# SWK 3805: Modules 3 & 4- Biological Models of Addiction

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# Contents

# Modules 3 & 4: Preface

Welcome to the online coursebook for Modules 3 & 4 of our Theories and Biological Basis of Addiction course. The material is designed to be read interactively or after downloading; while the embedded interactive exercises require internet connectivity, each can also be downloaded for offline work. These exercises are presented to help you test and apply what you are reading, challenge yourself, prepare for quizzes, and have a little fun along the way. The list of key terms at the end explains text ***highlighted in bold italics*** throughout the book—in the interactive mode you can click on a highlighted word to jump to its explanation in the key terms section. Use the back arrow to return to where you were reading.

# Modules 3 & 4: Introduction

The reading for Module 3 & 4 introduces concepts essential for understanding biological theories of addiction, as well as how alcohol and other substances affect the brain and other organ systems in the human body. This online coursebook is treated as a double volume because of the complexity of the content—in fact, the biological basis of addiction could be an entire course all on its own. Our Module 3 & 4 online textbook includes content developed by the National Institute on Drug Abuse (NIDA) and a chapter co-authored by this textbook's author.

**Module 3 & 4 Reading Objectives**

After engaging with these reading materials and learning resources, you should be able to:

- Explain basic principles of neuroscience as they relate to understanding substance use disorders/addiction (neuroanatomy and neurotransmitters)
- Identify evidence related to the role of genetics in substance use disorders/addiction
- Identify the ways that substance use affects the brain, behavior, and overall health
- Define several key terms related to substance use disorders.

# Ch. 1: Introduction to Biological Models of Addiction

A sizable body of research evidence addresses four domains of potential biological influence on the development of substance use disorders and addiction.

**Genetics:** Genetic studies paint a picture indicating that genetics are important in both the appearance of and resistance to substance use disorders. Individuals with genetically close relatives (parents or adult siblings) experiencing a substance use disorder involving opioids, cocaine, cannabis or alcohol have up to an eight times higher risk of developing a substance use disorder themselves (Merikangas, et al, 1998). However, genetics alone do not determine a person's destiny: genetic makeup interacts with environment and a person's lifetime of experiences and interactions with their environmental contexts to determine whether a substance use disorder emerges. It is critically important to note that a majority of individuals with a family history of substance use disorders never develop the problem themselves. Just to repeat that fact: most people with substance use disorders in their family history never develop the problem themselves.

Another fact that has emerged from decades of research is that there is no one specific "addiction gene" that applies to all different types of substances. Some of the genes involved are very specific to certain substances—what may "pull" for an alcohol use disorder may not "pull" for a problem with cocaine, for example. Some of the genes involved are not specific to substance use disorders per se, but to a class of problems that have substance misuse as an element—for example, depression. The more we learn about the specific combinations of genes that might be involved, exciting new biological tools for treating or even preventing addiction may emerge, including medications and perhaps even immunizations someday!

**Neurobiology**: The biological realm of addiction studies also includes neuroanatomy, neurophysiology, and neurochemistry. Together, neuroanatomy, neurotransmitters, and neurophysiology investigators have begun to develop increasingly complex, detailed, functional maps of the various regions of the brain involved with progression from the use of substances to a substance use disorder. These maps show how the brain's powerful pain, pleasure, reward, and memory systems interact in the complex process of developing an addiction. This also helps us understand how difficult

it can be to recover from addiction–difficult, but not impossible. Learning about the actions of specific substances on the neurochemistry (neurotransmitters) in our brains also helps us develop strategies for intervening with substance use disorders, including medications and the use of mindfulness meditation and neurofeedback approaches.

**Human Development**: Investigators also direct considerable attention to the developmental effects of a person's exposure to alcohol and other drugs. Many effects of prenatal exposure to alcohol or other drugs do not show up right away at birth; they may not show up until children enter school years later. You may have heard of fetal alcohol syndrome (FAS), which is at the most extreme end of the continuum; many of the neurological effects and birth defects are more subtle, but still have a profound impact on a person's development, learning, social skills, and other important functions. Many of these same effects and issues apply to substances other than alcohol to which a fetus might be exposed during a woman's pregnancy.

