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Human Genetics
Concepts and Applications
THIRTEENTH EDITION

Chapter 8
Genetics of Behavior
Thirteenth Edition

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Learning Outcomes [1]

1. Identify the physical basis of behavioral traits in the brain.
2. Explain how genes can affect behavior.
3. Describe how studies on dogs helped to find a narcolepsy gene.
4. Explain how mutations in the *period 2* gene disrupt sleep-wake cycles.
5. Describe intelligence tests.
6. List causes of intellectual disability.
7. State the two identifying characteristics of drug addiction.

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Learning Outcomes [2]

8. Discuss evidence that drug addiction is a biological phenomenon.
9. Describe two types of receptors that are implicated in drug addiction.
10. Explain how genes may affect risk of developing major depressive disorder.
11. Explain how the genetics of bipolar disorder is complex.
12. Explain how schizophrenia differs from the mood disorders.
13. Discuss how synaptic pruning may explain the origin of schizophrenia.
14. List risk factors for autism.

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Behavior

Behavior is a complex continuum of emotions, moods, intelligence, and personality that drives how we function on a daily basis.

Occurs in response to environmental factors, but how we respond has genetic underpinnings

Behavioral genetics considers nervous system function and variation

• Including the hard-to-define qualities of mood and mind

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The Human Brain

Weighs about three pounds, and resembles a giant gray walnut

Consists of 100 billion nerve cells, or **neurons** and at least a trillion other supportive and nurturing cells called **neuroglia**

• Neurons communicate across synapses using **neurotransmitters**

Genes encode diverse proteins that control the production and distribution of these chemical signals

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Neurotransmission
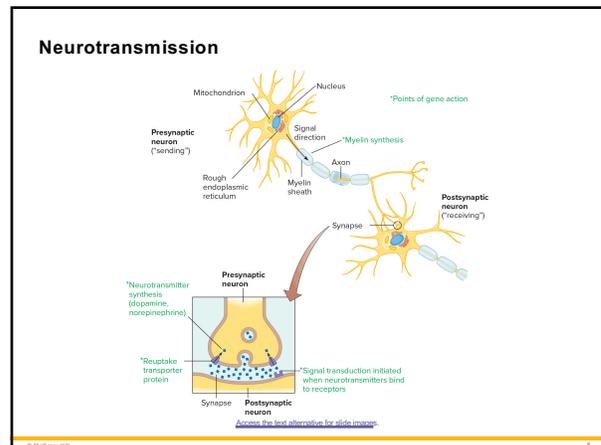
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Behavioral Genetics

Genetic studies of behavioral disorders are challenging traditional psychiatric classification

- Variants of hundreds of genes contribute in different degrees to behavioral disorders.

- People who have different behavioral disorders, such as depression, addiction, and schizophrenia, may share underlying gene variants.

Old and new genetic tools are being used to describe the biological causes of various behavioral disorders.

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Prevalence of Behavioral Disorders in the U.S. Population

Table 8.1 12-Month Prevalence of Some Behavioral Disorders in the US Adult Population	
Condition	Prevalence (%)
Anxiety	18.0
Social phobia	6.8
Posttraumatic stress disorder	3.5
Generalized anxiety disorder	3.1
Obsessive compulsive disorder	1.0
Panic disorder	2.7
Autism spectrum disorders (children)	1.5
Eating disorders	3.0
Anorexia nervosa	female 0.9, male 0.3
Binge eating	1.2
Bulimia nervosa	0.3
Mood disorders	9.5
Major depressive disorder	6.7
Bipolar disorder	2.6
Schizophrenia	1.1

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Sleep

Sleep has been called "a vital behavior of unknown function"

- Indeed, without sleep, animals die.

- We spend a third of our lives in this mysterious state.

Twin studies indicate 4 of the 5 stages of sleep have a hereditary component

- Fifth stage, REM sleep, is associated with dreaming and so reflects input of experience more than genes

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Narcolepsy with Cataplexy

- Daytime sleepiness with tendency to rapidly fall asleep **(narcolepsy)** and periods of muscle weakness **(cataplexy)**

- Genetic basis was first identified in dogs, then humans

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Familial Advanced Sleep Phase Syndrome

Disorder characterized by a very unusual sleep-wake cycle

Affected members of a large family enabled researchers to identify the first clock gene in humans

- *Period 2* gene on chromosome 2 enables a person to respond to day and night environmental cues

- A single DNA base mutation interferes with synchronization of the sleep-wake cycle with daily sunrise and sunset

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Intelligence

Intelligence is a highly variable complex trait that is subject to many genetic and environmental influences.

In general, intelligence refers to the ability to reason, learn, remember, connect ideas, deduce, and create.

