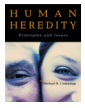
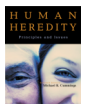
Chapter 18
Genetics of Behavior



Behavior

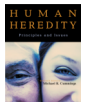
- Most human behaviors are polygenic and have significant environmental influences
- Methods used to study inheritance include
  - Classical methods of linkage and pedigree analysis
  - Recombinant DNA analysis
  - Combinations of twin studies and molecular methods
- It is important to refine the definitions of behavioral phenotypes in order to study the genetic basis of the behavior



Models

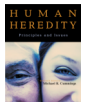
Table 18.1 Models for Genetic Analysis of Behavior

Model	Description
Single gene	One gene controls a defined behavior
Polygenic trait	Additive model that has two or more genes One or more major genes with other genes contributing to phenotype
Multiple genes	Interaction of alleles at different loci generates a unique phenotype

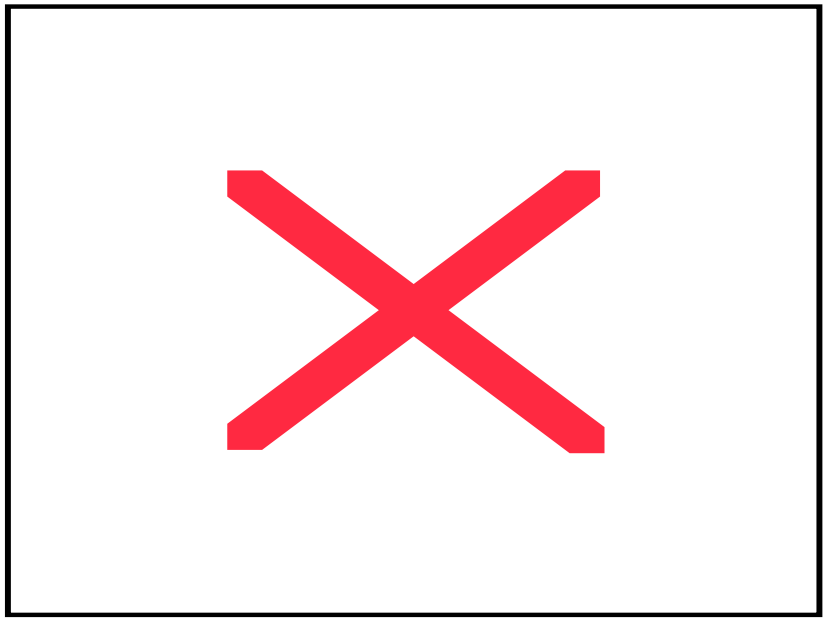


Animal Models

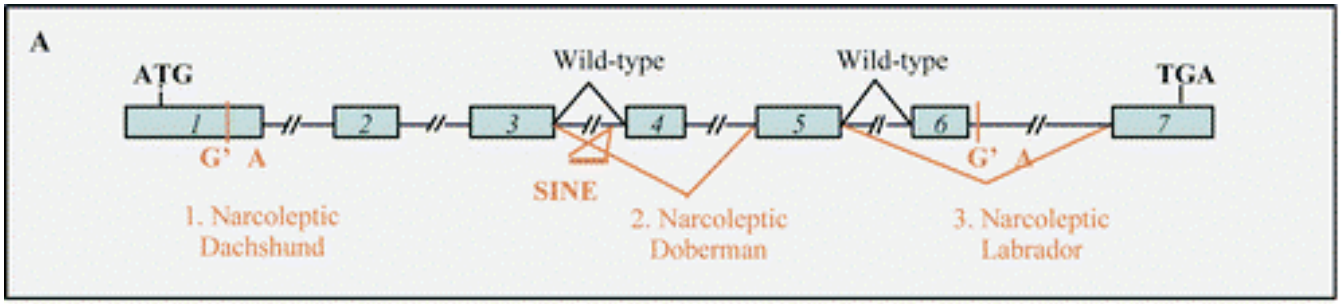
- Indicate that behavior is under genetic control and provide estimates of heritability
- Molecular basis of single gene effects on some forms of behavior have been identified
- Examples
  - Open-field behavior in mice
  - Narcolepsy

