Genetics of Behavior (Learning Objectives)

• Recognize that behavior is multi-factorial with genetic components
• Understand how multi-factorial traits are studied. Explain the terms: prevalence, incidence, empiric risk, heritability, genome-wide association studies (Chapter 7.3)

To be continued
Genes and Behavior

Behavior is a complex continuum of emotions, moods, intelligence, and personality.

Behavior occurs in response to environmental factors, but *how* we respond has genetic underpinnings, multi-factorial in nature.
Investigating Multifactorial Traits

Population Studies

**Incidence** is the number of new cases of a disorder diagnosed in a population within a specific time.

**Prevalence** is the proportion or number of individuals who have a particular trait within a specific time.
Statistical Measures for studies of multi-factorial traits

Variations in traits due to environmental influences

1. Empiric risk (monogenic traits)
2. Heritability (polygenic traits)
   - Coefficients of Relatedness
   - Twin Studies
3. Adopted Individuals
4. Genome-wide association
Empiric Risk

- A statistical measure of the likelihood that a monogenic trait will recur based on incidence
- Cleft lip is more likely in a person who has a relative with the condition

<table>
<thead>
<tr>
<th>Relationship to Affected Person</th>
<th>Empiric Risk of Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identical twin</td>
<td>40.0%</td>
</tr>
<tr>
<td>Sibling</td>
<td>4.1%</td>
</tr>
<tr>
<td>Child</td>
<td>3.5%</td>
</tr>
<tr>
<td>Niece/nephew</td>
<td>0.8%</td>
</tr>
<tr>
<td>First cousin</td>
<td>0.3%</td>
</tr>
<tr>
<td>General population risk (no affected relatives)</td>
<td>0.1%</td>
</tr>
</tbody>
</table>
Heritability describes the population, not individuals. Measures the fraction of phenotypic variation in a population that can be attributed to genetic variations. Heritability is specific to a particular population in a particular environment.

![Diagram](Figure 7.6)
Heritability (H)

Proportion of phenotypic variability due to a genetic component within a certain population over a specific period

Heritability is estimated using alternative statistical methods

- Comparing the proportion of people sharing a trait to the proportion predicted to share the trait if it was inherited in a Mendelian fashion

- Derived by knowing the blood relationships of the individuals (coefficient of relatedness)
Heritability (H)

Comparing actual proportion with the predicted one

H = 1.0 indicates that under particular conditions the phenotypic variability is genetically determined.

<table>
<thead>
<tr>
<th>Trait</th>
<th>Heritability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clubfoot</td>
<td>0.8</td>
</tr>
<tr>
<td>Height</td>
<td>0.8</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>0.6</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.5</td>
</tr>
<tr>
<td>Verbal aptitude</td>
<td>0.7</td>
</tr>
<tr>
<td>Mathematical aptitude</td>
<td>0.3</td>
</tr>
<tr>
<td>Spelling aptitude</td>
<td>0.5</td>
</tr>
<tr>
<td>Total fingerprint ridge count</td>
<td>0.9</td>
</tr>
<tr>
<td>Intelligence</td>
<td>0.5–0.8</td>
</tr>
<tr>
<td>Total serum cholesterol</td>
<td>0.6</td>
</tr>
</tbody>
</table>
Coefficients of Relatedness

The proportion of genes shared between two people related in a certain way

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Degree of Relationship</th>
<th>Percent Shared Genes (Coefficient of Relatedness)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibling to sibling</td>
<td>1°</td>
<td>50% (1/2)</td>
</tr>
<tr>
<td>Parent to child</td>
<td>1°</td>
<td>50% (1/2)</td>
</tr>
<tr>
<td>Uncle/aunt to niece/nephew</td>
<td>2°</td>
<td>25% (1/4)</td>
</tr>
<tr>
<td>Grandparent to grandchild</td>
<td>2°</td>
<td>25% (1/4)</td>
</tr>
<tr>
<td>First cousin to first cousin</td>
<td>3°</td>
<td>12 1/2% (1/8)</td>
</tr>
</tbody>
</table>
Separating Genetic and Environmental Influences

Dizygotic twins = Shared environment and 50% of genes

Monozygotic twins = Identical genotype and shared environment

Twins raised apart = Shared genotype but not environment

Adopted individuals = Shared environment but not genes
Twin Studies

**Concordance** measures the frequency of expression of a trait in both members of monozygotic (MZ) or dizygotic (DZ) twins

- Twins who differ in a trait are said to be discordant for it

For a trait largely determined by genes, concordance is higher for MZ than DZ twins
# Twins

<table>
<thead>
<tr>
<th>Trait</th>
<th>MZ (identical) twins</th>
<th>DZ (fraternal) twins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>Alzheimer disease</td>
<td>78%</td>
<td>39%</td>
</tr>
<tr>
<td>Anorexia nervosa</td>
<td>55%</td>
<td>7%</td>
</tr>
<tr>
<td>Autism</td>
<td>90%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>33–80%</td>
<td>0–8%</td>
</tr>
<tr>
<td>Cleft lip with or without cleft palate</td>
<td>40%</td>
<td>3–6%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>62%</td>
<td>48%</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>40–50%</td>
<td>10%</td>
</tr>
</tbody>
</table>
Adopted Individuals

• Similarities between adopted people and adopted parents reflect mostly environmental influences

• Similarities between adoptees and their biological parents reflect mostly genetic influences

• Therefore, information on both sets of parents can reveal how heredity and the environment both contribute to a trait
Genome-Wide Association Studies

Older techniques search for known gene variants, typically in only a few people.