In addition, investigators are concerned about the effects of exposure during adolescence and early adulthood. The use of alcohol or other drugs during these years can have profound, lasting effects on the still-developing brain; effects which have significant implications for how people think, behave, and feel, as well as for susceptibility to addiction later in life (see for example Spear, 2002; Squeglia, Jacobus, & Tapert, 2009). All of the evidence suggests that the earlier a person begins using alcohol or other substances, the greater the likelihood of eventually developing a substance use disorder, because of the interaction between exposure and these brain changes at a critical developmental point. Finally, consider the fact that a person's overall health and development may be affected by poor nutrition, physical trauma or injury, or exposure to diseases that often accompany substance misuse.

**Biopsychosocial Perspective:** Remember that we are only teasing out one piece of the biopsychosocial perspective in this module—only the biological. As we move into future modules, you will see how this piece fits together with the others to create the larger picture of complexity related to substance use, misuse, addiction.

### *Reflection: Your Family Tree*

*Draw a diagram of your family tree for at least three or four generations—this could include both your biological and adoptive family. Use a colored highlighter to mark everyone who you know or suspect had a problem with alcohol or other drugs during their lifetime. Is there a pattern to what you see? What are the implications for your own risk? What are the implications for your own resilience? Do you see how genetics are informative but not completely predictive of what happens related to people developing problems with alcohol or other drugs?*

# Ch. 2: Brain and Behavior

The second reading for Module 3 & 4 comes from the 2014 National Institute on Drug Abuse (NIDA) publication called *Drugs, Brains, and Behavior: The Science of Addiction*—the very publication that you started to read in Module 2. When you link to this material, read the following sections:

Part III (pp. 15-20): Drugs and the Brain

Part IV (pp. 21-24): Addiction and Health

(Don't worry, you will read the rest of this publication in other modules!)

In this chapter you will read about:

- three systems in the brain that play a role in substance use disorders/addiction;
- the human brain at the level of neurons;
- how drugs affect these systems to produce their immediate psychotropic effects and long-term brain changes;
- how drugs affect health; and,
- key terms used in the field of substance use disorders and addiction.


Click here for a link to our Carmen course where you can locate the assigned pdf file(s) for this chapter. You will need to be logged into our Carmen course, select Modules 3&4, and proceed to the Coursework area. Under the

Readings heading you will find a box with links to the readings for relevant coursebook chapters. Don’t forget to return here in your coursebook to complete the remaining chapters and interactive activities.

# Ch. 3: Biology of Addiction

This chapter goes into greater detail about some of the topics introduced in the NIDA publication, and some additional content mentioned in our classification system from Module 2. You will be reading a chapter about neurobiology and addiction from Begun and Brown (2014). As further assistance to your learning, this chapter also includes a case example in which many of the concepts are applied.

In this chapter you will read about:

- the role of genetics in substance use disorders/addiction;
- basic neuroanatomy as it relates to substance use disorders/addiction;
- basic neurophysiology as it relates to substance use disorders/addiction;
- substance use and human development;
- neurobiology and recovery from substance use disorders;
- clinical implications of this information; and,
- key terms used in the field of substance use disorders and addiction.


