Neuropharmacology
WORKSHEET 1

NEUROTOXINS IN VENOMOUS ANIMALS

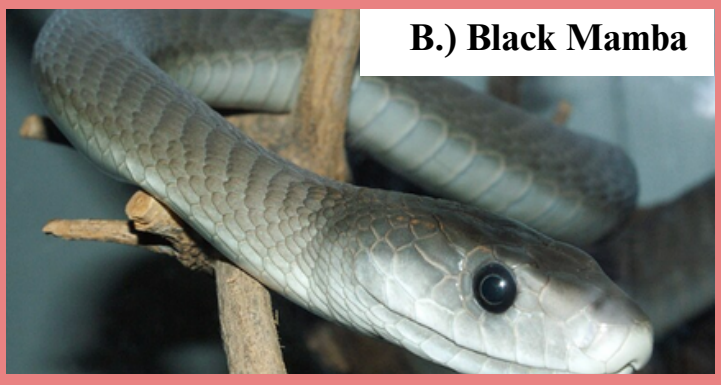
This activity will study those creatures to gain a better understanding of neurotoxins' mechanisms. There are **two questions.**

BACKGROUND

There are 3 main types of snakes that can cause acute neurotoxicity in humans: Elapidae (e.g. cobras, kraits, mambas, coral snakes, Australasian venomous snakes, sea snakes, etc.) which are characterized by: permanently erect fangs in the front of their mouths, typically uniform in color, and all possess pre- and post- synaptic toxins; Viperidae (e.g.: vipers, moccasins, rattlesnakes, etc.) which are characterized by: slow-movements but quick strikes, typically colorful dorsals, and some possess pre-synaptic toxins; and only one species in the typically non-venomous Colubridae family which can cause neurotoxic events.

PICK 2 OF THE FOLLOWING CREATURES TO RESEARCH

A.) Southeast Asian Banded Krait



B.) Black Mamba

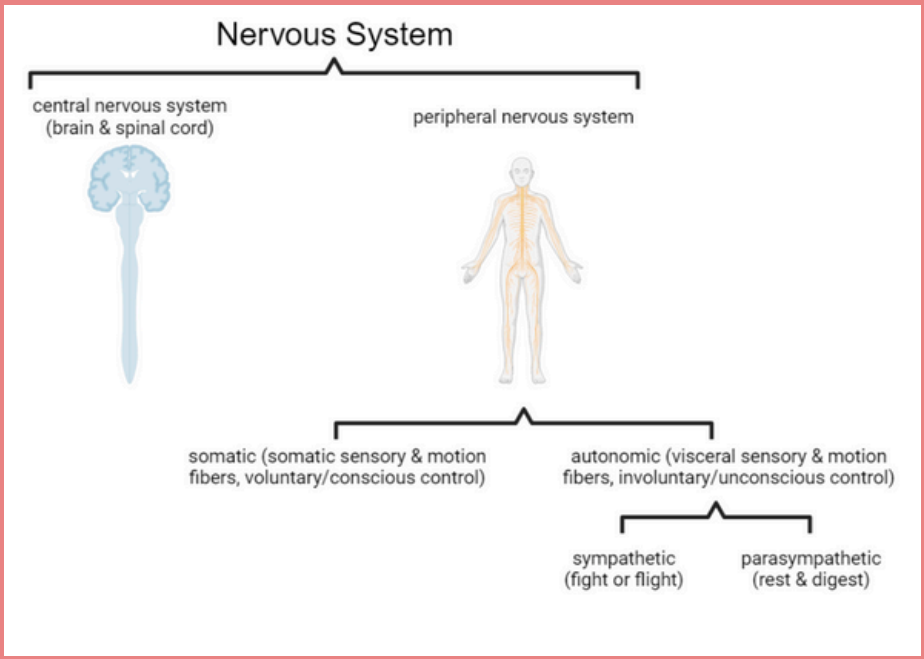
C.) Pufferfish

D.) Hooded Pitohui

Questions:

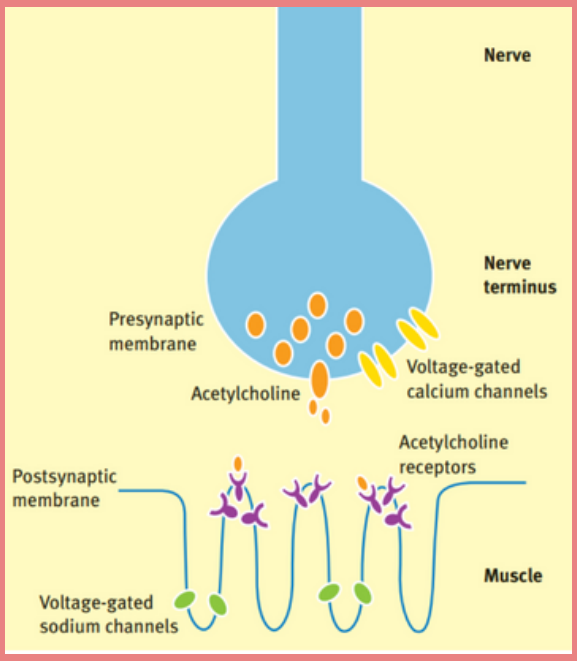
For EACH animal you chose- answer BOTH questions thoroughly! (Also, please specify which 2 animals you chose). You can put your answers in a separate document to submit.

1. **What part of the nervous system does this toxin affect? (Use the following image for assistance answering a-c)**



   a. **Central or peripheral nervous system?**
   b. **If peripheral: somatic or autonomic?**
   c. **If autonomic: sympathetic or parasympathetic?**

2. What is the synaptic mechanism of the animal's neurotoxin (where does it work in the synapse)?
Hint: Use the following graphic and description to help answer this question.



The neuromuscular junction has nerve signals from motor neurons transmitted to muscles via acetylcholine receptors (ACh), causing contraction of muscles. ACh-containing vesicles at the presynaptic terminals release in response to an action potential. At the nerve terminal, voltage-gated Ca++ channels open and Ca++ flows down the electrochemical gradient towards the nerve terminal, leading to fusion of the ACh-bound vesicles with the presynaptic membrane. Ion channels in the postsynaptic membrane open, causing positively charged ions (mostly Na+) to flow down their concentration gradient and depolarize the postsynaptic membrane. If this reaches an action potential threshold, an action potential is generated at the postsynaptic membrane, leading to muscle contraction. Acetylcholinesterase terminates ACh's action.