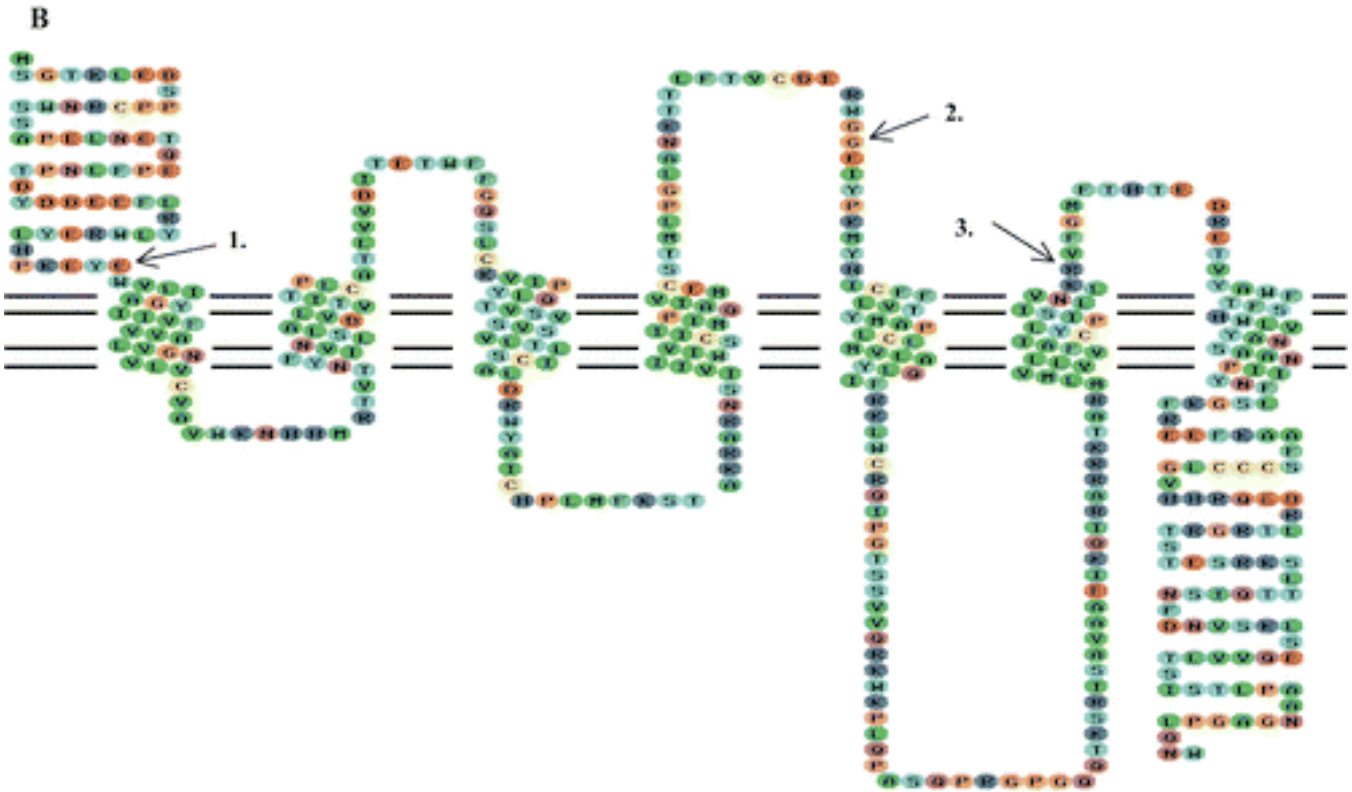


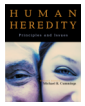
Narcolepsy



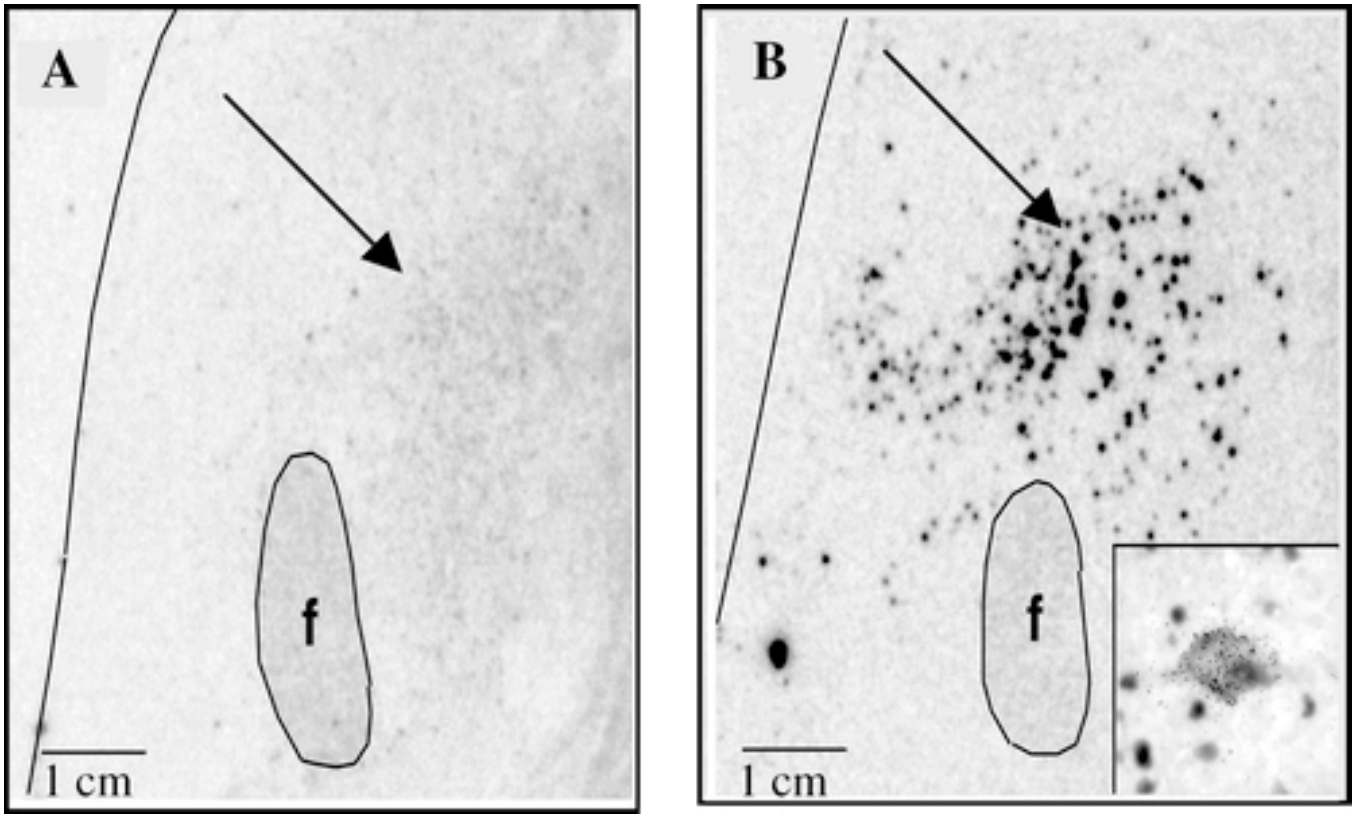
Mutations in hypocretin receptor (dogs)

