

When Jenn Lost Her Nerve: A Closer Look at Chemical Synapses

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Part I – What’s Wrong, Jenn?

It was time for Jenn’s weekly call to her parents, but she had a sinking feeling that the events of the past few weeks would make things difficult. She had managed to hide her problems with her boyfriend, but now she was worried that things had gone to a completely new level and they would know something was wrong. She picked up the phone and almost immediately Jenn’s mother knew that there was a problem.

“How do you do that? All I say is ‘Hi’ and you know something is wrong,” asked Jenn.

“It’s a mom-thing; you’ll understand when you and Rob have children.”

“You’ll be waiting a long time for kids from this direction. Maybe you should start working on Kate,” replied Jenn.

“What happened?”

“Rob left. Life’s been great since I transferred to the university. I was fine leaving my friends at State because it was more important to be with Rob and go into nursing, even though it’s going to take me an extra year. Everything was great for the first two years, but this semester’s courses have been tough and the oncology rotation is really difficult to deal with. It seems that all I see is terminal patients and it breaks my heart; it takes a special kind of person to do oncology and now I know I’m not one of them!”

Jenn’s mother tried to convey her sympathy over the phone. “But isn’t that rotation almost over? Don’t you have the pediatric rotation to look forward to next semester? You’ve said so many times that that is where your heart belongs, helping kids.”

“You’re right, but this semester has been rough on both of us and I’ve been unbearable to live with. Rob said that he can’t continue carrying me and deal with his own problems. We all know that the first-year of medical school isn’t easy and I’ve added to his burden at a time when we should be helping one another.” Jenn’s voice wavered as she tried to hold back the tears.

Searching for something positive to say, her mom replied “Well, the fact that you recognize that is good. Can’t you two just talk about it?”

“It seems that’s all we’ve done for the past semester. I see now that I’ve been acting like a spoiled brat, thinking only of myself. So I really wasn’t surprised when I got home from the hospital today to find that Rob has taken his things and moved out. I can’t say that I blame him; who would want to live with me? Now I’m alone and my only friends are in my nursing class, and I’ve ignored them because I’ve tried to spend all of my time with Rob. I have to question whether I’m cut out for this career.”

“Do you want to come home or would you like us to drive down?”

“No, it’s all right. I’ll be done with classes in a few days and then I’ll be home for Thanksgiving.”

“As long as you’re all right, Jennifer Katherine. You know I’ll worry until I see you. I love you.”

Jenn sighed, feeling the weight on her shoulders getting heavier.

“Why did I call home?” she wondered as the conversation ended and she hung up the phone.

Her mother, on the other hand, was worried because Rob’s influence had changed her daughter into a happy, confident young woman. She hoped that Jenn would not revert back to the quiet, introspective and withdrawn person she had been in high school.

Questions

1. What problems has Jenn been experiencing?
2. What do you think Jenn should do to deal with her problems?
3. How would you describe Jenn’s condition?

Part II – Back to the Happy Jenn

“It was so nice to see you with your old friends at Thanksgiving; you were so happy with them. But going to college and now back for Christmas, you seem to have gone back to the place you were when you called me a few weeks ago.”

“I know, Mom. Rob leaving really turned me upside down. We talked a lot but nothing changed. He’s going on with his life and I’ve buried myself in my work and my studies. But I’ve found it difficult to concentrate over the past few weeks so I barely passed my end-of-semester exams.”

“Would you like to talk to Dr. Smithers?” asked her mom. “She was at the party last night and said that she was worried about you.”

“I guess it can’t hurt to talk to her,” Jenn replied.

By the time Jenn was ready to go back to college she had worked with her doctor to adjust the level of her prescription medication so that she felt happy again. She persuaded a nursing friend, Ann, to move in and share the rent, which would help her financially and would insure that she wouldn’t be alone.

When Jenn returned to her apartment, she found Ann in the kitchen.

“Hi Ann; you beat me back to school.”

“I wanted to get a start on the books and I needed some time to complete those pre-semester assignments our wonderful professors are so fond of giving us,” Ann replied; they both smiled.