Thank you!

Neuropharmacology
WORKSHEET 2

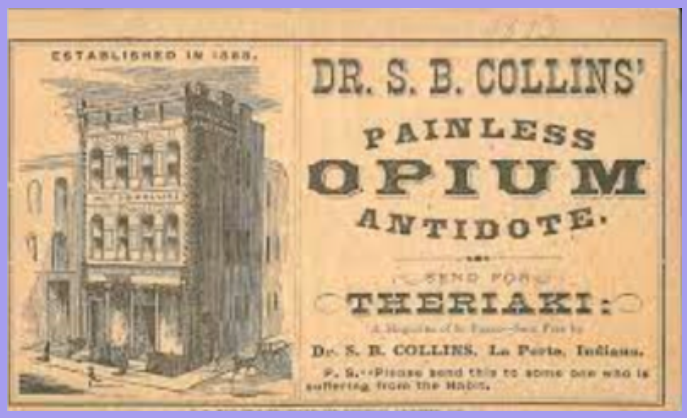
THE DRUG TRADE

This week, you will be reading an article regarding the drug trade and answering questions based on the reading. There are **five questions.**

Introduction Video: https://www.youtube.com/watch?v=k_2oIGofFr0

BACKGROUND

Opium has been known to relieve pain for millennia and can be traced back to empires, including the Sumerian tablets of 2100 BC and the Greek Minoan culture in 1500 BC. In the 1800s, during the Civil War era, soldiers were given opioids to treat their pain from wounds, injuries, and even psychological trauma such as PTSD. This resulted in many of these soldiers developing opioid addictions. Unfortunately, the opioid crisis has not yet been resolved, with a massive wave beginning in the 1990s for prescription opioid overdose deaths. Around 2010, a rise in heroin overdose deaths occurred, followed by a surge in synthetic opioid overdose deaths.



Throughout U.S. history- drug trafficking has included opium, marijuana, cocaine, and a variety of other substances that are illegally imported, sold, and distributed to the masses. Many drugs have been criminalized as they have been classified as having “abuse potential,” which is a threat to society. Some of these drugs include cocaine, heroin, marijuana, and amphetamines. The drug trafficking trade provides people with access to these drugs.

In medicine- some drugs are legal solely to help the patient; however, addiction to hospital-prescribed medications is a growing issue. Opioids continue to be prescribed in the hospital setting and are highly addictive. This is largely due to them activating the reward center within the brain, releasing endorphins that lead to a “good feeling” and momentarily muffle the perception of pain. These medications can lead to tolerance, dependence, addiction, and withdrawal, causing people to take more and more of the drug until they overdose. Physicians must now be wary of addiction signs before prescribing these types of medications due to their addictive nature.

QUESTIONS

Read the following article and then answer the questions:
Article Link: https://www.unodc.org/res/WDR-2023/WDR23_B3_CH1_Synthetic_drugs.pdf?fbclid=IwAR33GRFa9p-fYVJKYSb8YSCfVLKIbYgmTPM92gX4Gq8Q_cLh85J3uzh0xj4

1. How do synthetic drugs differ from naturally occurring drugs?

2. List three benefits of trafficking precursors, especially "designer" precursor drugs, as opposed to completed drugs.

3. What do the authors mean by enhanced synthesis routes?

4. Why does the increased potency of synthetic drugs make drug trafficking easier?

5. What are the benefits and risks of experimenting with a wide variety of diluents and adulterants in order to change a drug's pharmacology mechanism?

Thank you!

Neuropharmacology
WORKSHEET 3

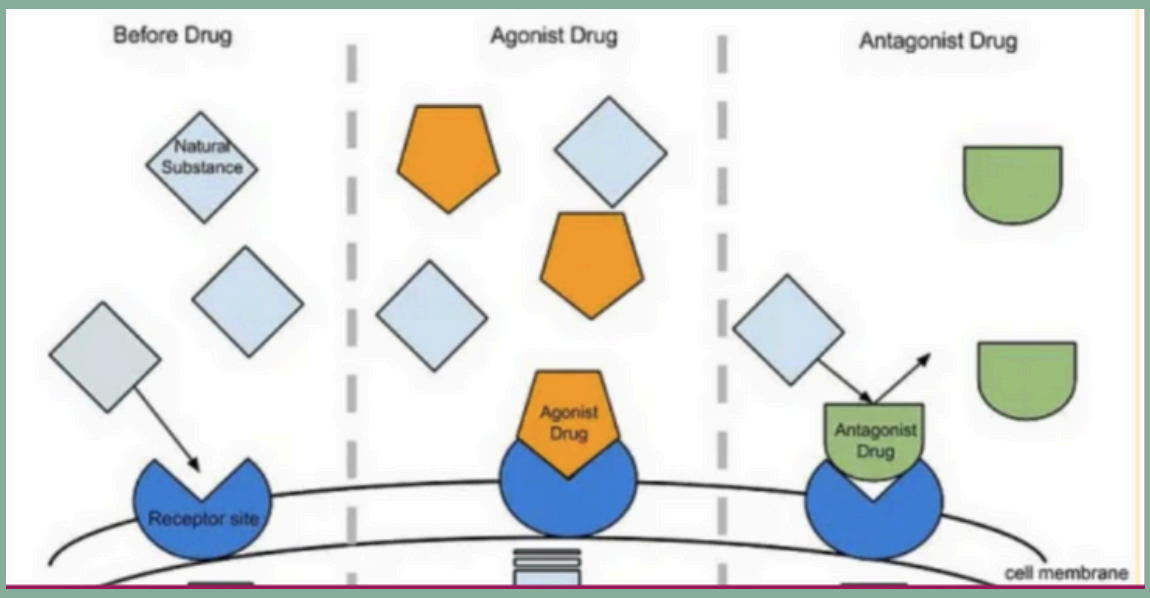
DRUG DOSAGE AND EFFICACY

In this worksheet, you will show your understanding of different groups of drugs and their responses. In addition, we will ask about affinity, efficacy, and your ability to read graphs relating to drug dosages. There are **three questions.**