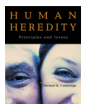




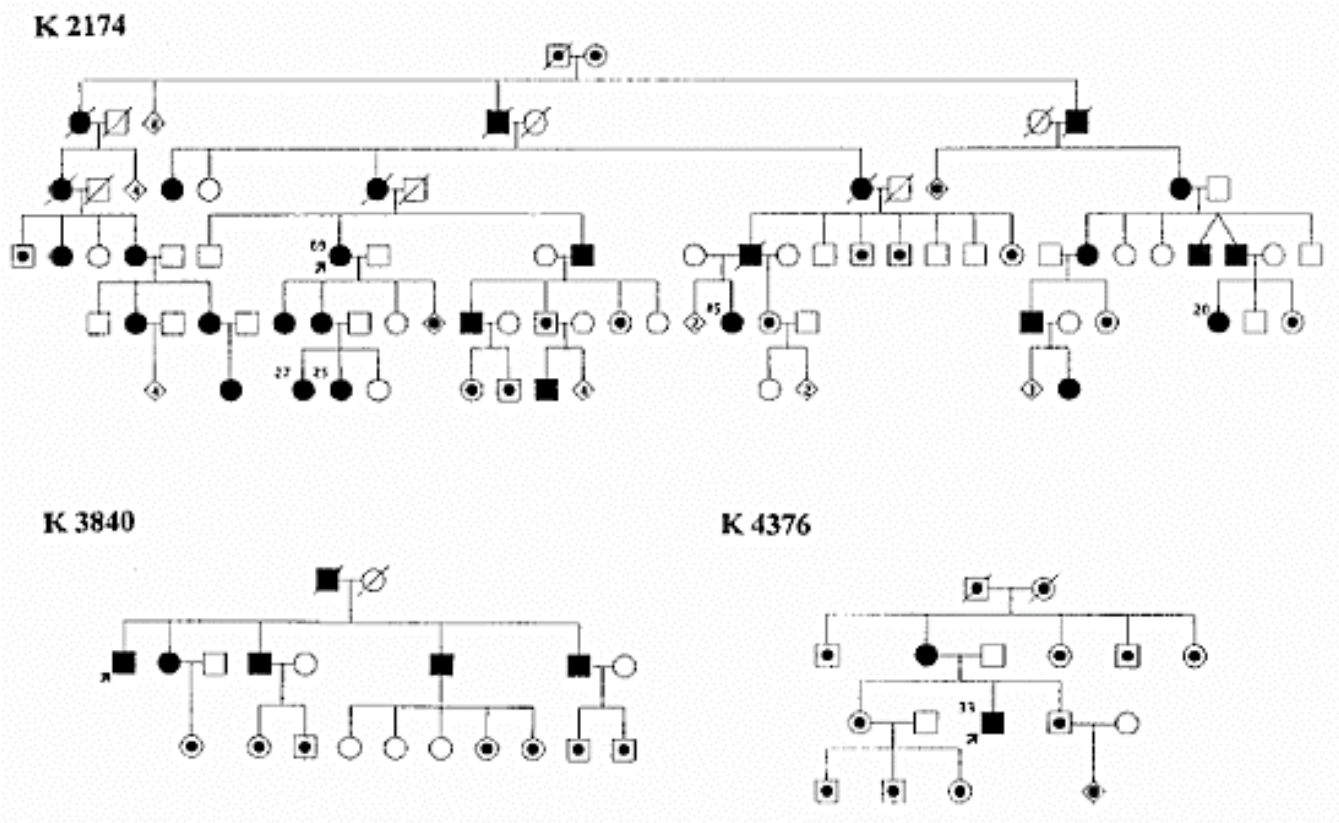


Loss of hypocretin immunostaining in narcoleptic hypothalamus



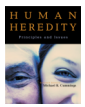


Familial advanced sleep phase syndrome



Jones et al., 1999

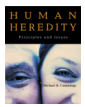
Period gene, others?



Neurodegenerative Diseases

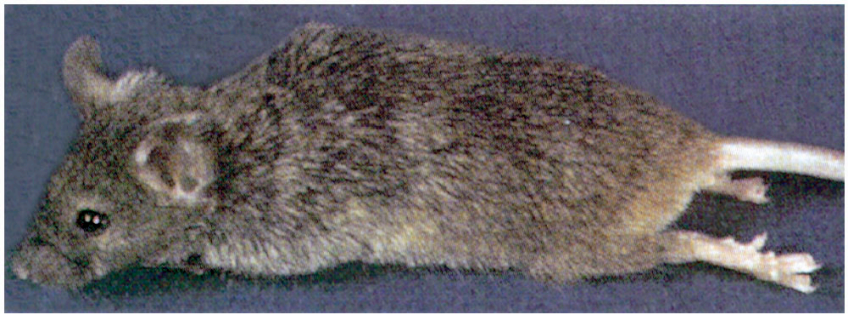
- Are progressive and fatal
- Examples
  - Alzheimer disease
  - Amyotrophic lateral sclerosis (ALS)
  - Parkinson disease

  Single genes have been identified for
  - Huntington disease
  - Spinocerebellar ataxia

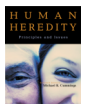


SOD1 Gene

Fig. 18.3

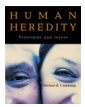


- 10% of all ALS cases are inherited as an autosomal dominant
- Some of these individuals have a mutation of *SOD1* gene
- The mutation causes the *SOD1* protein to become toxic
- Transgenic mice with mutant *SOD1* gene develop muscle weakness similar to humans



Other Transgenic Studies

- *Drosophila* studies
- Flies carrying the mutant human gene for HD and spinocerebellar ataxia 3
  - Demonstrate how mutant proteins kill nerve cells
  - Identify genes or chemicals that can slow or prevent loss of cells



