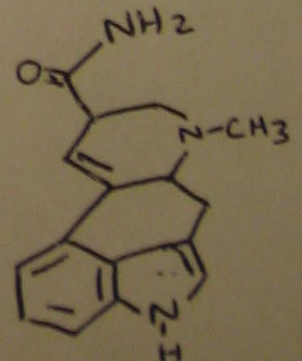
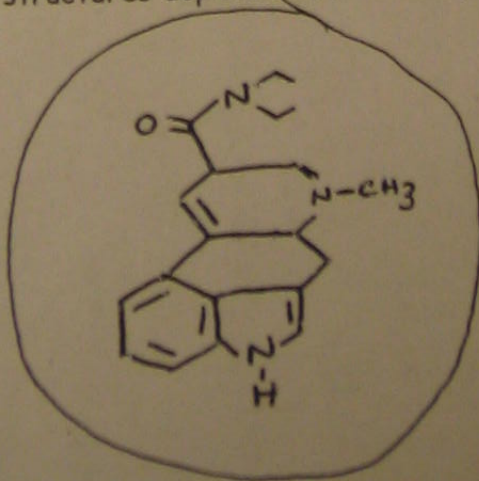
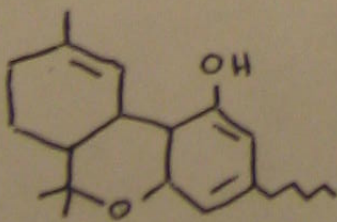


47. There are high densities of cannabinoid receptors in all of the following brain areas except: (1 point)
- hippocampus
 - brainstem
 - cerebral cortex
 - basal ganglia
 - cerebellum
48. Rats administered MDMA exhibit degeneration of serotonergic axon terminals. This degeneration can be reduced by giving the rats doses of vitamin C, vitamin E, or alpha-lipoic acid. What does this suggest about the axonal degeneration process? (2 points)
- it is related to vitamin deficiency
 - it is related to oxidative damage
 - it involves the serotonin transporter
 - it is temperature dependent
 - none of the above
49. The discovery of the primary psychoactive component from Cannabis took place in 1964. Most other common psychoactive plants had their chemistry elucidated in the 19th century. Cannabis chemistry took so long because: (1 point)
- the primary psychoactive compound is present in extremely low concentration in the plant
 - the primary psychoactive compound is not an alkaloid and everyone was looking for alkaloids
 - Cannabis researchers were always too stoned to get any research done
 - the primary psychoactive compound is not a molecule and everyone was looking for molecules
 - none of the above
50. The discovery of the cannabinoid receptor was hastened by: (1 point)
- new laws which allowed legal research on Cannabis
 - the availability of a low-affinity, lipid-soluble ligand, CP55,940
 - appreciation that Cannabis had psychoactive effects
 - new and better fractionation techniques for brain homogenates
 - none of the above
51. Which of the following molecular structures depicts LSD? Circle your answer. (2 points)



Circle your chosen answer for the multiple-choice questions. Each of these questions has a single best answer. For other questions, neatly print or draw your answer in the space provided. You should not need to exceed the space provided. Do not use abbreviations. Write out complete names. Hard to decipher answers will not receive credit.

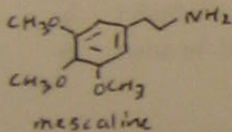
1. Serotonin is a potent agonist at the 5HT₆ receptor. Mescaline is a weak agonist at this same receptor. Which molecule would you suspect as having the larger k_D (equilibrium dissociation constant) for this receptor? (2 points)

Mescaline

2. What does k_D signify? (1 point)

- a. the concentration of ligand needed to equilibrate the receptor
- b. the concentration of ligand needed to dissociate the receptor
- ~~c.~~ the concentration of ligand needed to occupy 100% of the receptors
- ~~d.~~ the concentration of ligand needed cause neurotransmitter to bind to the receptor
- e. none of the above