QUESTIONS

1. Agonists and Antagonists

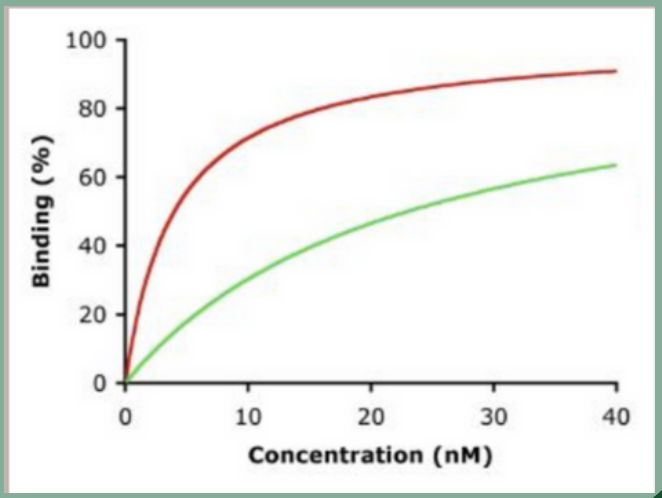
A) Based on the image below, define what agonist and antagonist drugs do in the context of cellular receptors.



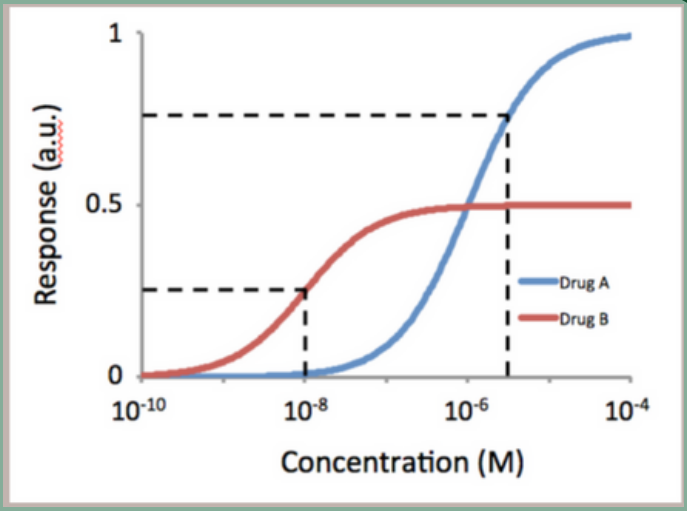
B) What would chronic use of an agonist lead to? Chronic use of an antagonist? Use the words upregulation and downregulation in your answer.

2. Affinity can be described by how well a ligand (drug, neurotransmitter, etc.) can bind to a receptor. Efficacy, on the other hand, refers to how much of a response said ligand can elicit. Potency refers to how much of a ligand is needed to elicit the response.

A) Is affinity, efficacy, and/or potency shown in the image to the right? Describe the graph and explain why the two lines are different.



B) Is affinity, efficacy, and/or potency being shown in the below right? Describe what the graph shows, and explain why the two lines differ.



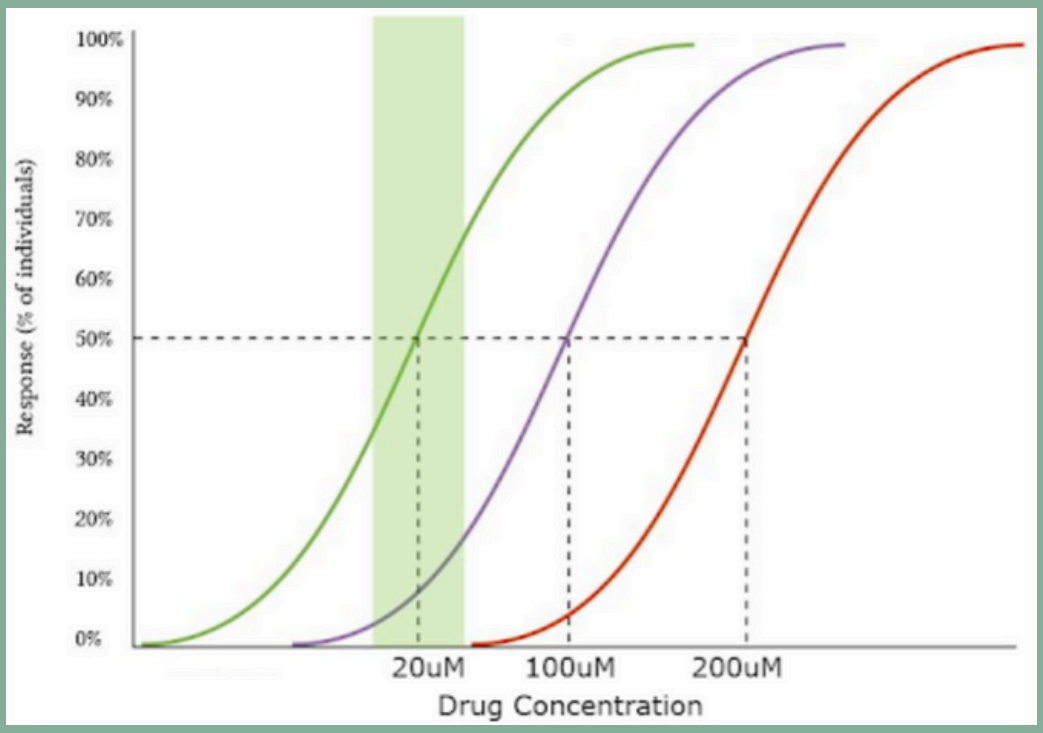
3. ED50, TD50, and LD50

A) Define ED50, TD50, and LD50. What is the relationship between these three values?

B) Label the diagram below with ED50, TD50, and LD50.

C) Calculate the therapeutic index (use the formula LD50 / ED50).

D) Explain how the therapeutic index of a drug can be used to assess its safety and efficacy.



