



Nicotine



MECHANISM OF ACTION

BACKGROUND

Tobacco, which comes primarily from the plant *nicotiana tabacum*, has been used for centuries. It can be smoked, chewed, or sniffed. The first description of addiction to tobacco is contained in a report from the New World in which Spanish soldiers said that they could not stop smoking.

When nicotine was isolated from tobacco leaves in 1828, scientists began studying its effects in the brain and body.

This research eventually showed that, although tobacco contains thousands of chemicals, the main ingredient that acts in the brain and produces addiction is nicotine. More recent research has shown that the addiction produced by nicotine is extremely powerful and is at least as strong as addictions to other drugs such as heroin and cocaine.

Some of the effects of nicotine include changes in respiration and blood pressure, constriction of arteries, and increased alertness. Many of these effects are produced through its action on both the central and peripheral nervous system.

Nicotine readily enters the body. When tobacco is smoked, nicotine enters the bloodstream through the lungs. When it is sniffed or chewed, nicotine passes through the mucous membranes of the mouth or nose to enter the bloodstream. Nicotine can also enter the bloodstream by passing through the skin. Regardless of how nicotine reaches the bloodstream, once there, it is distributed throughout the body and brain where it activates specific types of receptors known as cholinergic receptors.

Cholinergic receptors are present in many brain structures, as well as in muscles, adrenal glands, the heart, and other body organs. These receptors are normally activated by the neurotransmitter acetylcholine, which is produced in the brain, and by neurons in the peripheral nervous system. Acetylcholine and its receptors are involved in many activities, including respiration, maintenance of heart rate, memory, alertness, and muscle movement.

Because the chemical structure of nicotine is similar to that of acetylcholine's, it is also able to activate cholinergic receptors. But unlike acetylcholine, when nicotine enters the brain and activates cholinergic receptors, it can disrupt the normal functioning of the brain.

Regular nicotine use causes changes in both the number of cholinergic receptors and the sensitivity of these receptors to nicotine and acetylcholine. Some of these changes may be responsible for the development of tolerance to nicotine. Once tolerance has developed, a nicotine user must regularly supply the brain with nicotine in order to maintain normal brain functioning. If nicotine levels drop, the nicotine user will begin to feel uncomfortable withdrawal symptoms.

Nicotine

Recently, research has shown that nicotine also stimulates the release of the neurotransmitter dopamine in the brain's pleasure circuit. Using microdialysis, a technique that allows minute quantities of neurotransmitters to be measured in precise brain areas, researchers have discovered that nicotine causes an increase in the release of dopamine in the nucleus accumbens. This release of dopamine is similar to that seen for other drugs of abuse, such as heroin and cocaine, and is thought to underlie the pleasurable sensations experienced by many smokers.

Other research is providing even more clues as to how nicotine may exert its effects in the brain. Cholinergic receptors are relatively large structures that consist of several components known as subunits. One of these subunits, the β (beta) subunit, has recently been implicated as having a role in nicotine addiction. Using highly sophisticated bioengineering technologies, scientists were able to produce a new strain of mice in which the gene that produces the β subunit was missing. Without the gene for

the β subunit, these mice, which are known as "knockout" mice because a particular gene has been knocked out, were unable to produce any β subunits. What researchers found when they examined these knockout mice was that in contrast to mice who had an intact receptor, mice without the β subunit would not self-administer nicotine. These studies demonstrate that the β subunit plays a critical role in mediating the pleasurable effects of nicotine. The results also provide scientists with valuable new information about how nicotine acts in the brain, information that may eventually lead to better treatments for nicotine addiction.

However nicotine may not be the only psychoactive ingredient in tobacco. Using advanced brain imaging technology, it is possible to actually see what tobacco smoking is doing to the brain of an awake and behaving human being. Using one type of brain imaging, positron emission tomography (PET), scientists discovered that cigarette smoking causes a dramatic decrease in the levels of an important enzyme that breaks down dopamine.



Nicotine

The decrease in this enzyme, known as monoamine-oxidase-A (MAO-A), results in an increase in dopamine levels. Importantly, this particular effect is not caused by nicotine but by some additional, unknown compound in cigarette smoke. Nicotine itself does not alter MAO-A levels; it affects dopamine through other mechanisms. Thus, there may be multiple routes by which smoking alters the neurotransmitter dopamine to ultimately produce feelings of pleasure and reward.

That nicotine is a highly addictive drug can clearly be seen when one considers the vast number of people who continue to use tobacco products despite their well known harmful and even lethal effects. In fact, at least 90% of smokers would like to quit, but each year fewer than 10% who try are actually successful. But, while nicotine may produce addiction to tobacco products, it is the thousands of other chemicals in tobacco that are responsible for its many adverse health effects.

Smoking either cigarettes or cigars can cause respiratory problems, lung cancer, emphysema, heart problems, and peripheral vascular disease. In fact, smoking is the largest preventable cause of premature death and disability. Cigarette smoking kills at least 400,000 people in the United States each year and makes countless others ill, including those who are exposed to secondhand smoke. The use of smokeless tobacco is also associated with serious health problems.