3. Why does adding an alpha-methyl group to mescaline make it more potent? (3 points)



Makes it a stronger agonist at 5HT_{2A} (serotonin) receptor

-3

4. From which essential amino acid is the neurotransmitter histamine synthesized? (2 points)

Histidine

5. What chemical precursor to dopamine has been used for more than 30 years as the major pharmaceutical treatment for Parkinson's disease? (2 points)

L-dopa

6. When this chemical is given to treat Parkinson's disease, it is usually given in combination with another chemical which inhibits its enzymatic conversion to dopamine prior to entering the brain. What is the name of the enzyme being inhibited? (2 points)

Amino acid decarboxylase

7. The group of cells in the brain which are degenerating in Parkinson's disease is called: (2 points)

Substantia nigra

8. In which region of the brain is this group of dopaminergic neurons located? (1 point)
- ~~a.~~ basal ganglia
 - b. cerebellum
 - c. brainstem
 - ~~d.~~ limbic system
 - e. none of the above
9. For early onset Parkinson's disease, before age 50, monozygotic/identical twins exhibit a concordance of approximately: (1 point)
- a. 1%
 - b. 10%
 - c. 50%
 - d. 80%
 - e. 100%

For questions 10 and 11: Histamine is an excitatory neurotransmitter in the human brain. Acting at histamine H1 receptors, it depolarizes neurons by closing membrane channels which normally allow K⁺ ions to diffuse out of the cell when the cell is at rest, the so-called resting K⁺ conductance.

10. What kind of receptor is the histamine H1 receptor? (1 point)
- a. voltage-gated ion channel
 - b. ligand-gated ion channel
 - c. G-protein coupled
 - d. reuptake transporter
 - e. none of the above
11. What effect would anti-histamine medications have on postsynaptic neurons containing histamine H1 receptors? (1 point)
- ~~a.~~ depolarize
 - b. hyperpolarize
 - ~~c.~~ no effect on membrane potential
 - d. block histamine reuptake
 - e. none of the above
12. According to the DSM (Diagnostic and Statistical Manual), which of the following are not characteristic symptoms of schizophrenia? (1 point)
- ~~a.~~ delusions
 - ~~b.~~ hallucinations
 - c. emotional blunting
 - d. multiple personalities
 - e. all of the above are characteristic symptoms of schizophrenia

13. Jane's identical twin sibling has schizophrenia. What is the statistical likelihood that Jane will also develop schizophrenia? This is the identical-twin concordance. (1 point)
- a. 1%
 - b. 10%
 - c. 50%
 - d. 80%
 - e. 100%

14. Classical antipsychotic medications are ^{ant}agonists at dopamine D2 receptors. New-generation antipsychotic medications are ^{ant}agonists at dopamine D2 receptors and which other kind of neurotransmitter receptor type? (2 points)

Serotonin $5HT_{2A}$ receptors

15. New-generation antipsychotic medications are best known for which clinical property: (1 point)
- a. fewer sexual side effects
 - b. higher risk of tardive dyskinesia
 - c. lower risk of addiction
 - d. lower cost
 - e. none of the above

16. Brittany comes to her doctor complaining of severe insomnia, and a lack of appetite resulting in the loss of twenty pounds. She no longer wants to go on tour, or spend time with her boyfriend Justin - things she used to enjoy. What mental disorder should her doctor consider evaluating her for? (2 points)

major depression

17. Brittany's doctor puts her on phenelzine (Nardil®), an MAOI. What is the biochemical mechanism of this drug, and what three neurotransmitters are involved? (5 points)

MAOI ^{of} breaks down ^{or} prevents the monoamine neurotransmitter by monoamine oxidase
MAOI = monoamine oxidase inhibitor
3 neurotransmitters are dopamine, serotonin, ~~norepinephrine~~ norepinephrine

18. New generation antidepressant medications such as paroxetine (Paxil), sertraline (Zoloft), and citalopram (Celexa) have what primary neurochemical effect at synapses? (2 points)

Inhibit presynaptic reuptake of serotonin

19. The National Institute of Mental Health conducted a 16-week study comparing antidepressant medication, verbal psychotherapy and placebo in the treatment of depression. Of these, which had the best long-term success, measured at up to 18 months after treatment was completed. (1 point)
- a. tricyclic antidepressant medication
 - b. new-generation antidepressant medication
 - c. verbal psychotherapy
 - d. placebo
 - e. all of the above were equal in their efficacy at 18 months post-treatment