Intelligence quotient (IQ) test was first developed by Alfred Binet in France in 1904

- To predict academic success of developmentally disabled children in school

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IQ Test [1]

Later modified at Stanford University to assess white, middle-class Americans

IQ is normally distributed around a mean of 100

- Below 50—Severe intellectual disability
- 50 to 70—Mild intellectual disability
- 85 to 115—Average intelligence
- Above 115—Above average intelligence

Tests verbal fluency, mathematical reasoning, memory, and spatial visualization ability

"g" value measures a general intelligence factor that represents the inherited portion of IQ

Environment has less of an influence on IQ as a person ages

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IQ Test [2]

Genetics can explain some cases of intellectual disability, which affects 3 in 100 persons in the U.S.

- Noninherited birth defects
- Abnormal genes and chromosomes
- Environmental exposure to toxins
- Infections and malnutrition

The best-studied genetic causes of intellectual disability are Down syndrome and fragile X syndrome

Exome and genome sequencing have been helpful in assigning causative genes in children with intellectual disability who have no previously known causes

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Success and IQ

IQ has been a fairly accurate predictor of success in school and work.

IQ	70	80	90	100	110	120	130
Population percentages							
Total population distribution		5	20	50	20	5	
Lives in poverty		30	16	6	3	2	

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Drug Addiction

Compulsively seeking and taking a drug despite knowing its adverse effects

Has two identifying characteristics:

- **Tolerance**—Need to take more of a drug to achieve the same effect
- **Dependence**—Onset of withdrawal symptoms with cessation of drug

Heritability is 0.4 to 0.6

- Twin and adoption studies support role of genes in drug addiction.

Produces long-lasting changes in the brain

Brain changes that contribute to addiction are in the limbic system

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Events of Addiction [1]

Prefrontal cortex

Gene

Nucleus accumbens

Ventral tegmental area

Drug
Alcohol
Nicotine
Cocaine
→ Changes in expression of genes that control signal transduction; neurotransmitter synthesis; receptor abundance and activity
→ Changes in brain circuitry (neuron connections) in limbic system
→ Changes in behavior; dependence; tolerance

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Events of Addiction [2]

Proteins involved in drug addiction are those that:

- produce neurotransmitters, such as enzymes required for neurotransmitter synthesis;
- remove excess neurotransmitters from the synapse (called reuptake transporters);
- form receptors on the postsynaptic (receiving) neuron that are activated or inactivated when specific neurotransmitters bind; and
- convey chemical signals in the postsynaptic neuron.

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Drugs of Abuse [1]

Abused drugs are often derived from plants

- Cocaine, opium, and tetrahydrocannabinol (THC), the main ingredient in marijuana

- Chemicals bind receptors in human neurons

Endorphins and enkephalins are the human equivalents of opiates

- Relieve pain

LSD (lysergic acid diethylamide) causes effects similar to the symptoms of schizophrenia

- But is not addictive

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Drugs of Abuse [2]

Amphetamines are highly addictive drugs when misused.

- Promote the release of the neurotransmitter dopamine

- Addiction can lead to psychosis, which is a loss of contact with reality, causing delusions and hallucinations.

People addicted to various drugs share certain gene variants that must be paired with environmental stimuli for addiction to occur.

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Drugs of Abuse [3]

Discovering the genetic underpinnings of nicotine addiction is increasing our knowledge of addiction

- On a molecular level, nicotine does damage through a 5-part assembly of proteins called a nicotinic receptor.

- The receptor normally binds the neurotransmitter acetylcholine, but it also binds the similarly shaped nicotine molecule

- Certain variants of the receptor bind nicotine very strongly, which triggers a nerve impulse

  - Stimulates the pleasurable dopamine release into the synapse.

Nicotine in tobacco causes addiction and susceptibility to lung cancer

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Nicotine's effects at the cellular level

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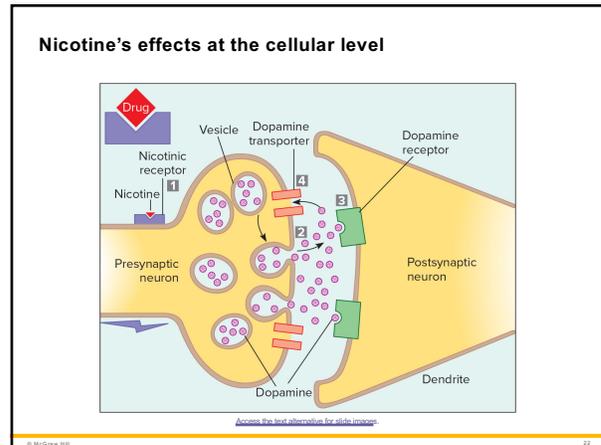
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Mood Disorders

Represent the extremes of normal behavior

The two most prevalent are:

- **Major depressive disorder**—Marked by unexplained lethargy, sadness, and chronic depression

- **Bipolar disorder**—Marked by depression interspersed with mania

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Major Depressive Disorder

A disabling condition that goes beyond sadness

Likely cause is a deficiency of the neurotransmitter **serotonin**

- Affects mood, emotion, appetite, and sleep

Many antidepressant drugs are selective serotonin reuptake inhibitors (SSRIs)

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Bipolar Disorder

Bipolar disorder is rarer than depression.