Chewing tobacco can cause cancers of the oral cavity, pharynx, larynx, and esophagus. It also causes damage to gums that may lead to the loss of teeth. Although popular among sports figures, smokeless tobacco can also reduce physical performance.



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OBJECTIVE

- ★ The student will become more familiar with the neuroscience concepts and terminology associated with the effects of nicotine and tobacco products on the brain and body.

OBJECTIVE

- ★ The student will understand that nicotine is a highly addictive drug and that once someone has become addicted, it is very difficult to stop smoking, even in the face of serious health consequences.

OBJECTIVE

- ★ The student will learn that cigarette smoke contains molecules that are deposited along the entire respiratory tract, including the lungs. These molecules not only turn the lungs and other parts of the respiratory system black, but they also cause cancers and other respiratory illnesses.

NICOTINE ACTIVITY ONE

The students will complete the Nicotine Word Find, and the teacher will then review the words and have the students discuss how the terms relate to tobacco use. A copy of the Word Find and Word Find Solution is included in the guide.

NICOTINE ACTIVITY TWO

The students will call local hospitals to obtain the names of physicians who provide treatment to people trying to stop their use of tobacco products. The students will then compose a letter to one or more of these physicians inviting them to come and speak to the class on the difficulties associated with quitting smoking or the use of other tobacco products. Prior to the visit by the physician, the students will prepare a list of questions that they would like to ask. These questions might include the following: 1) How many people succeed the first or even second time they try to stop smoking? 2) How many people try repeatedly to quit smoking without success? 3) Do people still smoke even when they have a life-threatening illness, such as heart disease or lung cancer?

NICOTINE ACTIVITY THREE

The students will conduct the following experiment:

Materials needed: cigarette, transparent plastic syringe, cotton balls, matches or lighter

Fill the syringe with the cotton balls. Insert the end of the syringe onto the filter of the cigarette. Light the cigarette and pull back the plunger to draw smoke into the barrel of the syringe. Have the students watch the cotton balls turn black as the smoke particles are deposited. Discuss with the students what they have observed. Students might consider what the effects of smoking several cigarettes a day for many years would have on the lungs if only one cigarette can turn a cotton ball black.

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WORD SEARCH

A	Z	W	S	A	M	E	S	Y	H	P	M	E
R	O	T	P	E	C	E	R	Q	Y	I	N	P
R	E	S	L	O	L	J	G	T	R	I	E	N
B	N	I	A	R	B	U	O	D	L	P	U	M
L	R	Z	W	A	R	T	M	O	O	T	R	K
O	X	Q	A	D	E	I	H	P	R	Z	O	R
O	Q	A	R	W	O	C	C	A	B	O	T	N
D	S	E	D	E	L	D	G	M	R	F	R	O
S	Y	G	H	Y	U	I	J	I	K	I	A	I
T	X	P	T	C	C	L	V	N	J	B	N	T
R	N	E	I	M	A	R	T	E	Y	I	S	C
E	C	Q	W	O	Z	C	D	O	P	M	M	I
A	D	D	R	Y	C	T	A	R	E	N	I	D
M	O	T	K	Z	Q	P	O	N	A	T	T	D
N	E	T	T	E	R	A	G	I	C	W	T	A
G	E	U	N	I	C	O	T	I	N	E	E	L
A	L	S	G	N	I	K	O	M	S	I	R	R

EMPHYSEMA

NEUROTRANSMITTER

CIGAR

DOPAMINE

ADDICTION

REWARD

SMOKING

WITHDRAWAL

CIGARETTE

CANCER

DRUG

ACETYLCHOLINE

BRAIN

BLOODSTREAM

RECEPTOR

NICOTINE

TOBACCO

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WORD SEARCH

SOLUTION

A	Z	W	S	A	M	E	S	Y	H	P	M	E
R	O	T	P	E	C	E	R	Q	Y	I	N	P
R	E	S	L	O	L	J	G	T	R	I	E	N
B	N	I	A	R	B	U	O	D	L	P	U	M
L	R	Z	W	A	R	T	M	O	O	T	R	K
O	X	Q	A	D	E	I	H	P	R	Z	O	R
O	Q	A	R	W	O	C	C	A	B	O	T	N
D	S	E	D	E	L	D	G	M	R	F	R	O
S	Y	G	H	Y	U	I	J	I	K	I	A	I
T	X	P	T	C	C	L	V	N	J	B	N	T
R	N	E	I	M	A	R	T	E	Y	I	S	C
E	C	Q	W	O	Z	C	D	O	P	M	M	I
A	D	D	R	Y	C	T	A	R	E	N	I	D
M	O	T	K	Z	Q	P	O	N	A	T	T	D
N	E	T	T	E	R	A	G	I	C	W	T	A
G	E	U	N	I	C	O	T	I	N	E	E	L
A	L	S	G	N	I	K	O	M	S	I	R	R

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NEUROTRANSMITTER

CIGAR

DOPAMINE

ADDICTION

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