“Listen, Ann, I hope I know you well enough to tell you that I’ve been diagnosed with depression and have been put on a medication called sertraline. I remember that you aced pharmacology so if I forget to take a pill I hope you’ll be understanding and maybe help me along.”

“Sure, I remember that drug but I would feel better if I had a refresher on how it works. Maybe I should consult my old notes?” suggested Ann.

“Great idea, thanks,” Jenn replied.

Questions

1. Use the word bank to fill in the flow chart (next page) describing the mechanism of synaptic release of serotonin from the pre-synaptic neuron to a post-synaptic neuron in the brain.
2. If the SSRI slows the rate of serotonin uptake back into the presynaptic terminal, what would be the effect of the SSRI on the amount of serotonin in the synaptic cleft?
3. If the number of receptors in the postsynaptic membrane is indirectly proportional to the amount of serotonin in the synaptic cleft, what would be the effect of the SSRI on the number of postsynaptic receptors?
4. Why was it important for Jenn to adjust the level of sertraline she takes?

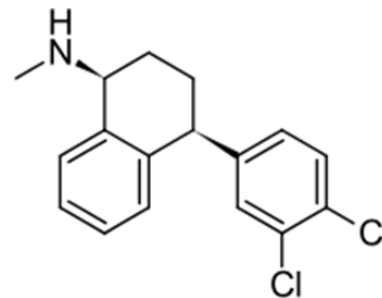
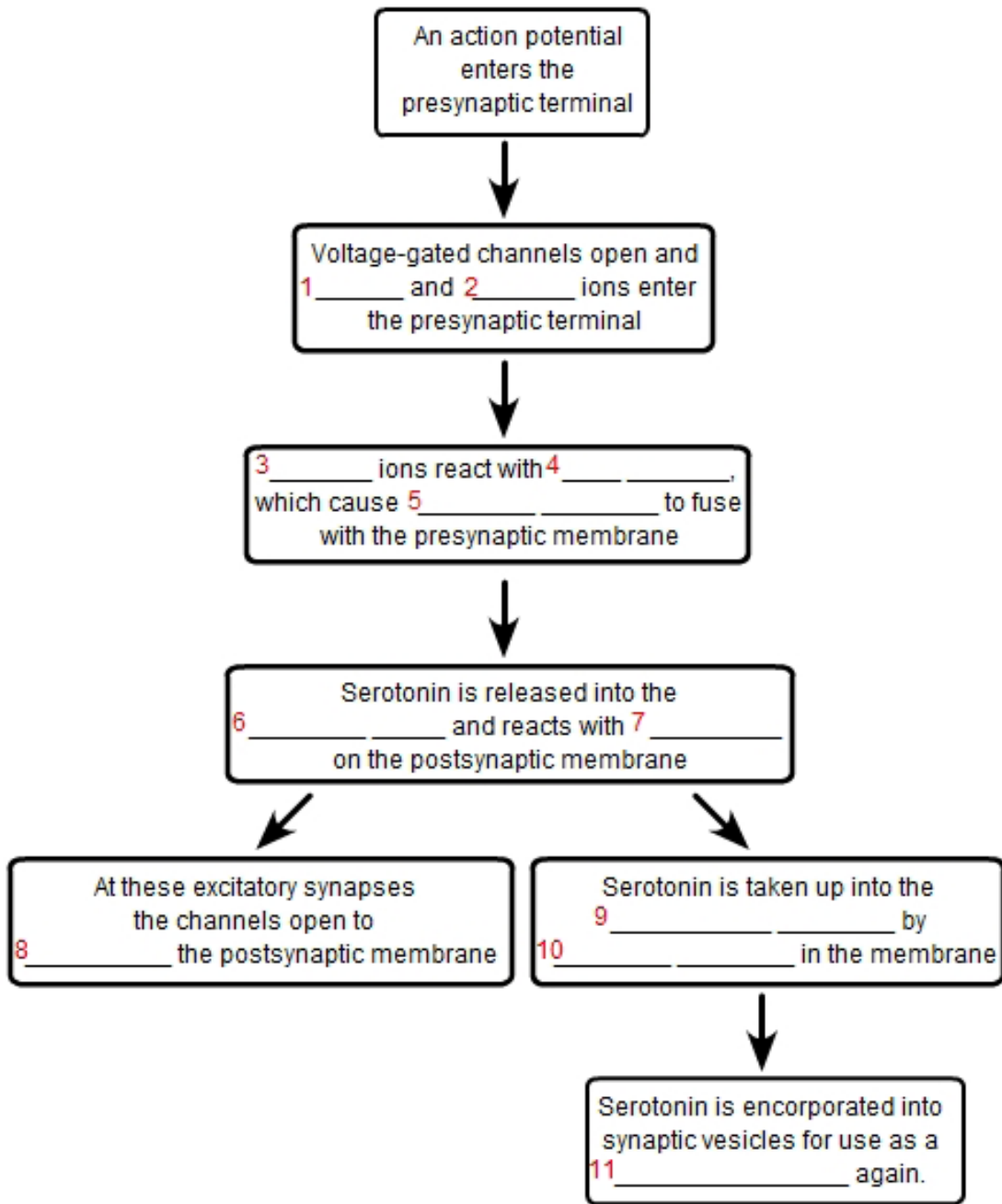


