *Desensitizing Agent* A drug that causes the AP to stay in a depolarized state; refusing to let the neuron go through another AP, and it stays in the absolute refractory period. (Antagonist)

Neurotransmitter Classes and Related Molecules

Glutamate Synthesized from precursor glutamine by an enzyme called *glutaminase*. It is the most common excitatory neurotransmitter in the brain.

NMDA A type of glutamate receptor that is important for synaptic plasticity and memory formation.

Ketamine A drug that blocks NMDA receptors and is used as an anesthetic and antidepressant.

GABA Synthesized from precursor glutamate by an enzyme called *glutamic acid decarboxylase*. It is the most common inhibitory neurotransmitter in the brain.

Glycine An inhibitory neurotransmitter that is important for motor control and is synthesized from serine.

Excitatory Amino Acid Transporters (EAATs) Facilitates reuptake of glutamate from the synaptic cleft. Important to reduce excitotoxicity.

Excitotoxicity The process by which excessive stimulation of neurons by excitatory neurotransmitters leads to cell death. (ALS, Lou Gehrig's disease)

Amines (monoamines) Derived from amino acids.

- **Catecholamines** Derived from tyrosine. Includes dopamine, norepinephrine, epinephrine. Uses dopaminergic, noradrenergic, and adrenergic systems.
- **Indoleamines** Derived from tryptophan. (Serotonin, melatonin)

Peptides Endogenous opioids. (endorphins, enkephalins, dynorphins)

Acetylcholine (ACh) A neurotransmitter that is involved in muscle contraction, learning, and memory. It is synthesized from choline and acetyl-CoA by the enzyme choline acetyltransferase (ChAT).

Cholinergic Refers to neurons that use acetylcholine as their neurotransmitter.

Lipids Endocannabinoids.

- **Anandamide** An endocannabinoid that binds to cannabinoid receptors and is involved in pain modulation, appetite, and mood regulation. (Sanskrit for "bliss")

Gases Nitric Oxide (NO) diffuses across membranes and acts as neurotransmitters.

Nucleosides (adenosine) Involved in sleep regulation and has inhibitory effects on neurotransmission.

Colocalized When two or more neurotransmitters are released from the same neuron.

Enzymes and Proteins

Monoamine Oxidase (MAO) An enzyme that breaks down monoamines (dopamine, norepinephrine, serotonin) in the presynaptic neuron.

"Vagusstoff" The original name given to acetylcholine by its discoverer, Otto von Loewy.

Choline Acetyltransferase (ChAT) The enzyme that synthesizes acetylcholine from choline and acetyl-CoA.

acetylcholinesterase (AChE) Breaks down ACh into acetate and choline. The choline is taken back up by active transport and reused, and the acetate is broken down and eliminated.

Synaptic Structures and Neural Pathways

Neuromusclar Junction The synapse between a motor neuron and a muscle fiber.

Paravertebral Ganglion A ganglion located next to the spinal cord.

Sympathetic Chain A chain of ganglia that runs parallel to the spinal cord. This is the reason for when you get anxious, ALL of your body gets anxious.

Basal Forebrain Activates the cortex and facilitates learning.

Nucleus Basalis Projects to the cortex

Medial Septal Nucleus and *Nucleus of Diagonal Band* Projects to the hippocampus through the fornix for memory and learning.

Pedunculopontine nucleus (PPT) and Laterodorsal Tegmental Nucleus (LDT) Projects to the pons and thalamus to facilitate REM sleep generation.

Receptors

Nicotinic Receptors Agonist at low doses, but antagonist at high doses. Also iontropic. They are found predominately at the Neuromusclar Function in the PNS.

Muscarinic Receptors Comes from a hallucinogenic mushroom (Amanita muscaria). Predominates in the CNS, but also found in the PNS. They are metabotropic receptors.

Drugs and Toxins Affecting Acetylcholine

Curare (direct antagonist) A drug that blocks nicotinic receptors, causing paralysis.

Muscarine (direct agonist) A drug that activates muscarinic receptors, causing hallucinations and other effects.

Atropine (direct antagonist) A drug that blocks muscarinic receptors, causing pupil dilation and increased heart rate. Comes from the belladonna alkaloids (deadly nightshade) plant.

Scopolamine (direct antagonist) A drug that blocks muscarinic receptors, causing sedation and amnesia. Comes from the belladonna alkaloids (deadly nightshade) plant.

Botulinum Toxin A waste product of *Clostridium botulinum*, which are bacteria who grows without oxygen. It interferes with Ca^{2+} influx channels, preventing the release of ACh. Because Botox causes paralysis, it can interfere with emotional *expression* because it paralyzes muscles like the orbicularis oculi. Additionally, since we know that expression influences experience, when we paralyze these muscles, then the emotional *experience* is also negatively affected.

Botox Derived from botulinum toxin, a neurotoxin that blocks the release of ACh at the neuromuscular junction, causing paralysis. It is used for cosmetic purposes to reduce wrinkles by paralyzing facial muscles. It can also be used to treat various medical conditions such as chronic migraines, hyperhidrosis (excessive sweating), and muscle spasms. The effects of Botox typically last for several months before the muscle activity gradually returns.

Black Widow Spider Venom A neurotoxin that causes the release of ACh at the neuromuscular junction, causing continual release of ACh and paralysis.

Cobra and Krait Venom A neurotoxin that blocks the binding of ACh to nicotinic receptors, causing paralysis.