Pedigree of KE family

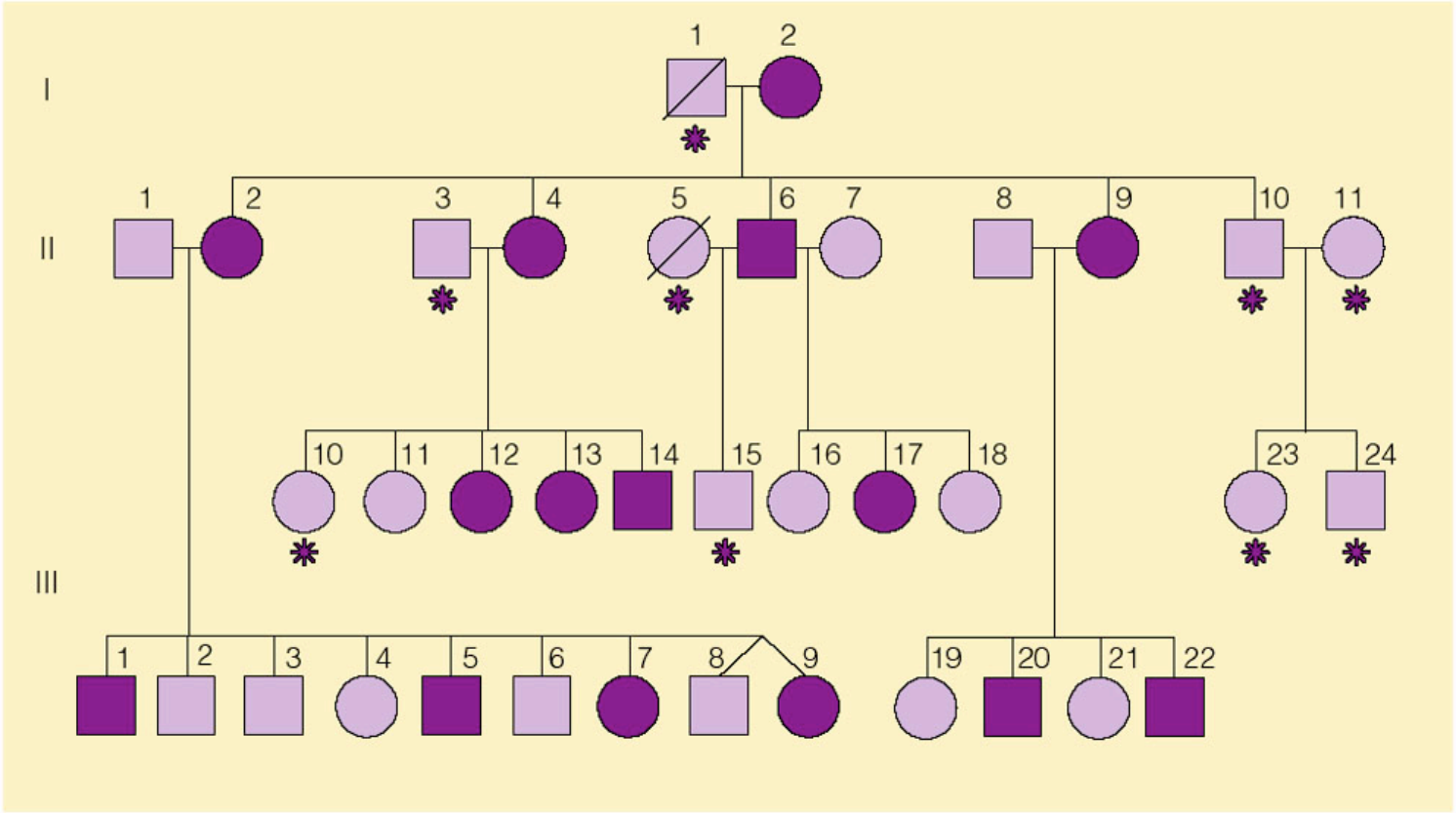
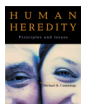


Fig. 18.6

Language and Brain Development

- *SPCH1* region of chromosome 7 involved in development of speech
- First identified in KE family
- Non-family member with same speech deficit allowed discovery of *FOXP2* gene
- *FOXP2* gene encodes for transcription factors
- Understanding the action of this gene may assist in treatment of language disorders and explain evolutionary changes

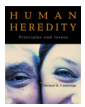


Neurotransmitters

Neurotransmitters transmit the impulse across the synapse

Table 18.2 Some Common Neurotransmitters

Acetylcholine
Dopamine
Norepinephrine
Epinephrine
Serotonin
Histamine
Glycine
Glutamate
Gamma-aminobutyric acid (GABA)