For questions 20 and 21: You have developed a new drug to block serotonin reuptake. Your drug has one asymmetric carbon. The following table describes the activity (IC₅₀ in nM) of the stereoisomers of your drug on different reuptake transporters.

	serotonin	histamine	dopamine
racemic mixture	1.8	6000	8000
S-enantiomer	1.8	12000	16000
R-enantiomer	1.8	800	500

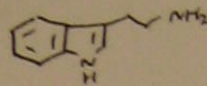
20. Which stereoisomer of the drug would you select as having potentially the fewest side effects? (2 points)
R-enantiomer
21. If you wanted to use your new drug to try to treat amphetamine addiction, which stereoisomer of the drug would you select? (2 points)
R-enantiomer
22. Which of the following plants has been used as a botanical antidepressant medication and has recently been studied by the National Institute of Mental Health for these effects? (1 point)
- coca
 - Catha edulis*
 - Ephedra sinica*
 - Saint John's Wort
 - none of the above
23. Studies with mice, rats, and monkeys have demonstrated that in sufficient dose, the amphetamine derivative fenfluramine, once widely marketed as an appetite suppressant, produces a prolonged decrease in CNS serotonin and a degeneration of axon terminals in serotonergic neurons. Both these effects are prevented by the presence of fluoxetine (Prozac). Given this information, how do you suppose the compound causing problems for the serotonin neurons gets into the nerve cell. Explain your reasoning. (4 points)
- The compound enters through the serotonin ~~reuptake transporter~~ ^{receptor or transporter} and destroys the ~~serotonin reuptake cell~~ ^{serotonergic neuron}. This would cause degeneration of axon terminals. Decrease in serotonin may occur by non-vesicular release into the synapse and subsequent degradation by MAO.*
24. DMT is a potent psychedelic when smoked or snorted. It is not active when ingested orally. Why? (2 points)
- MAO in digestive system breaks down DMT
 (monoamine oxidase)*
25. When DMT is taken as part of ayahuasca, a preparation developed by native South American shamans which contains the plant *Banisteriopsis caapi*, the DMT becomes active orally. What is happening? (2 points)
- The plant contains a monoamine oxidase inhibitor (MAOI) that prevents DMT from being broken down in the digestive system.*

26. What are 3 potentially medically-useful properties of Cannabis? (3 points) (You will be penalized 1/2 point for each incorrect answer)

anti-emetic
anti-seizure
increase appetite "munchies"

27. Which of the following molecules is not considered to be a tryptamine? (1 point)

- a. mescaline
- b. MDMA
- c. dopamine
- d. phenylalanine
- e. all are considered to be tryptamines
- f. none are considered to be tryptamines



For questions 28, 29, and 30: While working in the Fresno General Hospital emergency room, you are asked to evaluate the following case: A 24-year-old female is brought to the hospital by the police after having been injured in an automobile accident. The patient had been "surfing" on the hood of a car on the road when she fell off. You note that the patient appears easily distracted and highly agitated, and is talking rapidly in a grandiose, exaggerated manner. She insists that she does not use drugs and a urine test for the presence of commonly used psychoactive drugs comes back "negative". She claims to have not slept in 35 hours, and says that she feels "great!" You find in her medical records that she has attempted suicide several times in the past, and has been unsuccessfully treated with tricyclic antidepressant medications for depression.