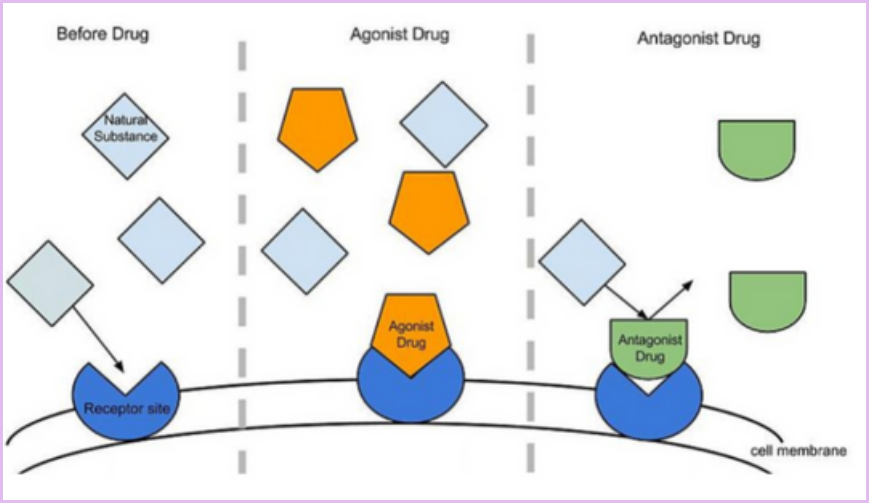
Thank you!

Neuropharmacology
WORKSHEET 4

This assignment is structured like a case study. Please read the background and answer the questions. There are **four questions.**

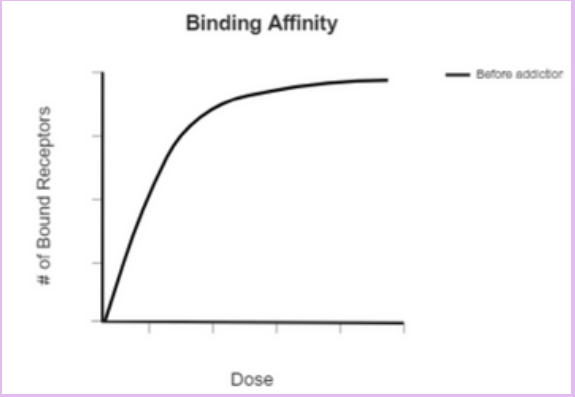
BACKGROUND

An **agonist** is a chemical substance that binds to then activates a receptor, mimicking the role of a neurotransmitter or hormone. Some examples of opioid receptor agonists include fentanyl, oxycodone, morphine, heroin, methadone, and endorphins. **Partial agonists** like buprenorphine also bind and activate a receptor, but are less powerful relative to **full agonists**. Partial agonists are commonly used to transition to abstinence, usually combined with an antagonist. An **antagonist** is a chemical substance that binds to and blocks the activation of a receptor. Some examples include naloxone (brand name Narcan) and naltrexone.

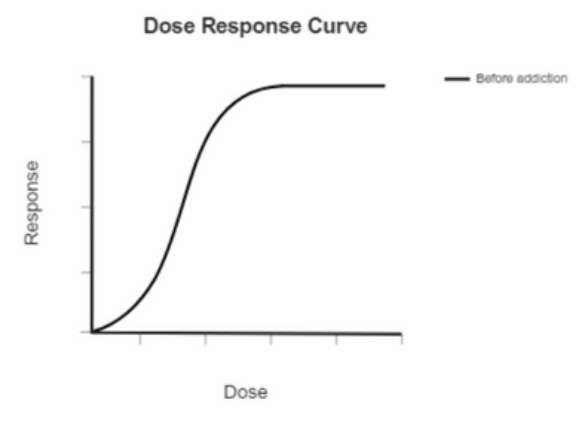


CASE PART 1: Peter is suffering from an addiction to fentanyl.

1. Sketch how his binding affinity curve would shift before and after addiction. The baseline curve prior to his addiction is shown in black. Did his kD and Bmax increase, decrease, or stay the same? What happened to the number of receptors in the synapse? Explain



2. Sketch how his dose-response curve would shift before and after addiction. The baseline curve prior to his addiction is shown in black. Did his ED50 and max efficiency of the drug increase, decrease, or stay the same? Explain.

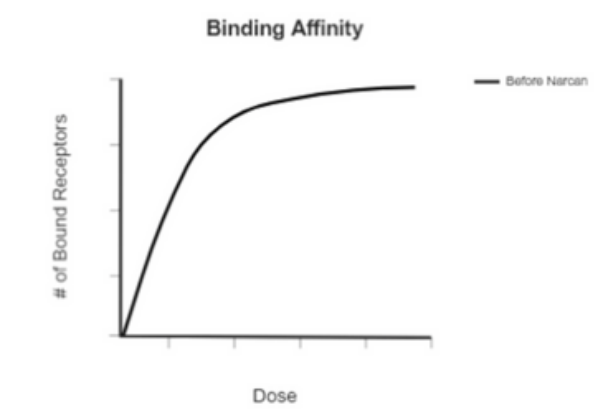


CASE PART 2:

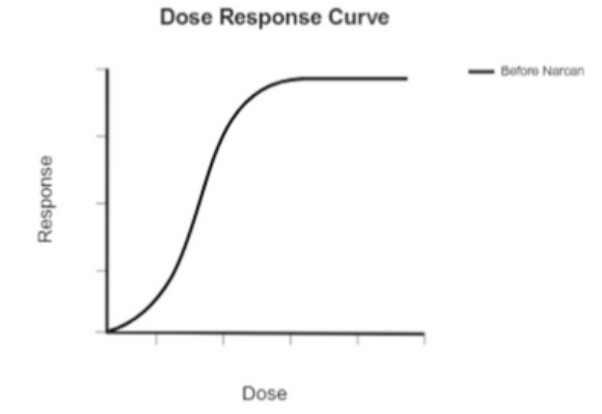
Now that Peter developed an addiction to an addictive drug, he developed tolerance, meaning repeated administration of that drug leads to a decreased effect. His body also developed a compensatory response or drug administration ritual, meaning his body anticipates the effects of the drug and attenuates them. The compensatory response often includes the environment. In Peter's case, he normally takes the drug in his room, so that location is now an environmental cue. However, Peter decided to take his drugs at a party (new environment), which didn't elicit his normal compensatory response, causing a larger actual drug response. Peter unfortunately suffered from an overdose! However, someone was with him and helped administer Narcan (naloxone). Important note: Narcan (nalaxone) is a competitive antagonist.