Sequencing of the human genome and the HapMap project (which identifies SNPs) have led to a new tool.
SNPs

SNPs (single nucleotide polymorphisms) are sites in a genome where the DNA base varies in at least 1% of the population.

In these studies, SNPs span the genome, rather than define a single gene.

- A SNP can be *anywhere* among our roughly 3.2 billion base pairs.

SNPs

PTC gene, non-taster allele

1  atgttgactc taactcgcctt ccgcacactgtg tcctatgaag tcaggagtaac atttctgttct
61.. atttcaggctc tggagtttgc agtggggttt gctgaccaatgc cttgcttttt cttggtgaat
121.. ttttgggatg agtgaagag gcatgacactg agcaacagtg atttctgtgct gctgtgttctc...

781  tgtgccgttc ctatctctgt gcccctactgt attctgtggc gcgcacaatgt agggtgtagtg
841  gtttgggttg ggtatatggc agctttgctcc tctgggcagcg ccgactttct gatctcaggc
901  aatgcagaaagt gtagagaggg tcctgatgacc atttctgtctt gggctcagag cagcctgaag
961  gtaagagcccg accacaaggg aagtttccgg acacttgtgct ga

PTC gene, taster allele

1  atgttgactc taactcgcctt ccgcacactgtg tcctatgaag tcaggagtaac atttctgttct
61.. atttcaggctc tggagtttgc agtggggttt gctgaccaatgc cttgcttttt cttggtgaat
121.. ttttgggatg agtgaagag gcatgacactg agcaacagtg atttctgtgct gctgtgttctc...

781  tgtgccgttc ctatctctgt gcccctactgt attctgtggc gcgcacaatgt agggtgtagtg
841  gtttgggttg ggtatatggc agctttgctcc tctgggcagcg ccgactttct gatctcaggc
901  aatgcagaaagt gtagagaggg tcctgatgacc atttctgtctt gggctcagag cagcctgaag
961  gtaagagcccg accacaaggg aagtttccgg acacttgtgct ga
Genome-wide association studies

- Seek correlations between SNP patterns and phenotypes in large groups of individuals
- Microarrays

http://highered.mcgraw-hill.com/olcweb/cgi/pluginpop.cgi?it=swf::535::535::/sites/dl/free/0072437316/120078/micro50.swf::Microarray
Genome-wide association studies seek SNPs that are shared with much greater frequency among individuals with the same trait than among others.

Figure 7.9
Behavioral Genetics

Considers nervous system function and variation, including mood and mind

Uses studies of
- Empirical risk
- Twin studies
- Adoption studies
- Association studies with SNPs and
- Analysis of specific mutations that are present in individuals with the behavior
The Human Brain

brain weighs about 3 pounds

- Consists of 100 billion neurons and at least a trillion other supportive and nurturing cells called neuroglia

Animated Neuroscience DVD

Neurons communicate across synapses using neurotransmitters

http://outreach.mcb.harvard.edu/animations/synaptic.swf

Genes control the production and distribution of these chemical signals
Neurotransmission

Figure 8.1
Behavioral Genetics

Genetic studies of behavioral disorders are challenging traditional psychiatric classification.

- These disorders may lie on a continuum with many genes having input.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer disease</td>
<td>4.0</td>
</tr>
<tr>
<td>Anxiety</td>
<td>8.0</td>
</tr>
<tr>
<td>Phobias</td>
<td>2.5</td>
</tr>
<tr>
<td>Posttraumatic stress disorder</td>
<td>1.8</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>1.5</td>
</tr>
<tr>
<td>Obsessive compulsive disorder</td>
<td>1.2</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>1.0</td>
</tr>
<tr>
<td>Attention deficit hyperactivity disorder</td>
<td>2.0</td>
</tr>
<tr>
<td>Autism spectrum disorders</td>
<td>0.1</td>
</tr>
<tr>
<td>Drug addiction</td>
<td>4.0</td>
</tr>
<tr>
<td>Eating disorders</td>
<td>3.0</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>7.0</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>6.0</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>1.0</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Prevalence of Behavioral Disorders in the U.S. Population

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Eating Disorders

In the US, 5-10 million people have eating disorders

- About 10% are male

Twin studies reveal a heritability ranging from 0.5-0.8

Genes whose products control appetite or regulate certain neurotransmitters may predispose to eating disorders
Eating Disorders