28. What is your diagnosis? (2 points)

bipolar disorder

29. You recommend the most widely-used medication for this condition. What is it? (2 points)

lithium

30. Specify the biochemical action of the agent you recommend - that is, with what neurochemical system and in what way does the drug act? (3 points)

Inhibits the enzyme used to resynthesize phosphatidylinositol in G_q-protein coupled ~~system~~ receptor systems

31. Why is 5-hydroxy-DMT less lipid soluble than 4-hydroxy DMT? (3 points)

4-hydroxy DMT forms an intramolecular hydrogen bond, so it doesn't attract hydrogen ions like 5-hydroxy DMT. After the hydrogen ion, 5-hydroxy DMT becomes charged and ~~therefore~~ therefore less lipid soluble

33. Who first synthesized LSD and discovered its potent psychoactive effects? (2 points)

Hofmann

34. What is the full name for the chemical abbreviated by LSD? (2 points)

Lysergic acid diethylamide

35. What does the abbreviation MDMA stand for? (2 points)

3,4 - methylenedioxy amphetamine

36. Arthur Heffter identified which psychoactive substance which he extracted from a plant in 1887? (2 points)

~~_____~~ Cactus -2

37. The primary psychoactive chemical from psychedelic/hallucinogenic mushrooms from Oaxaca Mexico is: (2 points)

~~_____~~ Psilocybin

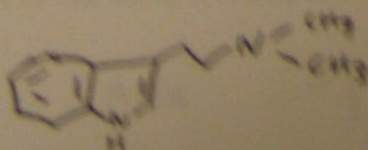
38. MDMA causes nonvesicular release of which two neurotransmitters from presynaptic axon terminals? (2 points)

serotonin & dopamine

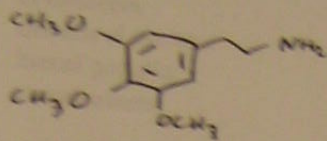
39. You synthesize a new molecule which you determine to be an inhibitor of presynaptic uptake of norepinephrine and serotonin. What clinical condition might this be useful in treating? (2 points)

major depression

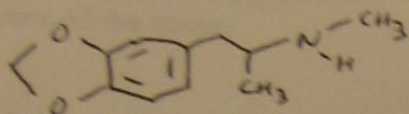
40. Draw the chemical structure of dimethyltryptamine. (3 points)



40. Draw the chemical structure of mescaline. (3 points)



41. Draw the chemical structure of MDMA. (3 points)



42. Classical psychedelics are all agonists at which specific type of receptor? (2 points)

serotonin (5HT_{2A})

43. What is the name of the endogenous ligand for the cannabinoid receptor? (2 points)

Anandamide

44. Name one specific plant where mescaline is found. (2 points)

Peyote cactus

45. What part of the world is the Cannabis plant believed to be native to? (2 points)

Asia -|

46. What is believed to be the primary psychoactive compound in Cannabis? (2 points)

Cannabinoid -|

90

MCB 165

Midterm Exam #2 (100 points)

April 8, 2003

Name: Wade Lee

SID: 14872663

(please print clearly)

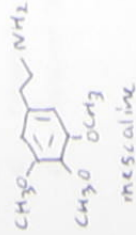
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1. Serotonin is a potent agonist at the $5HT_6$ receptor. Mescaline is a weak agonist at this same receptor. Which molecule would you suspect as having the larger k_d (equilibrium dissociation constant) for this receptor? (2 points)

Mescaline

2. What does k_d signify? (1 point)
- the concentration of ligand needed to equilibrate the receptor
 - the concentration of ligand needed to dissociate the receptor
 - ~~the concentration of ligand needed to occupy 100% of the receptors~~
 - ~~the concentration of ligand needed cause neurotransmitter to bind to the receptor~~
 - none of the above

3. Why does adding an alpha-methyl group to mescaline make it more potent? (3 points)



Makes it a stronger agonist at $5HT_{2A}$ (serotonin) receptor

-3

4. From which essential amino acid is the neurotransmitter histamine synthesized? (2 points)

Histidine

5. What chemical precursor to dopamine has been used for more than 30 years as the major pharmaceutical treatment for Parkinson's disease? (2 points)

L-dopa

6. When this chemical is given to treat Parkinson's disease, it is usually given in combination with another chemical which inhibits its enzymatic conversion to dopamine prior to entering the brain. What is the name of the enzyme being inhibited? (2 points)

Amino acid decarboxylase

7. The group of cells in the brain which are degenerating in Parkinson's disease is called: (2 points)

Substantia nigra