CASE PART 2 QUESTIONS:

3. Draw the binding curve of fentanyl after the Narcan took effect. The baseline prior to the Narcan is in black. Would this have changed if a non-competitive antagonist was given? If so, please draw how the curve would look with a non-competitive antagonist.



4. Draw the dose response curve of fentanyl after the Narcan took effect. The baseline prior to the Narcan is in black. Would this have changed if a non-competitive antagonist was given? If so, please draw how the curve would look with a non-competitive antagonist.

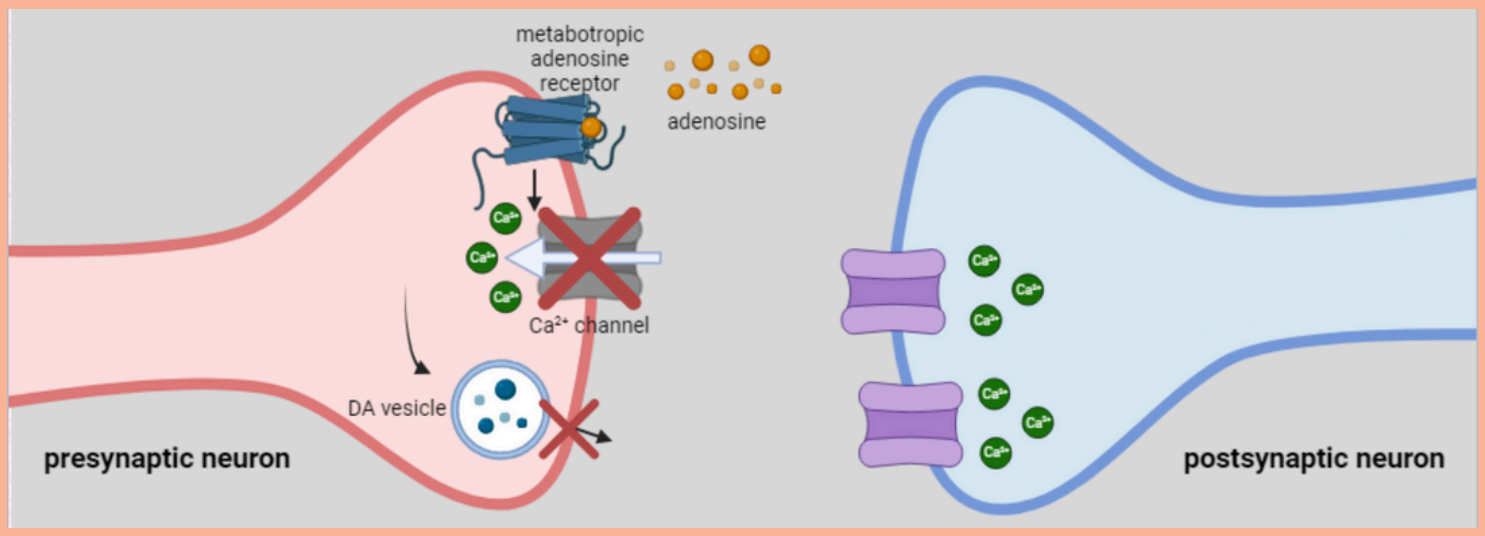


Thank you!

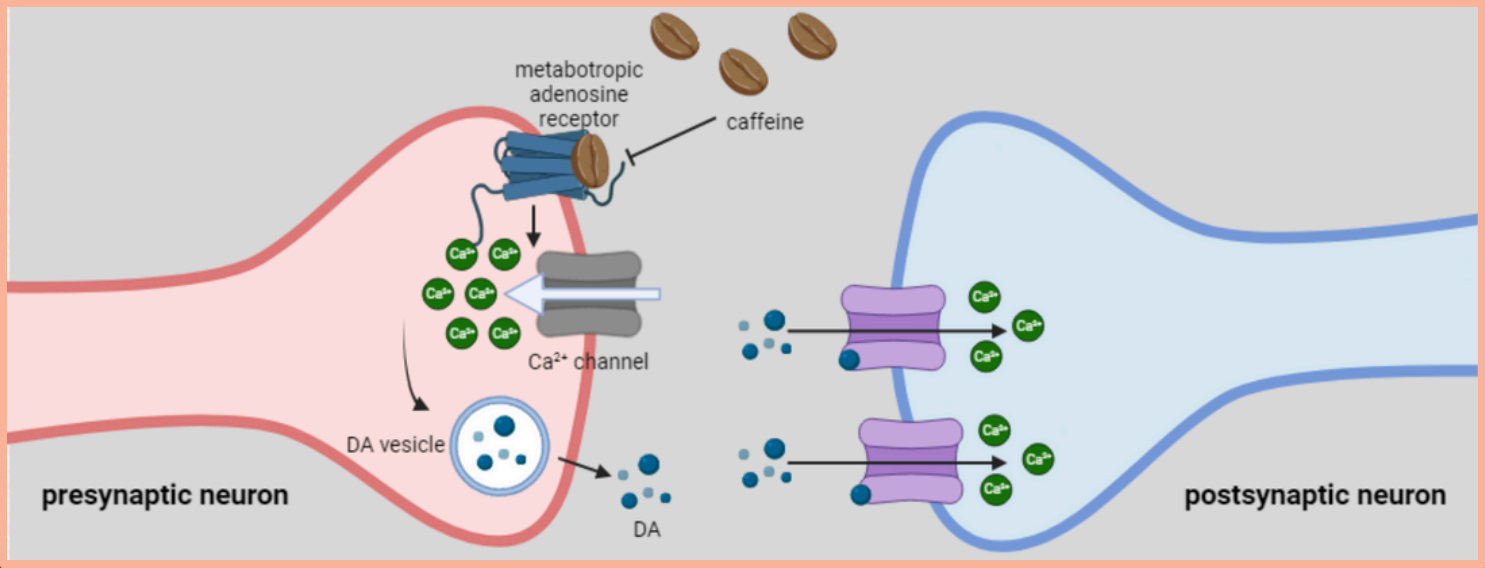
Neuropharmacology
WORKSHEET 5

Please look over the mechanisms below and then answer the questions on a separate document. There are **seven questions.**

ADENOSINE MECHANISM OVERVIEW



CAFFEINE MECHANISM OVERVIEW



Consider Carl, a healthy 19-year-old UCI student who is taking Bio Sci 36 Drugs and the Brain. He is struggling with staying awake in class, so he starts drinking coffee. (Refer for Q1 and 2).