Synapse

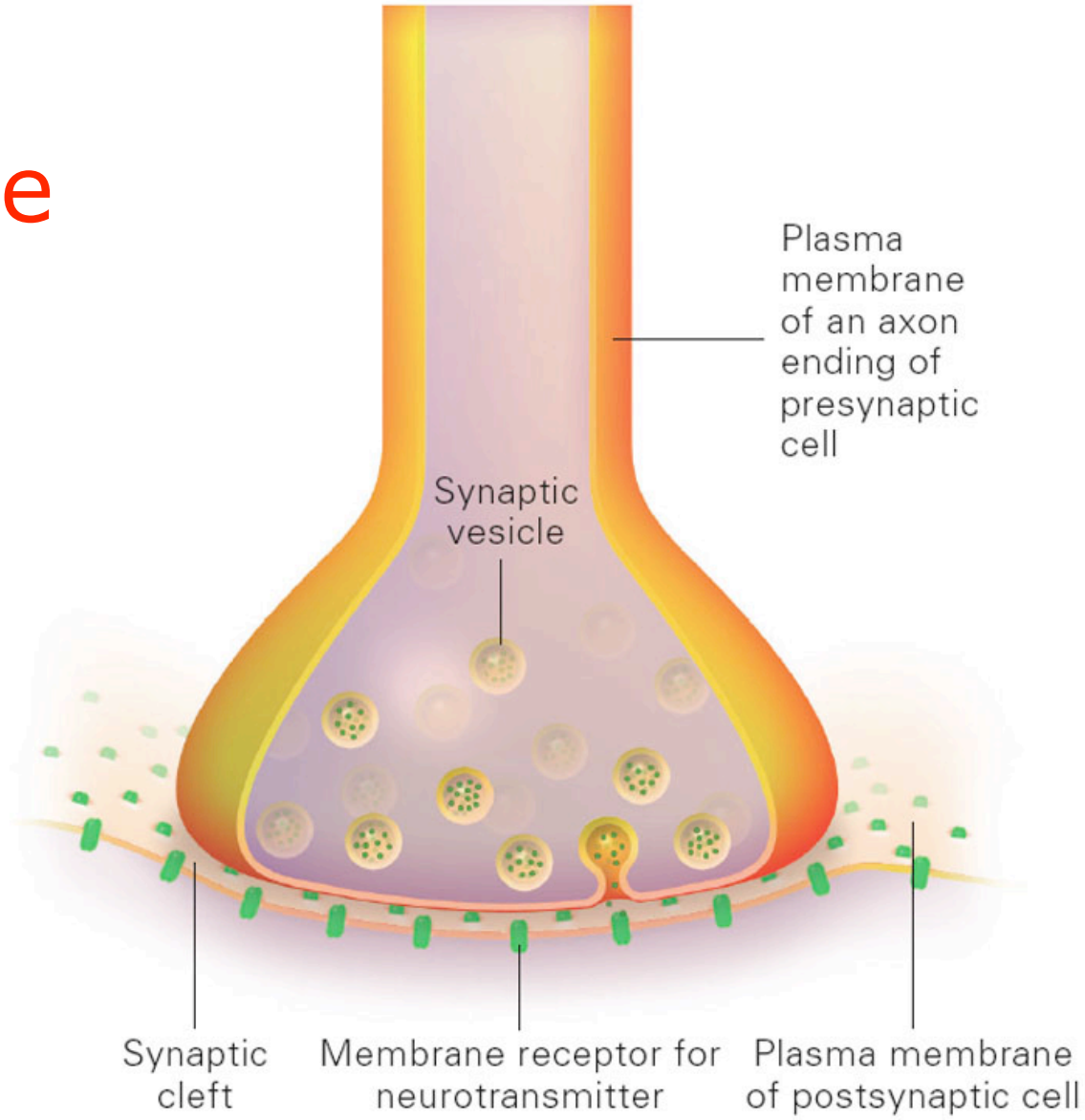


Fig. 18.8a

Nerve Impulse Triggers Release of Neurotransmitter

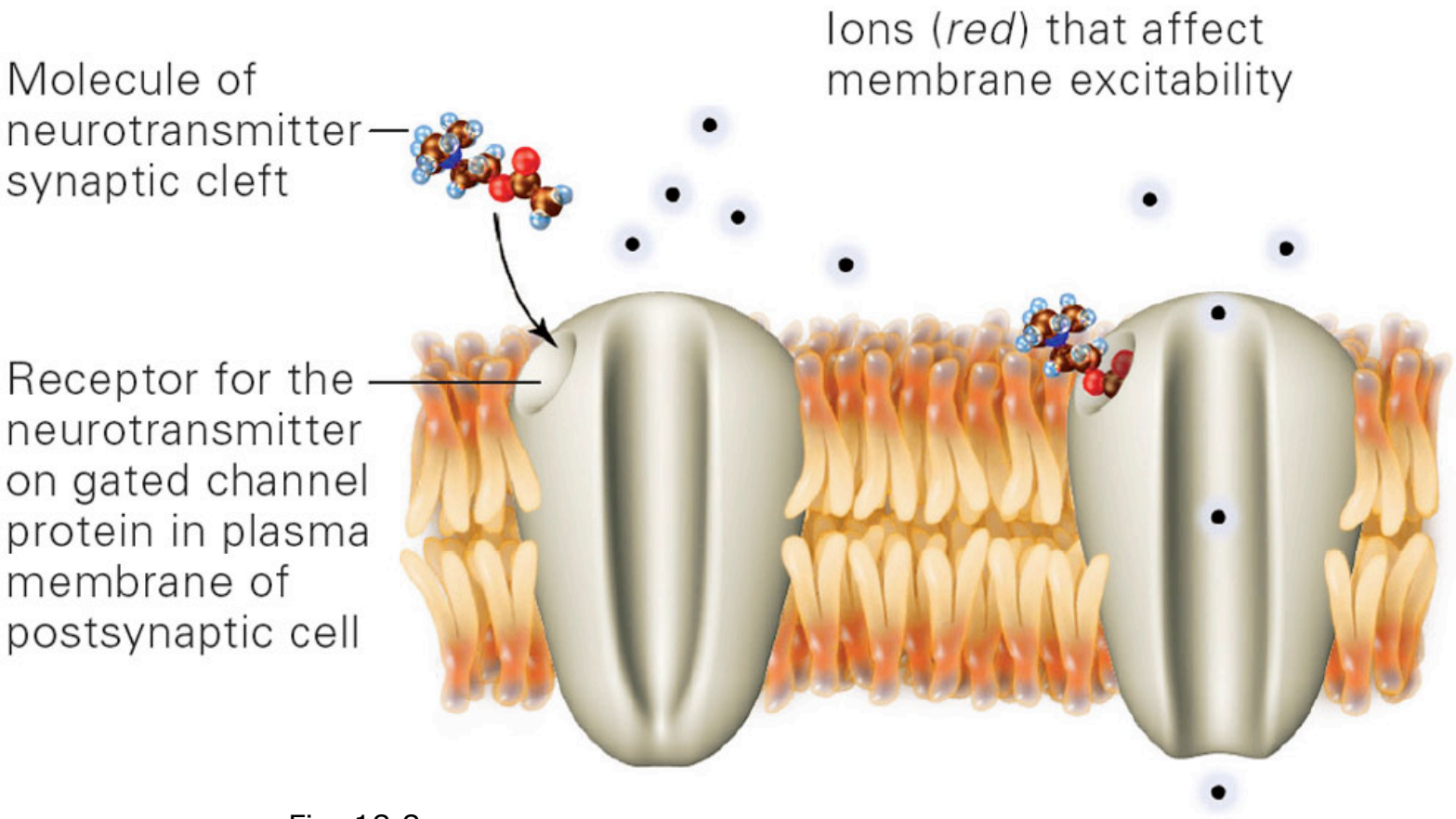
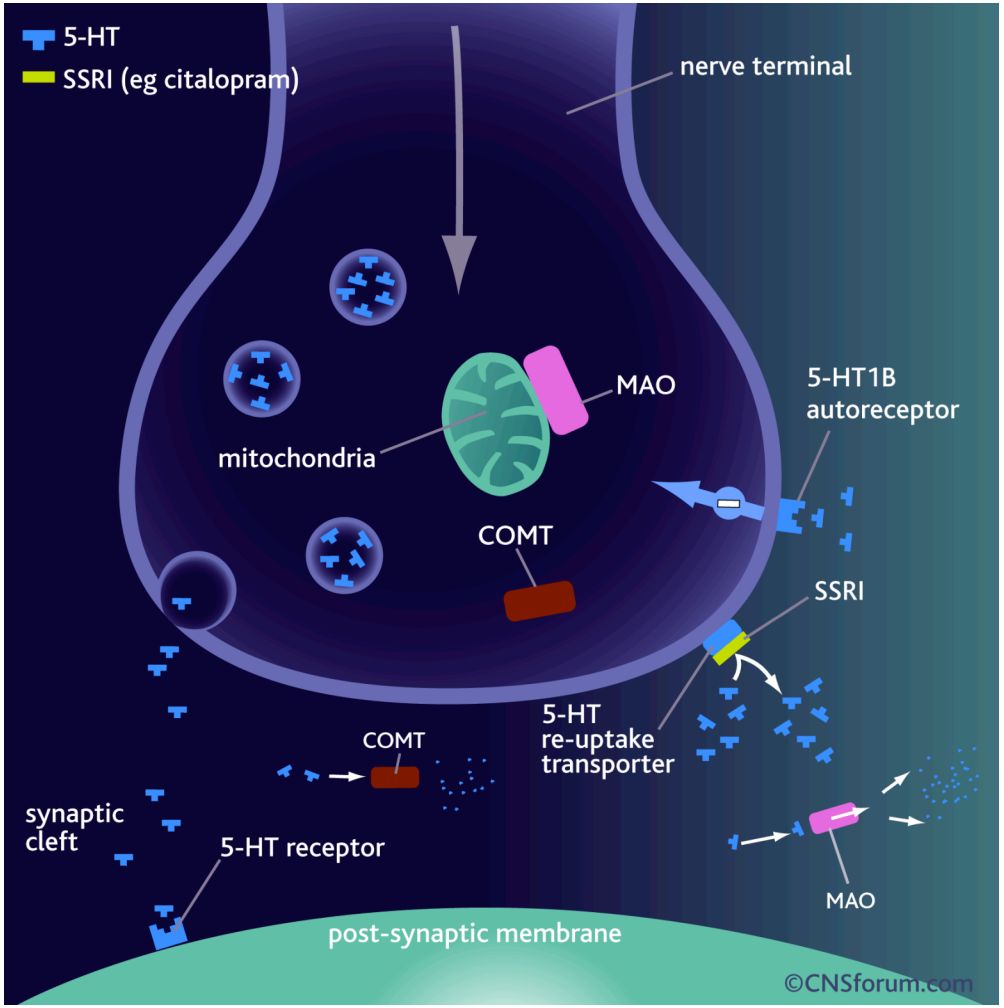