Figure 1. Sertraline. Sertraline is used to treat depression and panic attacks in adults. Treatment may improve sleep, appetite, mood and energy levels. Sertraline is an SSRI, or a selective serotonin reuptake inhibitor, and is thought to rebalance the level of serotonin in the brain. Abrupt interruption of sertraline treatment may result in withdrawal or discontinuation syndrome. During the 5–8-day period when sertraline was replaced by placebo, the most frequent symptoms (reported by > 25% of patients) were nausea, irritability and agitation.



Word Bank: calcium, calcium channels, calmodulin, depolarize, docking, exocytosis, hyperpolarize, neurotransmitter, metabolic enzymes (MAO), neurotransmitter, presynaptic terminal, postsynaptic, postsynaptic cell, presynaptic terminal, potassium, receptors, reuptake proteins, sodium, SNARE proteins, synaptic cleft, synaptic vesicles, synapsin.

Part III – From Good to Bad

Jenn smiled as she reflected on the past six weeks and remembered the children she had helped during her rotation. She had transferred from her previous university because she wanted to be with Rob, but that was now a memory. Another reason she had transferred was that the nursing program had an international component, where all seniors finish their first half-semester courses one week early and start their second half-semester courses one week late. This freed up one week on either side of spring break so that all students could have a “solid three week immersion” (as her advisor called it) into nursing in a third-world country. Jenn looked down and saw a lake and a primitive airport surrounded by a green jungle.

The customs officers took a long time inspecting the medical supplies provided by the university, and then asked each student the same question: “Do you have any drugs?”

Fortunately the instructors had warned them about this and Jenn decided to leave the sertraline at home. She didn’t want anyone, apart from Ann, to know about her difficulties and her prescription medication. She was initially concerned about not taking sertraline but comforted herself with the knowledge that she was through that phase of her life and was now truly happy and content with herself and her career choice. All doubts were gone, but Ann had warned her that going cold turkey was not a good idea. But Jenn thought that she had no choice if she wanted to satisfy the program requirements and go on this trip.

Jenn loved nursing even though the facilities were limited and the supplies they had brought were being used at an alarming rate. Towards the end of the first week, Jenn had a problem.

“This child has a bad cut and I need to clean and dress it, otherwise it may become infected,” Jenn said.

“You are absolutely right, Jenn, but we are running low on supplies. All I am saying is that we need to conserve as much as we can to make what we have left go as far as possible,” replied the instructor.

“Well it’s not my fault that we didn’t bring enough supplies and that these people live in conditions not fit for a dog!” Everything went quiet and a second instructor entered the room.

“I think it’s time to take a break, Jenn,” suggested the instructor

Jenn turned and reached the sink just in time to throw up. “I hate this place; it’s disgusting and the food sucks!”

Questions

1. What problems is Jenn experiencing?
2. Why is Jenn experiencing these problems?
3. The SSRI sertraline inhibits the reuptake of serotonin into the presynaptic terminal. Jenn stopped taking the drug and the reuptake transporter could function at a faster rate. What would you predict would happen to the level of serotonin in the synaptic cleft?
4. If Jenn’s feeling of well-being is directly proportional to the level of serotonin in the synaptic cleft, predict what happened to Jenn’s feelings of well-being when she stopped taking the SSRI.