AchE Blockers Comes into contact with the enzyme that breaks down ACh, causing an increase in ACh in the synaptic cleft.

- **Parathion** Insecticide. Crosses the blood-brain barrier and causes CNS effects.
- **DFP (Diisopropylfluorophosphate)** It is used as a chemical warfare agent and can cause paralysis and respiratory failure.
- **Sarin** It is highly toxic and can cause convulsions, paralysis, and death.

Pralidoxime A drug that reactivates AChE, allowing it to break down ACh again. Also used as an antidote for nerve gas poisoning.

Diseases and Related Treatments

Myasthenia Gravis A disease that causes muscle weakness and fatigue. It is caused by an autoimmune response that attacks nicotinic receptors at the neuromuscular junction, leading to a decrease in ACh receptor availability.

***Neostigmine*, *Physostigmine* (Prostigmin, Antilirum)** Drugs that inhibit AChE. Does not cross the blood-brain barrier. Used to treat myasthenia gravis.

***Donepezil*, *Rivastigmine* (Aricept, Exelon)** Drugs that inhibit AChE. Cross the blood-brain barrier. Used to treat Alzheimer's disease and Parkinson's disease (only the cognitive part).

***Xanomelne*, *trospium chloride* (Cobenfy)** A drug that blocks the muscarinic receptors in the CNS, but not in the PNS. Used to treat schizophrenia.

Additional Neurotransmitter Synthesis/Metabolism and Neural Systems

Tyrosine Hydroxylase The rate-limiting enzyme in the synthesis of catecholamines.

Nigrostriatal System Starts in the substantia nigra and ends in the striatum (caudate nucleus and putamen).

Reserpine (**Raudixin**) Used to decrease blood pressure (Not in use anymore because it caused Parkinson's-like symptoms). Works by blocking monoamine transporters.

MPTP Neurotoxin for DA cells in the Nigrostriatal System (which is not endogenous).

MPPP Opioid analgesic drug.

Lewy Bodies Misfolded proteins that are found in the brains of people with Parkinson's.

Huntington's Chorea A genetic disorder that leads to uncontrolled movements and cognitive decline.

Pallidotomy A surgery that affects the Globus Pallidus to inhibit movement.

Choreoathetotic Movements Too much movement

Athetosis Slow continually writing movements

Choreic *to dance*; rapid, purposeless, involuntary movements.

Dopaminergic Drugs

***Deprenyl*, *Selegiline* (Eldepryl, Jumex)** Drugs that inhibit MAO, can slow down progression of the disease.

***Tetrabenazine* (Xenazine)** Drug that inhibits the DA vesicle transporters. It is used to treat Huntington's disease.

***Methylphenidate* (Ritalin)** A drug that increases DA and NE in the brain, used to treat ADHD, but can also be used for narcolepsy.

Neuropeptides and Sleep-Regulating Molecules

Hypocretine A neuropeptide that is involved in the regulation of sleep and wakefulness.

Orexin Another name for hypocretin; makes you want to eat.

***Suvorexant* (Belsomra)** An antagonist for the orexin receptor, which is used to treat insomnia.

TAK-994 OX2R (Orexin-2 receptor) agonist. Used to treat narcolepsy by stimulating the orexin receptors in the brain, promoting wakefulness and alertness.

Hcrt-1 Intranasal hypocretin-1 (orexin-1) agonist. Also treats narcolepsy by the same mechanism as TAK-994.

Opioids

Receptors

Mu Receptors Responsible for analgesia and euphoric effects.

Delta Receptors Responsible for analgesia.

Kappa Receptors Colocalized with certain catecholamines. Plays a role with analgesia and in learning and memory, emotional control, and stress response.

Endorphins Endogenous opioids that bind to mu receptors.

Enkephalins Endogenous opioids that bind to delta receptors.

Dynorphins Endogenous opioids that bind to kappa receptors.

Antagonists

***Naloxone* (Narcan)** An opioid antagonist that is used to reverse opioid overdoses. It works by blocking the effects of opioids at the mu-opioid receptors in the brain.

***Naltrexone* (Vivitrol)** An opioid antagonist that is used to treat alcohol and opioid dependence. It works by blocking the effects of opioids at the mu-opioid receptors in the brain, reducing cravings and withdrawal symptoms.

NonOpioid Pain Relief

VS-548 Used in acute post-surgical pain relief and has no addiction risk. It works by blocking Na^+ channels in PNS pain fibers.

NSAIDS

Proprionic Acid Derivatives These include Ibuprofen, naproxen, and ketoprofen.

Salicylates These include aspirin, diflunisal, and salsalate.

COX-2 Inhibitors These include *celecoxib* (**Celebrex**) and *rofecoxib* (**Vioxx**). They are used to treat arthritis and other inflammatory conditions. COX-2 is an enzyme that is involved in the production of prostaglandins, which are responsible for pain and inflammation.

Dopamine-Related Systems

Mesocortical System From ventral tegmental nucleus to prefrontal cortex, limbic CORTEX, hippocampus, all frontal lobes, and association areas of parietal and temporal lobes in primates. Involved with short-term memories, planning, and problem-solving.

Mesolimbic System (MLS) Responsible for reward and reinforcement. Runs from the ventral tegmental nucleus to the limbic system. Consists of the nucleus accumbens, amygdala, and hippocampus.