Fig. 18.8c

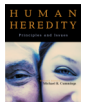
SSRI and MAOI action



http://www.cnsforum.com/content/pictures/imagebank/hirespng/Drug_SSRI_2.png

Aggressive Behavior and Brain Metabolism

- Most forms of mental retardation are genetically complex multifactorial disorders
- One form of X-linked retardation associated with aggressive behavior is linked to abnormal metabolism of a neurotransmitter



Mental Retardation, Aggression, and a Mutation of *MAOA* Gene

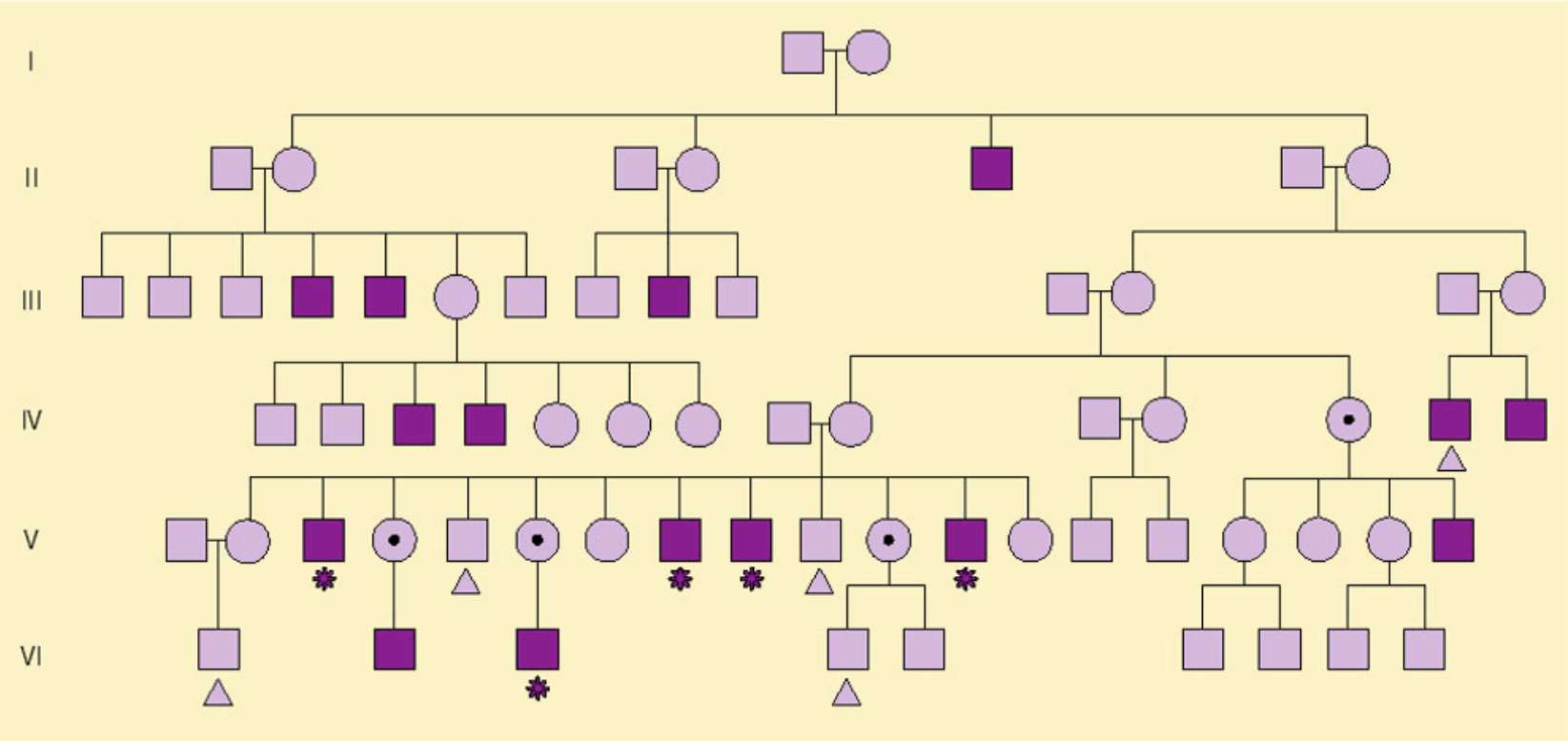
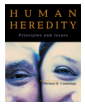
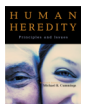