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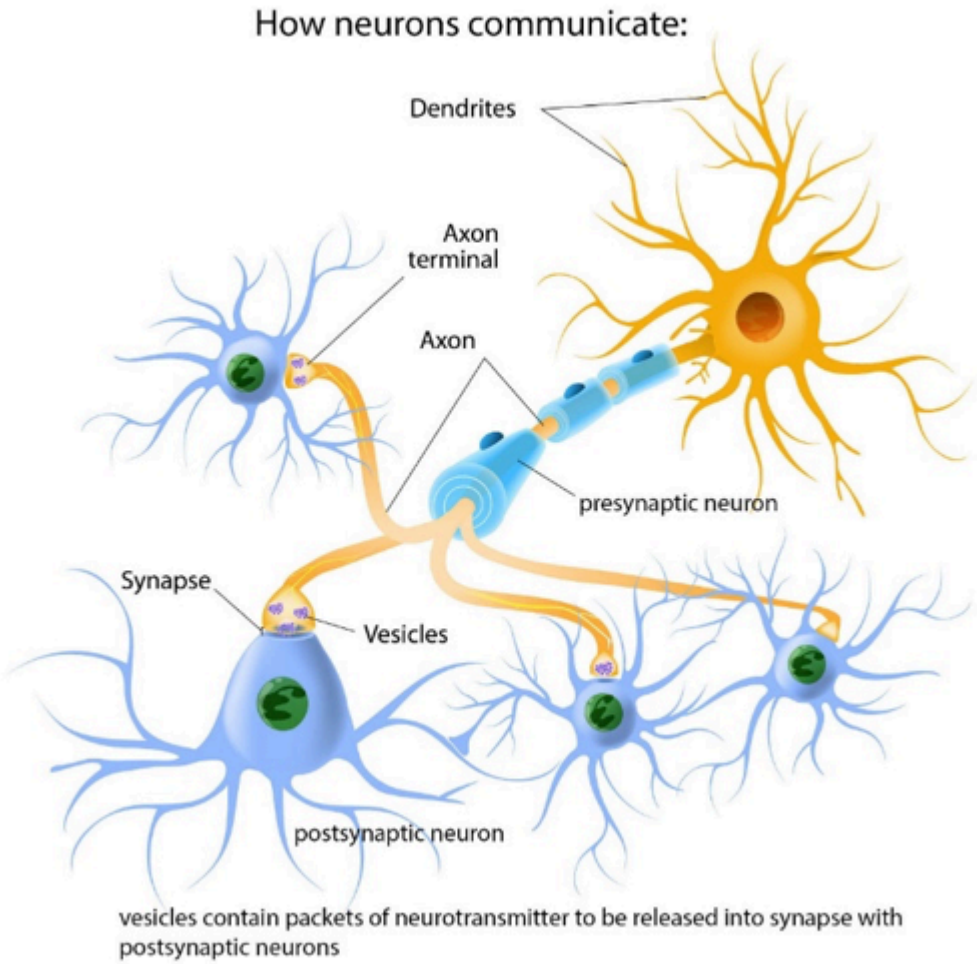
Please answer these short questions to assess your knowledge of the readings.

# Ch. 4: More about Neurotransmitters and How Neurons Communicate

It is helpful to take a closer look at what happens at the level of neurons and their communication with each other through neurotransmitters. This is relevant because the psychotropic effects of the substances we are studying are very often related to the impact these substances have at the level of neurotransmission.

Figure 1 shows the layout of what happens when brain neurons in close physical proximity to each interact or communicate. It makes sense to consider this microscopic level because these are the building blocks of the brain regions that play a role in how substance use can become a substance use disorder. The ***neurotransmitters*** that you have been reading about are contained in packets called vesicles, located in the terminal area of a neuron's axon—the area that comes into close contact with the neighboring neurons. The space between the neurons is the ***synapse*****,** or***synaptic cleft***. And this space between neurons is where those neurotransmitters are released to work their changes on their neighboring neurons. The "sending" neuron is the presynaptic neuron, while the receiving neuron is the postsynaptic neuron.

Figure 1.




Several neurotransmitters are known to play a role in the development, maintenance, and recovery from alcohol or other substance use disorders, as well as other forms of addiction. These include:

- ***anandamide***
- ***dopamine***
- ***endorphins***
- ***epinephrine***
- ***GABA***
- ***glutamate***
- ***norepinephrine***
- ***serotonin***

Several things are very important to understand about neurotransmitters and the system of communication in which they are involved:

- Each type of neurotransmitter is concentrated in one or more specific regions of the brain—they are not

distributed evenly all over the brain.