Q1.) What is the general mechanism for caffeine's effect on the Central Nervous System? Is it an agonist or antagonist?

Q2.) If Carl is only drinking 1 cup of coffee (low dose) before class, which receptors will be involved in the caffeine's effect?

Carl has his first exam for the Drugs and the Brain class coming up, and he does not feel ready. As a result, he significantly increases his caffeine consumption so he can study more for the test.

Q3.) With the increased dosage of caffeine, what is the overall effect on neural excitation in the brain?

Q4.) Considering that Carl is a relatively new coffee drinker, how would his withdrawal symptoms compare to a habitual drinker if his regular coffee shop was closed for the day?

Carl failed his test, and he is absolutely crushed as a result. He tries to cheer himself up with his favorite shows, but nothing seems to work. At a Halloween party one of his friends offers him a vape, and he tries it, allowing Carl to take his mind off the test.

Q5.) Which receptor in the central and peripheral nervous systems are actiavted by nicotine?

Q6.) What is the general mechanism for nicotine's reinforcing effect on the Central Nervous System? Is it an agonist or antagonist?

Q7.) Considering the synaptic mechanism underlying nicotine tolerance, how does addiction to nicotine occur?

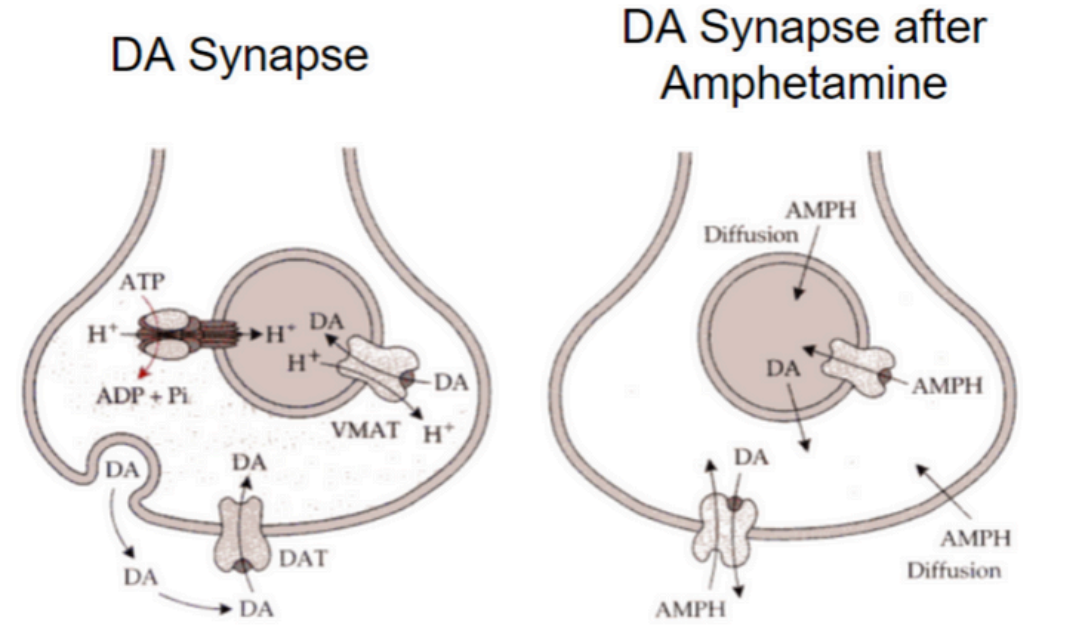
Q8.) How might high doses of nicotine lead to toxicity in the peripheral nervous system (autonomic nervous system)?

Thank you!

Neuropharmacology
WORKSHEET 6

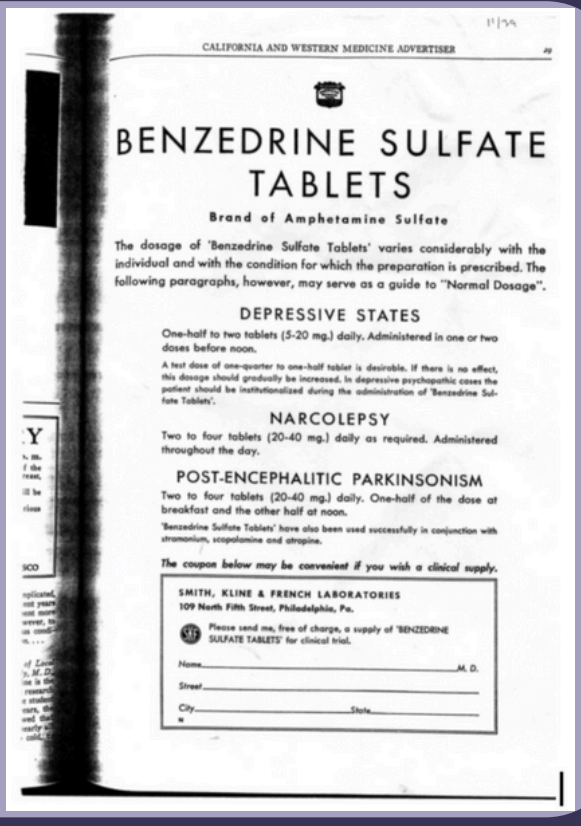
Please read each question below and then answer them on a separate document.
There are **seven questions.**

Q1.) Using the schematic of the mechanism of amphetamine shown below, list the steps of which amphetamine acts on the synapse.



The image to the right shows a 1939 advertisement with Benzedrine (a form of amphetamine), the first Rx drug for treating "discouragement." The original findings of the drug were based on its effects for narcolepsy and Parkinson's, but its use was expanded because "Patient numbers in these groups [narcoleptics and Parkinson's sufferers] were too small to create a profitable market."

Q2.) Why do you think amphetamines had seemingly positive effects in treating narcolepsy?



CALIFORNIA AND WESTERN MEDICINE ADVERTISER

BENZEDRINE SULFATE TABLETS

Brand of Amphetamine Sulfate

The dosage of 'Benzedrine Sulfate Tablets' varies considerably with the individual and with the condition for which the preparation is prescribed. The following paragraphs, however, may serve as a guide to "Normal Dosage".

DEPRESSIVE STATES

One-half to two tablets (5-20 mg.) daily. Administered in one or two doses before noon.