Fig. 18.7



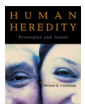
Mood Disorders and Schizophrenia

- **Unipolar disorder** is characterized by prolonged periods of deep depression
- **Bipolar disorder** is characterized by mood swings
- **Schizophrenia** is characterized by disordered thought processes and withdrawal from reality
- Common and likely to be caused by multifactorial inheritance



Unipolar and Bipolar Disorder

- Unipolar disorder (depression) is most common and more common in females
- Concordance for bipolar disorder is 60% for MZ twins and 14% for DZ twins
- Adoption studies indicate genetic factors
- Environmental factors are also important
- No genes or markers have been identified



Frequency of Bipolar Disorder in Families

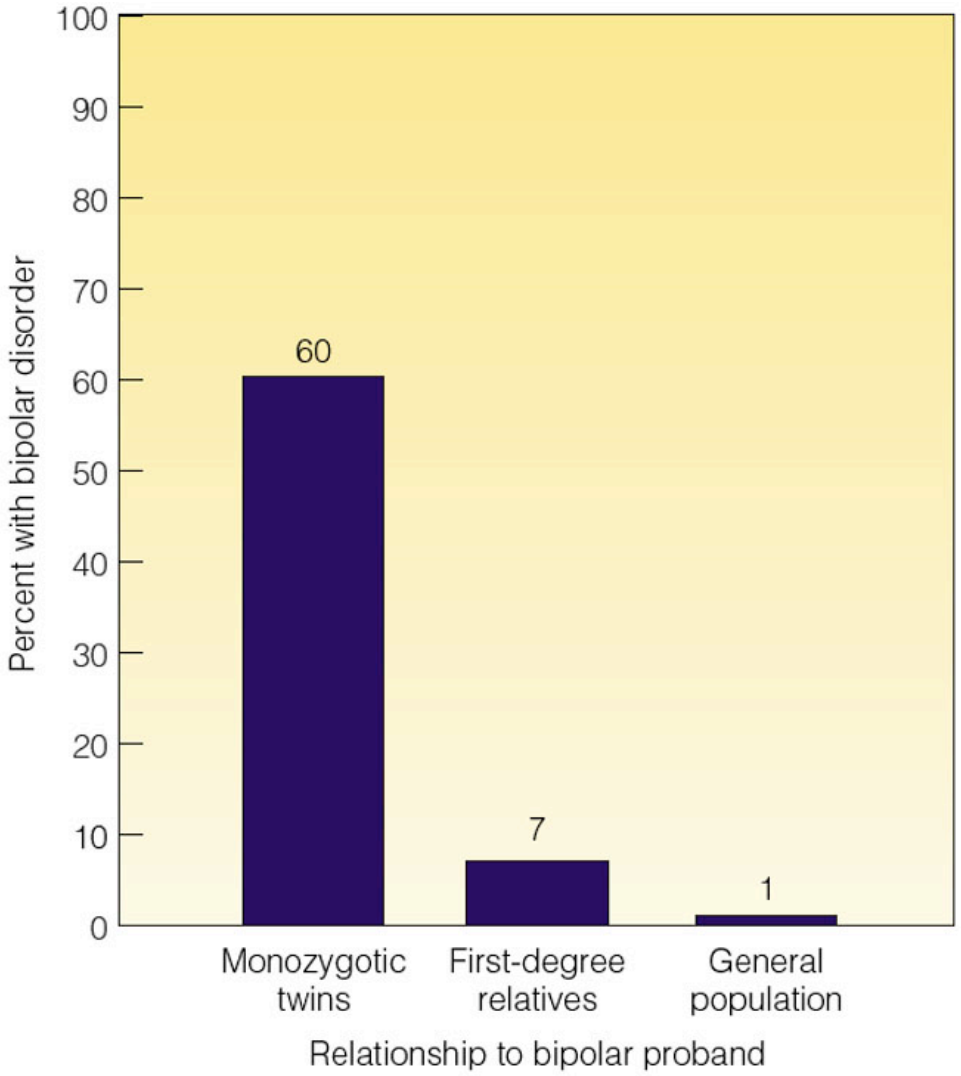
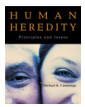


Fig. 18.9



Areas with Genes Possibly Associated with Bipolar Disorder

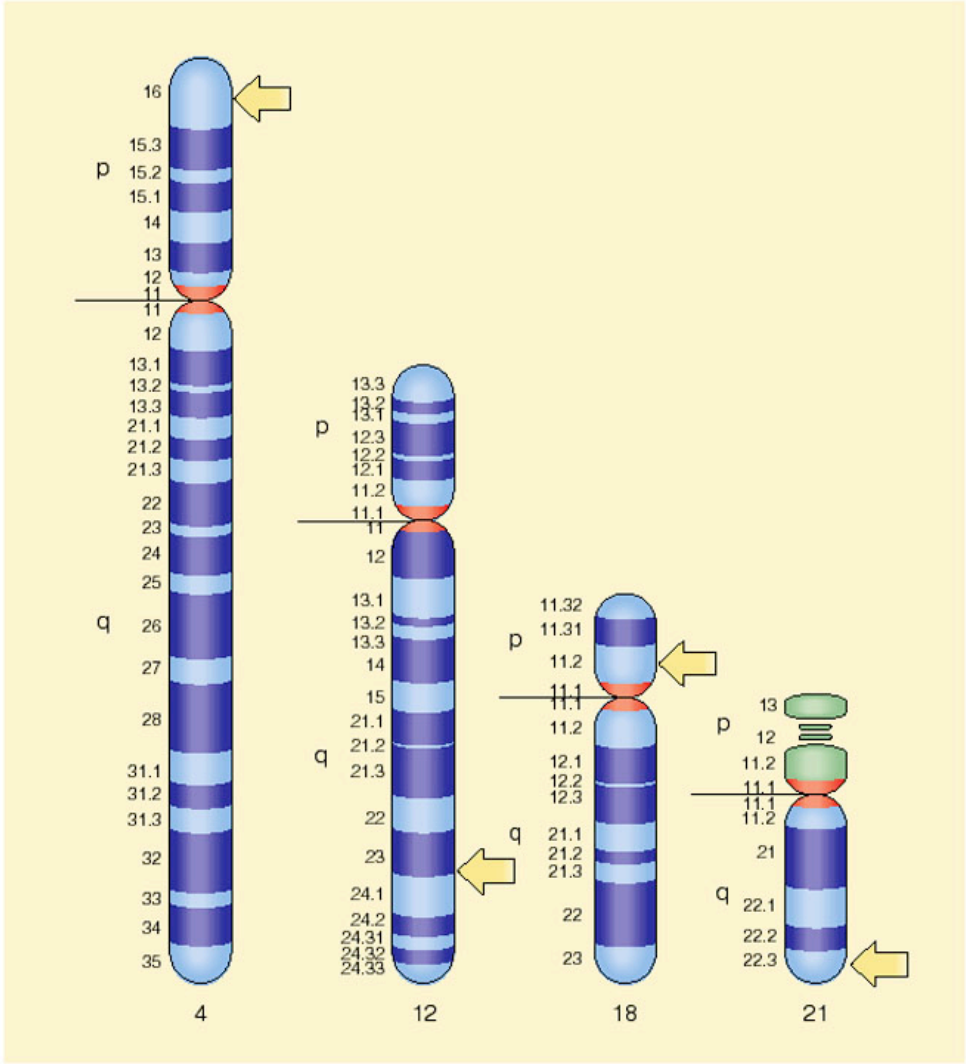
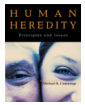