- We used to believe that a neuron could only release one type of neurotransmitter. More recent research indicates that in many cases the same neuron can release two and possibly more types depending on the frequency of the stimulation its receives—at one frequency it might release one type of neurotransmitter, at another frequency it might release a different type.
- Most neurotransmitters occur naturally as important chemicals in other parts of the body (including the peripheral nervous system and other organs) where they have other health-related functions, not just in the brain (central nervous system).
- Neurotransmitter release is triggered by many natural behaviors, not just by drugs. For example, dopamine release is involved in the natural reward systems associated with food, sex, humor, pair-bonding (mates), listening to music, video games. The addictive potential of a psychotropic drug increases when the concentration of dopamine released is higher compared to what is released by natural behaviors (Johnson, 2014).
- Fast uptake of a drug, for example getting it to the brain by injection rather than ingesting it orally, produces a stronger "high" and therefore a greater potential for addiction. This is because more dopamine is released at once, so it is more powerfully rewarding (Volkow et al., 2010).
- Neurotransmitters released by the ***presynaptic neuron*** must be received by their specific receptors on a postsynaptic neuron. If the ***postsynaptic neuron*** does not have the right receptors, the release of the neurotransmitter into the synapse/synaptic cleft between them has no effect.
- The brain has specific receptors for certain substances (like the cannabinoid or opioid receptors) because there are ***endogenous*** forms of these or chemically similar substances. An example are the naturally occurring ***enkephalins*** that bind to the body's opioid receptors, similar to how ***endorphins*** work.
- ***Transporters*** return the "spent" neurotransmitter substances back to the original (presynaptic) neuron to prepare for release again in the future. Transporters serve to clean up and reduce the concentration of the neurotransmitter in the synaptic space/cleft.
- Neurotransmitters tend to be either ***excitatory*** or ***inhibitory*** in nature, although a few can do both/either function (an example is dopamine). Excitatory neurotransmitters turn "on" or stimulate a neuron to fire, inhibitory neurotransmitters turn "off" or block a neuronl from firing.
- ***Agonist*** substances trigger a receptor to produce a response, because the receptors "recognize" and bind to it. For example, the THC in marijuana (cannabis) is an agonist that activates the cannabinoid receptors.
- ***Antagonist*** substances prevent a receptor from producing its response by blocking the binders or otherwise preventing the response. For example, naloxone treats a heroin/opioid overdose by blocking the effects of the drugs on the body's opioid receptors.
- Certain substances, when combined, create a stronger neurotransmitter response than either could alone. This is called ***potentiation***.

## Neurotransmitters and Withdrawal

At this point, you have developed a basic understanding of how neurotransmitters play a role in substance use, and

have come to recognize the names of some of the key players. Let's take a brief look at the other side of the coin: how neurotransmitters play a role in the experience of withdrawal from certain substances and why this might make a difference in keeping a person motivated to maintain a "quit" attempt after developing a substance use disorder. Here, we can draw from content presented in articles published by Koob and Simon (2009) and Trevisan et al (1998). They tell us that:

- A decrease in dopamine or serotonin (as well as something called the opioid peptide) contributes to the experience of ***dysphoria***. What is dysphoria? Dysphoria is the experience of a profound sense of unease, unhappiness, and general dissatisfaction, often associated with major depression and anxiety. [Your other readings also talked about the experience of ***anhedonia*** during recovery/prolonged withdrawal, as you may recall. The idea is the same: it is a punishing emotional/psychological experience.]
- A decrease in GABA contributes to the experience of anxiety, even panic attacks, due to the resulting nervous system hyperactivity.
- An increase in norepinephrine contributes to the experience of stress.
- An increase in glutamate contributes to hyperexcitability.