A test dose of one-quarter to one-half tablet is desirable. If there is no effect, this dosage should gradually be increased. In depressive psychopathic cases the patient should be institutionalized during the administration of 'Benzedrine Sulfate Tablets'.

NARCOLEPSY

Two to four tablets (20-40 mg.) daily as required. Administered throughout the day.

POST-ENCEPHALITIC PARKINSONISM

Two to four tablets (20-40 mg.) daily. One-half of the dose at breakfast and the other half at noon.

'Benzedrine Sulfate Tablets' have also been used successfully in conjunction with stramonium, scopolamine and atropine.

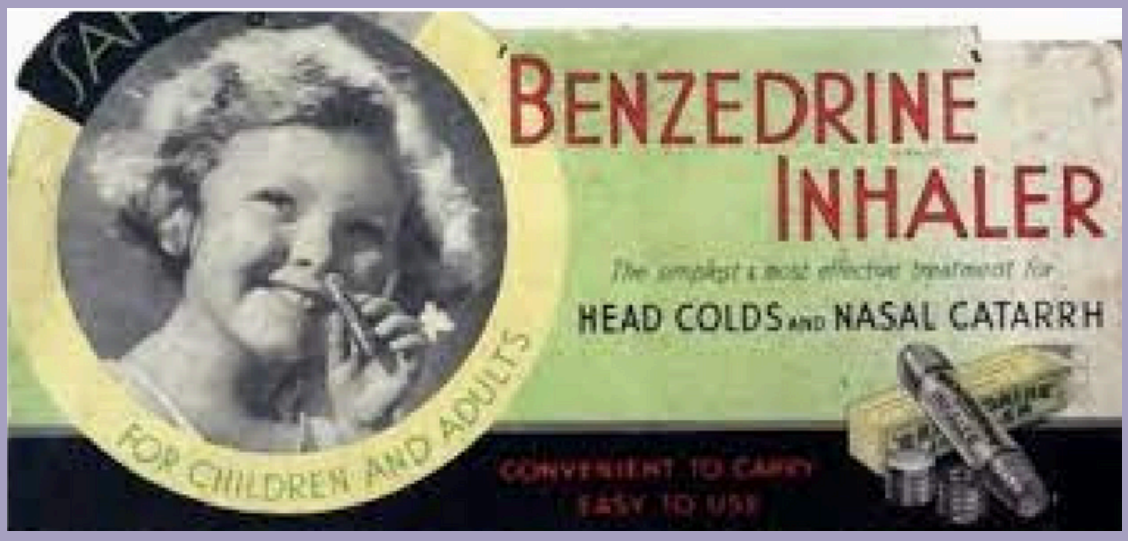
The coupon below may be convenient if you wish a clinical supply.

SMITH, KLINE & FRENCH LABORATORIES
109 North Fifth Street, Philadelphia, Pa.

Please send me, free of charge, a supply of 'BENZEDRINE SULFATE TABLETS' for clinical trial.

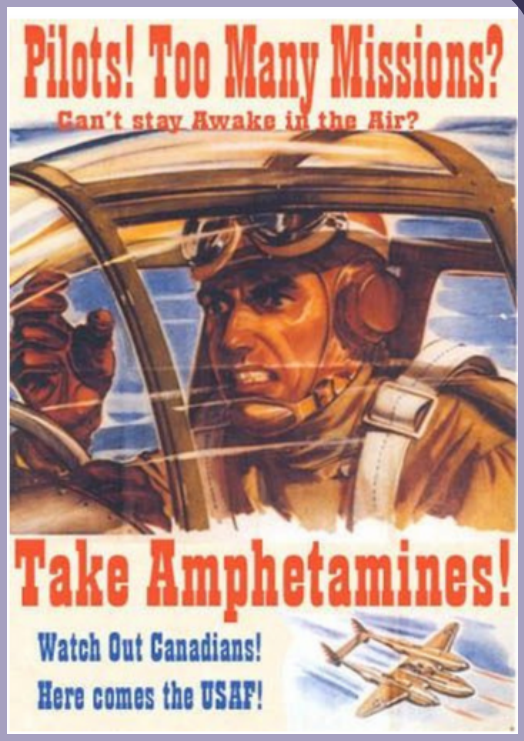
Name _____ M. D.
Street _____
City _____ State _____

UCLA researcher Gordon Ailes developed mind-altering drugs and synthesized amphetamine sulfate in 1928. He experimented on himself, taking an IV containing 50 ng of amphetamine (a very large dose!). Seven minutes after administering the drug, his nose was dry and clear, his blood pressure increased, and he had a "feeling of well-being." He self-reportedly became chatty, unusually witty, and had a restless night. Ailes entered a business relationship with Smith, Kline, and French (SFK). SFK introduced a benzedrine inhaler in 1932. SFK also offered benzedrine sulfate tabs in 1936 for free to any physician despite no clinical trials being performed. Initially an off-the-counter treatment for decongestion, it was eventually banned by the United States Food and Safety Administration in 1965 after decades of reported abuse.



Q3.) Why do you think amphetamines had seemingly positive effects in decongestion?

During World War II, both the Axis and Allied Powers experimented with giving amphetamines to servicemen. One notable amphetamine user was Adolf Hitler, who took them in the summer of 1936 after being prescribed a drug cocktail including methamphetamine by Dr. Theodor Morell for stomach cramps. During WWII, German pharmaceutical company Temmler marketed nonprescription methamphetamine tablets called Pervitin (nicknamed "Assault Pills." Over 35 million Assault Pills were consumed by the Wehrmacht during the 6-week Battle of France in 1940, as the German army ordered front-line soldiers and fighter pilots to take military-issues stimulants containing methamphetamine. Britain purchased 72 million Benzedrine tablets from SKF, and America 250 million.



Q4.) What are some of the potential reasons why servicemen were put on amphetamines?

Q5.) What might methamphetamine be prescribed for stomach cramps and clear airways?

In 1937, George Still used amphetamines to treat a group of boys who didn't comport properly at school and/or home because they had headaches. Those boys called it their "math pill" because it helped them concentrate in class. Amphetamine was used successfully for a long time before Ritalin (methylphenidate) and Adderall (amphetamine and dextroamphetamine). At present, methamphetamines are a standard treatment for ADHD (attention-deficit hyperactivity disorder) by increasing attention and decreasing restlessness.