Anorexia nervosa – Psychological perception of obesity and intentional starvation

Bulimia – Psychological perception of obesity and intentional vomiting

Muscle dysmorphia – Psychological perception of being too small
Sleep

Without sleep animals die

Stages of sleep

http://www.youtube.com/watch?v=qEWbu37fH9k
http://www.youtube.com/watch?v=uWYwMnMMEoU&NR=1

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

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

http://www.ninds.nih.gov/disorders/brain_basics/understanding_sleep.htm
Narcolepsy with Cataplexy

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

The genetic basis was first identified in dogs, then humans.

http://www.youtube.com/watch?v=l2x14qETS7E
Familial Advanced Sleep Phase Syndrome

An autosomal dominant disorder characterized by a very unusual sleep-wake cycle (fall asleep at 7:30 pm and wake up at 4:30 am)

Affected members of a large family enabled researchers to identify the first “clock” gene in humans
- The *period* gene enables a person to respond to day and night environmental cues
Intelligence

A complex and variable trait subject to multiple genes, environmental influences, and intense subjectivity

The IQ (intelligence quotient) test was first developed in France in 1904
  - To predict academic success of developmentally disabled children

Refers to the ability to reason, learn, remember, synthesize, deduce, and create
Intelligence

The **IQ** test was modified at Stanford University to assess white, middle-class Americans
tests verbal fluency, mathematical reasoning, memory, and spatial visualization ability
The IQ Test

IQ is normally distributed around a mean of 100

- Below 50 = Severe mental retardation
- 50-70 = Mild mental retardation
- 85-115 = Average intelligence
- Above 115 = Above average intelligence
Drug Addiction

Compulsively seeking and taking a drug despite knowing its adverse effects

Serotonin

http://www.youtube.com/watch?v=iLVxickzsNs

Characteristics:

- **Tolerance** = The need to take more of a drug to achieve the same effect
- **Dependence** = The onset of withdrawal symptoms with cessation of drug
Drug Addiction

Heritability is 0.4-0.6

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

Drug addiction produces long-lasting changes in the brain

Brain changes that contribute to addiction are in the limbic system

http://www.youtube.com/watch?v=lZ4mdXAtnEs&feature=related
http://www.youtube.com/watch?v=g6KpIrKCDwg&NR=1
http://www.youtube.com/watch?v=BHfOui9hSg4&NR=1
The Events of Addiction

![Diagram showing the events of addiction involving genes, prefrontal cortex, nucleus accumbens, and ventral tegmental area.](image)

**Figure 8.6**

- **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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Proteins Involved in Drug Addiction

Enzymes involved in biosynthetic pathways of neurotransmitters

Neurotransmitter-reuptake transporters

Cell-surface receptors

Members of signal transduction pathways in postsynaptic neuron
Drugs of Abuse

Abused drugs are often derived from plants
- Cocaine, opium, and tetrahydrocannabinol (THC), the main ingredient in marijuana
- These chemicals bind receptors in human neurons

Endorphins and enkephalins are the human equivalents of opiates
- Are pain relievers
Candidate Genes for Drug Addiction

Nicotine binds a receptor that normally binds acetylcholine, causing dopamine release and pleasure.

Candidate genes for addiction include those that encode:
- The dopamine D(2) receptor
- The nicotine receptor parts
- The protein neurexin-1, which ferries nicotinic receptors to neuron’s surface
Mood Disorders

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 affective disorder** = Marked by depression interspersed with mania
Major Depressive Disorder

Affects 6% of the US population

A likely cause is a deficiency of the neurotransmitter serotonin, which affects mood, emotion, appetite, and sleep

Many antidepressant drugs are selective serotonin reuptake inhibitors (SSRIs)
Major Depressive Disorder

Figure 8.7
Bipolar Disorder

Also called manic-depression

Affects 1% of the population

Associated with several chromosome sites

Its genetic roots are difficult to isolate
Schizophrenia

Loss of ability to organize thoughts and perceptions – withdrawal from reality

Worldwide – 1% affected

Typically early adult onset

Progression

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

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

Figure 8.8
Schizophrenia

A heritability of 0.8 and empiric risk values indicate a strong genetic component for schizophrenia.

Dozens of genes may interact with environmental influences to cause this disease.

One powerful candidate is infection during pregnancy.

- Prenatal exposure to the influenza or herpes viruses.
Autism

Autism is a spectrum of disorders
- Characterized by loss of language, communication, and social skills, beginning in early childhood
- Seizures and mental retardation may occur

Autism affects 3-6 children out of every 1,000
- It strikes four times as many boys as girls
Autism

More than 30 genes so far have been associated with autism

Two genes in particular may finally explain how autism develops
- They encode the cell adhesion proteins neurexins and neuroligins
- These proteins strengthen synaptic connections in neurons associated with learning and memory
Understanding Autism

Autism may arise from failure of synapses to form that enable a child to integrate experiences.