Part IV – Enter Tim

Jenn was sent home from the trip.

“So what happened, Jenn?” asked Dr. Smithers.

“I didn’t realize that one of the other students was on sertraline, so the instructors borrowed a few pills, which settled me down. I got back to school just in time for spring break, so I picked up my meds and came home. My friends are on their nursing trip in a distant land, and I’m stuck here. Could life get any worse?” says Jenn.

“I understand how you feel but I think when we get you stabilized you’ll feel better. I appreciate that you want to get off the drug, so I suggest you come see me around Easter and we can think about slowly weaning you off the sertraline,” suggested Dr. Smithers

Jenn rejoined her class but felt it would never be the same. Getting herself sent home was embarrassing enough but now she found it difficult to be in the same room as the instructors, even though she apologized and explained her problems. The instructors were nice and seemed understanding, but Jenn still felt awkward.

Jenn committed to working hard in an effort to do well in her remaining classes so that her instructors would have something positive to remember her by. She refused invitations to go out in the evenings, so Ann and her classmates eventually stopped asking and went without her. Jenn didn’t mind because it gave her peace and quiet to study.

As exam time approached, Jenn usually went to the library to study. One day she met Tim, Rob’s best friend from high school and his college roommate. He did not get into medical school with Rob, so he was pursuing a master’s degree to improve his GPA and give him time to retake his MCATs.

“How do you do it, Tim? You’re a teaching assistant, you go to classes, you do lab research and you still have enough energy to attend the MCAT course.”

“I couldn’t do it on my own, Jenn. These little pills are a wonder. They help me concentrate; I’m more productive and I don’t even want to sleep.”

“Wow, I’m at a point where I’ve worked so hard this last half of the semester that I’m just about out of gas. And with exams in a few weeks, this is the wrong time to be tired. What are these pills?”

Tim took some pills out of a plastic bag and put them on the desk. “Amphetamines. They are all over campus at this time of the semester; everyone is taking them.”

“But I don’t have ADHD.”

“Me neither, but they’re only 20 milligrams and they really help. Try one; it’ll give you so much energy.”

“Maybe some other time. But thanks anyway. I’m bushed; I think I’ll go home.”

As she left the library she saw Tim staring at a computer screen, his right knee bouncing up and down. Jenn was relieved that she refused the drugs, although she had to admit it was tempting; but she didn’t want to get addicted to amphetamines, especially since she was almost off the sertraline.

Questions

1. What unusual behavior does Tim exhibit?
2. Tim said that he felt more energized. Which hormone is responsible for mobilizing glucose from the liver?
3. From which division of the autonomic nervous system is this chemical secreted as a neurotransmitter?
4. Given what you know about antidepressant drugs like SSRIs, speculate how amphetamines may affect synaptic function in the autonomic nervous system.

Part V – A Trip to the ER

“Did you even go home last night, Tim?” asked Jenn when she returned to the library the next morning.

“I told you amphetamines are sensational. I had a mountain of grading and a research paper to write and I’m almost done. I just pop a few more pills and I’m good to go for another couple of hours.”

Tim gulped down the last of his giant cup of coffee and got up for a refill.

“Did it suddenly get hot in here, Jenn? Could you open a window? I feel like I’m going to throw up.”

Tim staggered and collapsed across a desk. A couple of students lifted him off the desk and placed him on the floor while Jenn called security.

Jenn arrived at the emergency room in time to see Rob.

“Is he okay? He was pulling an all-nighter in the library and I guess he over did things and collapsed.”

“I’m afraid it’s much more than that, Jenn. Do you know whether he was taking any drugs?”

“He offered me pills last night; amphetamines. He said they helped him with all of the work he had due.”

“I’ll tell the doctor.”

Rob could see Tim lying in a bed with a nasal cannula providing oxygen to his friend. The nurse was taking vitals and entered them into his chart. The doctor shined a light into Tim’s eyes and observed that his pupils remained dilated.

“Did you contact his parents yet, nurse?”

“I’m afraid the university is reluctant to give us his home number.”