Q6.) Considering the fact that amphetamines improve concentration, what does that tell you about the receptor population's underlying focus and attention?

"Tweaker" is a common word used to describe someone who appears to be under the influence of very potent drugs- namely Meth. The street name for meth is "speed," and tweakers can display behaviors similar to stereotypy seen in lab animals.

Q7.) What regions of the brain are responsible for these behaviors?

Thank you!

Neuropharmacology
WORKSHEET 7

Please read each question below and then answer them on a separate document.
There are **seven questions.**

Case study: Chris is a 30-year-old man with schizophrenia. He began presenting with trouble concentrating and sleeping at 25, but now has progressed to showing symptoms of hallucinations, rigid muscles, delusions of persecution, lack of movement, odd expressions in his face, lack of speech, and extreme social withdrawal.

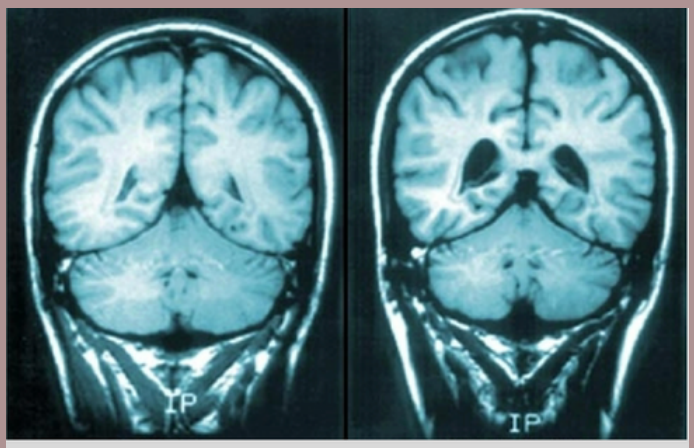
Q1.) What type of schizophrenia is Chris undergoing and why?

Q2.) Which of his symptoms would be considered positive and which would be considered negative?

Although Chris doesn't usually take his medicine, because it is Thanksgiving, he takes his indicated dose of haloperidol so he can properly meet up with his brother Cage. Upon taking his dose, his hallucinations, delusions, and rigid motor activity were relieved.

Q3.) How does haloperidol work? What is its mechanism of action?

Cage, Chris's twin brother, is not schizophrenic and he is a relatively healthy adult. Consider their brain scans below.

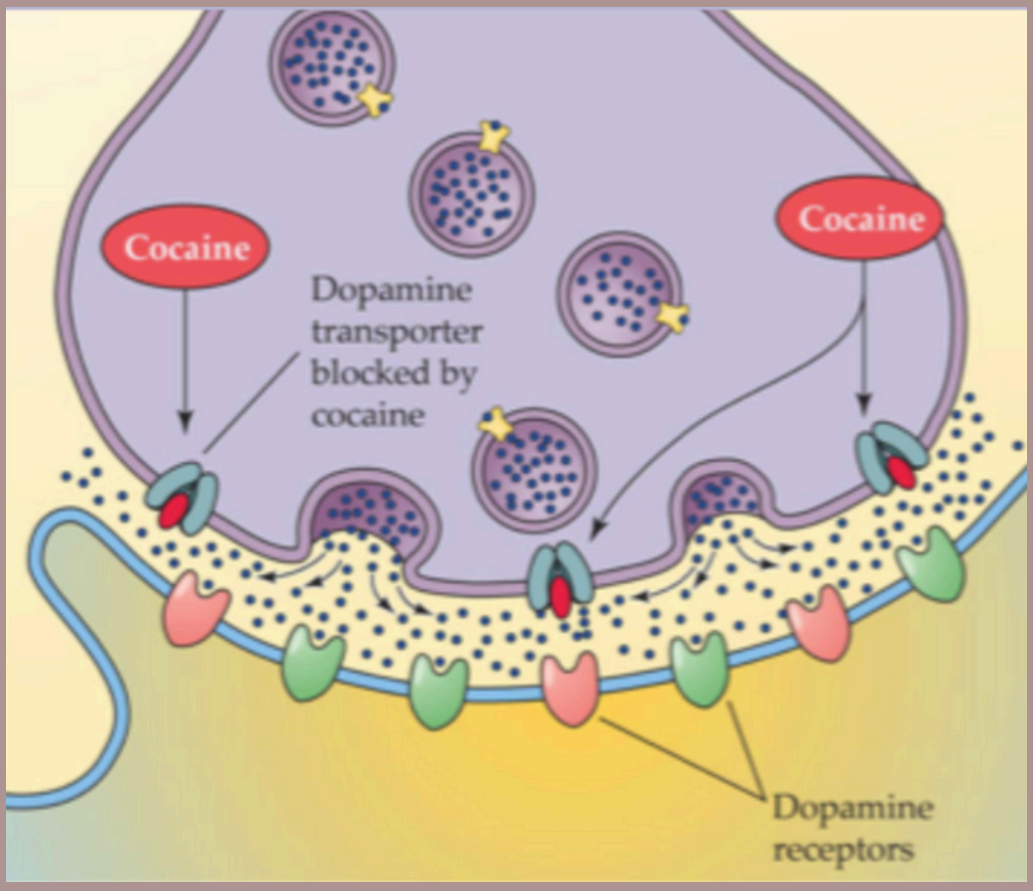


Q4.) Compare and contrast Chris and Cage's brains (refer back to slides for help on this question). Enlarged ventricles in Chris's brain, suggest what has occurred.

Q5.) Another region showing tissue loss is the limbic region. Which symptoms of schizophrenia might be associated with this region?

Cage began taking cocaine and has been using it consistently for 6 months now. Recently, he took a much larger dose and entered a state of psychosis. Interestingly enough, Cage's state of psychosis matched up pretty well with Chris's state of schizophrenia.

Q6.) Considering the dopamine hypothesis for psychosis, explain why Cage and Chris's symptoms lined up. Refer to the below mechanism to help with your explanation.



Q7.) Chris gives a dose of his haloperidol to Cage in an attempt to relieve his psychosis. Would the haloperidol have any effect on cocaine-induced psychosis? Give a brief description of why or why it wouldn't work.

Thank you!