It is also called **manic depression**

Bipolar disorder includes depressive periods and periods of mania or hypomania.

Many gene variants contribute to developing bipolar disorder.

- As much as 10% of the genome is part of the clinical picture

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Schizophrenia 1

Schizophrenia is a debilitating loss of the ability to organize thoughts and perceptions, which leads to a withdrawal from reality.

- It is a form of psychosis, which is a disease of thought and sense of self.
- In contrast, the mood disorders are emotional, and the dementias are cognitive.

It affects about 1% of the word's population

- 10% of affected individuals commit suicide

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Schizophrenia 2

Symptoms typically begin in early adulthood

Progression

- Difficulty in paying attention, memory and learning difficulties, psychosis (delusions and hallucinations)

Schizophrenia means "split mind," but it does not cause a split or multiple personality.

In many patients the course of schizophrenia plateaus (evens out) or becomes episodic.

- It is not a continuous decline, as is the case for dementia.

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Schizophrenia 3

Disjointed drawings by schizophrenic patients display the characteristic fragmentation of the mind.

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Risks of Schizophrenia

Heritability of 0.9 and empiric risk values indicate a strong genetic component for schizophrenia.

Table 8.2 Empiric Risks for Schizophrenia	
Relationship	**Risk**
MZ twin	48%
DZ twin	17%
Child	13%
Sibling	9%
Parent	6%
Half-sibling	6%
Grandchild	5%
Niece/nephew	4%
Aunt/uncle	2%
First cousin	2%
General population	1%

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Causes of Schizophrenia 1

- Dozens of genes may interact with environmental influences to cause this disease.
- Environmental influences include birth complications, fetal oxygen deprivation, herpesvirus infection at birth, and traumatic brain injury or malnutrition in the mother.
- Infections during pregnancy is a well-studied environmental factor causing schizophrenia.
- It is not the infection that sets the stage for later schizophrenia, but the maternal response to it.
- High levels of the cytokine interleukin-8 are associated with a child developing schizophrenia.

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Causes of Schizophrenia 2

- An important new gene finding associated with schizophrenia are the *C4* genes associated with the complement system.
- Certain variants of the *C4A* genes are much more common among individuals with schizophrenia.
- The *C4A* variant gene causes too much pruning of synaptic connections in the brain.
- Microglial cells bind to C4A protein tags to perform the pruning.

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Synaptic Pruning 1

Presynaptic neuron

Neuron

Synapse

Synaptic pruning

Postsynaptic neuron

Neuron

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Synaptic Pruning 2

15-year-old

Synaptic pruning

20-year-old, no schizophrenia

Excess pruning

20-year-old, schizophrenia

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Autism

Autism spectrum disorders impair socialization and communication skills, with symptoms appearing before age 3.

- Seizures may occur

Affects one in 40 children in the United States

- Strikes four times as many boys as girls

Although 70% of people with autism have intellectual disability, others are very intelligent

Many are talented in science or the arts

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Famous People Who Had Autistic Behaviors

Table 8.3 Famous People Who Had Autistic Behaviors	
Person	**Characteristics**
Albert Einstein	Did not like to be touched
	Difficulty learning in school
	Awkward in social situations
Charles Darwin	Preferred letter writing to face-to-face interactions
	Fixated on certain objects and topics
Emily Dickinson	Heightened sense of smell
	Preferred white clothing
	Reclusive
	Fascinated with flowers
Michelangelo	Limited interests but obsessed with work
	Poor communication and social skills
	Relied on rigid routines

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Causes of Autism

In most cases of autism, many genes contribute to different degrees against a backdrop of environmental influences.

- Prenatal exposures to rubella (German measles), the drug valproate, and folic acid supplements increase the risk of autism.

Heritability of autism is high: about 0.90 (90% of variability due to genetics).

Autism is part of many genetic syndromes, but these account for a small % of autism cases.

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Discovering Autism Genes 1

Three approaches are used to identify gene variants that contribute to autism.

- The "multiple unrelated affected subjects" approach seeks gene variants in individuals with autism that are not in population databases of unaffected children.

- "Trio analysis" distinguishes carrier parents from *de novo* mutations in children.

- "Recessive analysis" searches for gene variants that two or more affected siblings share.

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Discovering Autism Genes 2

(a) Five unrelated children who have autism

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Discovering Autism Genes 3

(b) Trio analysis

(c) Recessive analysis

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Understanding Autism 1

Two genes in particular may finally explain how autism develops.

- Encode cell adhesion proteins found at synapses

Neurexins and **neuroligins** are embedded in the plasma membranes of presynaptic and postsynaptic neurons, respectively.

- Mutations misfold the two proteins so that they cannot interact properly

- If this interference happens in early childhood when synapses naturally form as child experiences environment, learning & memory may be impacted

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Understanding Autism 2

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