“Maybe I can help, Dr. Franks. I’m a first-year medical student and Tim was my roommate in college. I know the family.”

“Call. Don’t give them any details, just get them here,” said the doctor not taking his eyes off his patient.

“Nurse, I need blood and tox screens, stat.”

Tim was sleeping comfortably when his parents arrived at the hospital.

“What’s wrong, Rob? Why is Tim in the ER?”

“He collapsed in the library. Fortunately, Jenn was there and they got him here quickly. I’m afraid that’s all I know except that I was told that he’s sleeping comfortably right now.”

Dr. Franks looked at Tim’s chart and hoped that the results of the blood and tox screen would soon come back from the lab.

Test	Normal	Tim
EKG	-----	arrhythmia
Resting heart rate	70–80 b/m	140 b/m
Blood pressure	120/80 mmHg	160/92 mmHg
Pupil diameter	sensitive to light	fixed & dilated
Skin color	pink	pale
Breathing rate	12–15 breaths/m	30 breaths/m

Questions

1. What signs and symptoms was Tim exhibiting before he went to the hospital?
2. What signs and symptoms became evident after he went to the hospital? For each sign or symptom, state which division of the autonomic nervous system is responsible for Tim’s condition.
3. If Tim’s problems are induced by an overdose of amphetamines, predict their effect on the concentration of the neurotransmitter in the synaptic cleft.

Part VI – Conclusion

“How are you feeling Tim?” asked Dr. Franks.

“I feel really sleepy and my head is pounding.”

“That’s quite normal for someone who has been what you have been through. Your toxicology screen came back with high levels of amphetamines in your blood which is a clear sign of abuse. Now, your parents are in the waiting room and are very concerned about you. By law I am not allowed to give them information without your consent. Would you like to see them?”

“Absolutely. I know they will be angry but I hope they will understand. I think it may be easier on everyone if you give us the information at the same time.”

Tim’s parents came into the room and immediately hugged their son.

“Oh Tim, are you okay? Will he get better doctor?”

“I was dumb,” interjected Tim. “I felt like a failure. I didn’t get into medical school first time around and I felt forced into doing something I didn’t want to do—grad school. Work became hectic and I wasn’t motivated so when a friend offered me a way out I took it. I wanted you to be proud of me, just like Rob’s parents feel about him.”

“Oh Tim, we are proud of you,” said his mother.

“And we’re behind you every step of the way,” said his Dad.

The doctor stepped up to the family. “I know you’re doing a master’s in biology, Tim, so that should make it easier for me to explain what seems to have been going on. Amphetamines do many things including target synapses that secrete catecholamines, like norepinephrine and dopamine. These effects include inhibition of the transporter proteins in the presynaptic membrane and inhibition of the enzyme that breaks down the catecholamines. These effects combine to increase the level of neurotransmitter in the synaptic cleft. In the case of norepinephrine, stimulation of the sympathetic nervous system gave you more energy. And high levels of dopamine in the limbic system in your brain are associated with pleasure, so the amphetamines gave you a sense of well-being. However, over time your body compensated for the increased levels of the neurotransmitters by decreasing the number of receptors in the postsynaptic membranes.”

“Yes I learned about that in physiology and in pharmacology—down regulation of the postsynaptic receptors. I guess that’s why I had to take more to get the same effect.”

“That’s correct, and had you continued you may have experienced some hallucinations. Unfortunately, maintained use of high doses of amphetamines can turn on the expression of certain genes that initiate what is called an addictive state. These effects may take months to reverse, so there is a long road ahead of you before you fully recover.”

Questions

1. What happens to the level of neurotransmitter in the synaptic cleft when a drug decreases reuptake into the presynaptic cleft?
2. What happens to the level of neurotransmitter in the synaptic cleft when a drug inhibits its breakdown in the presynaptic cleft?
3. What happens to the number of postsynaptic receptors if a drug increases the level of neurotransmitter in the synaptic cleft in the long term?
4. If a person takes the drug in the long term and then suddenly stops, what happens to the level of neurotransmitter in the synaptic cleft when the effect of the drug is no longer evident?
5. If a person takes the drug in the long term and then suddenly stops, what happens to the response in the postsynaptic cell?