Why does this matter? Because these negative emotional and psychological states make it difficult to sustain one's motivation to avoid taking drugs and contribute to the pressure a person might feel to relapse back to using again. And, depending on the nature of the substances involved, withdrawal may lead to decreased dopamine, serotonin, or GABA, as well as increased norepinephrine or glutamate. Knowing about these links between neurotransmitter changes during prolonged withdrawal from using a substance has contributed to the development of several medications to help manage these negative experiences; this, in turn, may help a person to sustain a quit attempt over time. (We will learn more about these medications in Module 13 when we study pharmacotherapy strategies.) Another reason why all of this matters: it helps us to understand the biology behind the frequently reported observation that, during withdrawal and early recovery from many types of substances, the risk for suicide is greater than in the general population.

## Interactive Exercise:

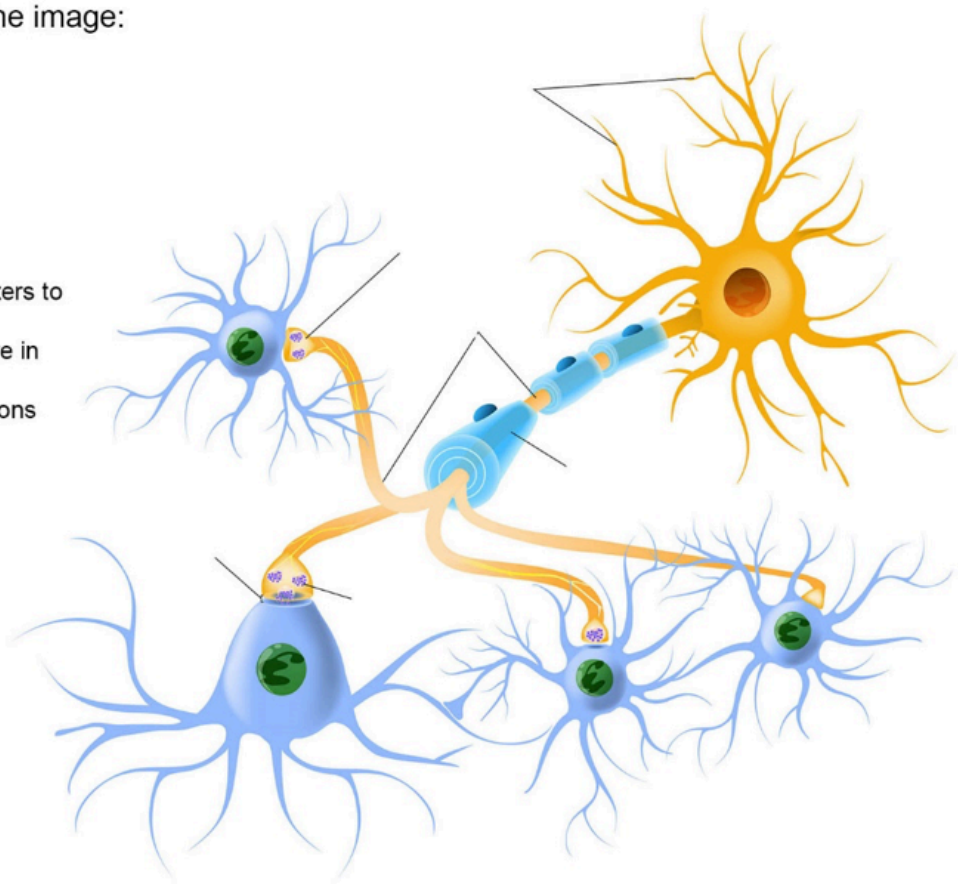
See if you can complete this picture laying out how neurons in the brain interact and communicate–refer back to Figure 1 above for the answers.

# Do you know how neurons communicate?

locate the following in the image:

axons
axon terminals
dendrites
presynaptic neuron
postsynaptic neurons
synapse
vesicles

Where are the neurotransmitters to be found?
How many axon terminatls are in this picture?
How many postsynaptic neurons do you see?



# Ch 5: Summary

In this Module 3 & 4 online coursebook, you learned about some basic principles of neuroscience as they relate to understanding what happens with substance use, substance misuse, substance use disorders and addiction. We explored the world of genetics, and how this can both contribute to and protect from the development of a substance use disorder. We also learned why a person's genetic makeup is not sufficient to predict the outcome because of the key role played by the interaction with environment and experience. You were also introduced to a great deal of information concerning how drugs affect the brain at a neurotransmitter level, as well as at the level of neuroanatomy, and how other body systems might be affected by substance use. Furthermore, you saw how this knowledge relates to drug exposure and use at different periods of development across the lifespan and how it relates to treatment, recovery, and prevention issues.

You are now ready to review some of the key terms related to substance use disorders that were introduced in this book.

# Modules 3 & 4: Key Terms

**agonist**: a drug that stimulates or promotes a receptor's response; an agonist can cause a similar effect to the drug for which it serves as an agonist by replacing the drug in the neurotransmitter response system (being recognized by the binders)

**anandamide**: neurotransmitter responsible for relaxation and analgesia (pain reduction)

**anhedonia**: a person's inability to experience feelings of pleasure in situations which are usually found to be enjoyable

**antagonistic**: a relationship between a drug and its specific receptors in the brain whereby the antagonist drug prevents or blocks the receptor response to another substance

**dopamine**: neurotransmitter involved in the reward and pleasure centers of the brain with a significant role in the development of substance use disorders involving many different drugs, as well as non-substance addiction; usually inhibitory

**dysphoria**: the experience of a profound sense of unease, unhappiness, and general dissatisfaction, often associated with major depression and anxiety.

**endogenous**: occurs naturally, internal to the body (compared to exogenous, introduced from outside the body)

**endorphins**: inhibitory neurotransmitter with an effect of blocking pain signals, similar to opioids; occurs naturally in the body (endogenous)

**enkephalins**: occurring naturally in the body (endogenous), bind to the body's opioid receptors and act as a "natural" painkiller

**epinephrine**: a neurotransmitter that is usually excitatory, involved in the "fight or flight" response

**excitatory**: stimulating action

**GABA**: nickname for the inhibitory neurotransmitter gamma-aminobutyric acid that reduces nervous system excitability; alcohol mimics some effects of GABA by binding to GABA receptors and inhibiting neurons from passing signals

**glutamate**: excitatory neurotransmitter involved in cognition, memory, and learning; its release is suppressed by alcohol, which causes slower brain activity inhibitory: blocking or suppressing action

**neurotransmitters**: naturally occurring (endogenous) chemical messengers between neurons

**norepinephrine**: acts as a neurotransmitter playing a role in attention/arousal, emotion, sleep, dreaming, and learning (also called noradrenaline); part of the "fight or flight" response of the autonomic nervous system for calming after excitation

**potentiation**: an interaction between two substances that produces a combined effect greater than the sum of the individual responses.

**presynaptic neuron**: the neuron sending communication to a neighboring neuron by releasing neurotransmitters across the synapse (synaptic cleft) between them

**postsynaptic neuron**: the neuron receiving communication from a neighboring neuron by accepting the neurotransmitters released into the synapse (synaptic cleft) between them

**serotonin**: a neurotransmitter that is usually inhibitory and has an indirect effect by affecting the responses of neurons to other neurotransmitters like dopamine and norepinephrine (keeps them from overreacting); affected by many different drugs, playing a significant role in the brain's reward systems, thus is involved in substance use disorders and addiction

**synapse/synaptic cleft**: the communication space between two neurons where released neurotransmitters are concentrated until received/retrieved

**transporters**: responsible for returning neurotransmitter chemical units back to the presynaptic neuron after they have been released into the synaptic cleft (reloading for next time)

# Modules 3 & 4: References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