Fig. 18.10

Schizophrenia

- 1% of U.S. population
- Genetic and environmental components
- Features of the illness include
  - Psychotic symptoms
  - Disorders of thought
  - Perceptual disorders
  - Behavioral changes
  - Withdrawal from reality



PET Scans of Monozygotic Quadruplets with Varying Degrees of Schizophrenia

Normal

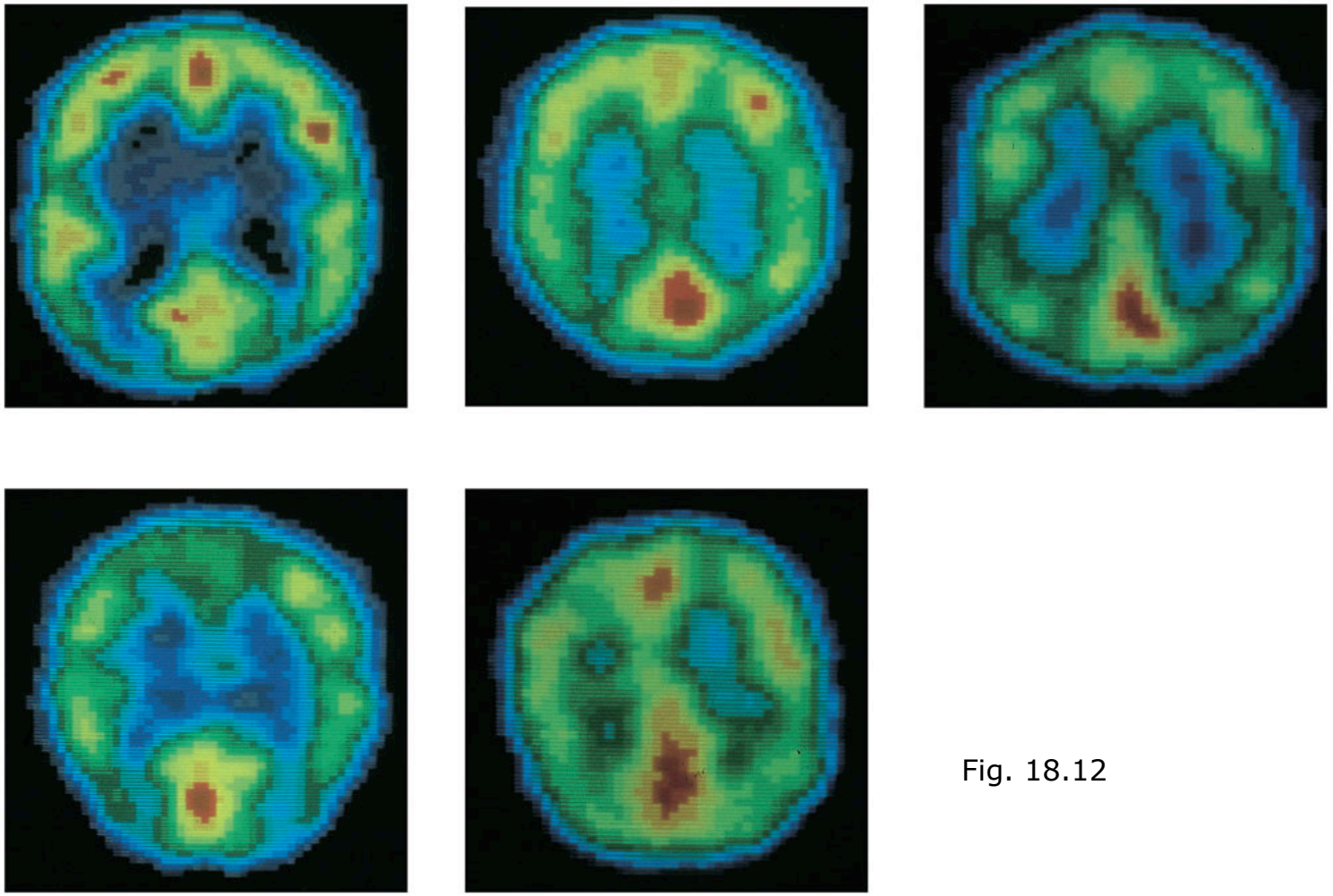
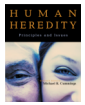
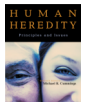


Fig. 18.12



Schizophrenia Risk

- Concordance for MZ twins is 46% versus 14% for DZ twins
- With a broader definition of phenotype, concordance for MZ approaches 100%
- Some linkages have been identified but studies are contested
- Possibly polygenic and associated with genes involved in nerve cell myelination



Lifetime Risk

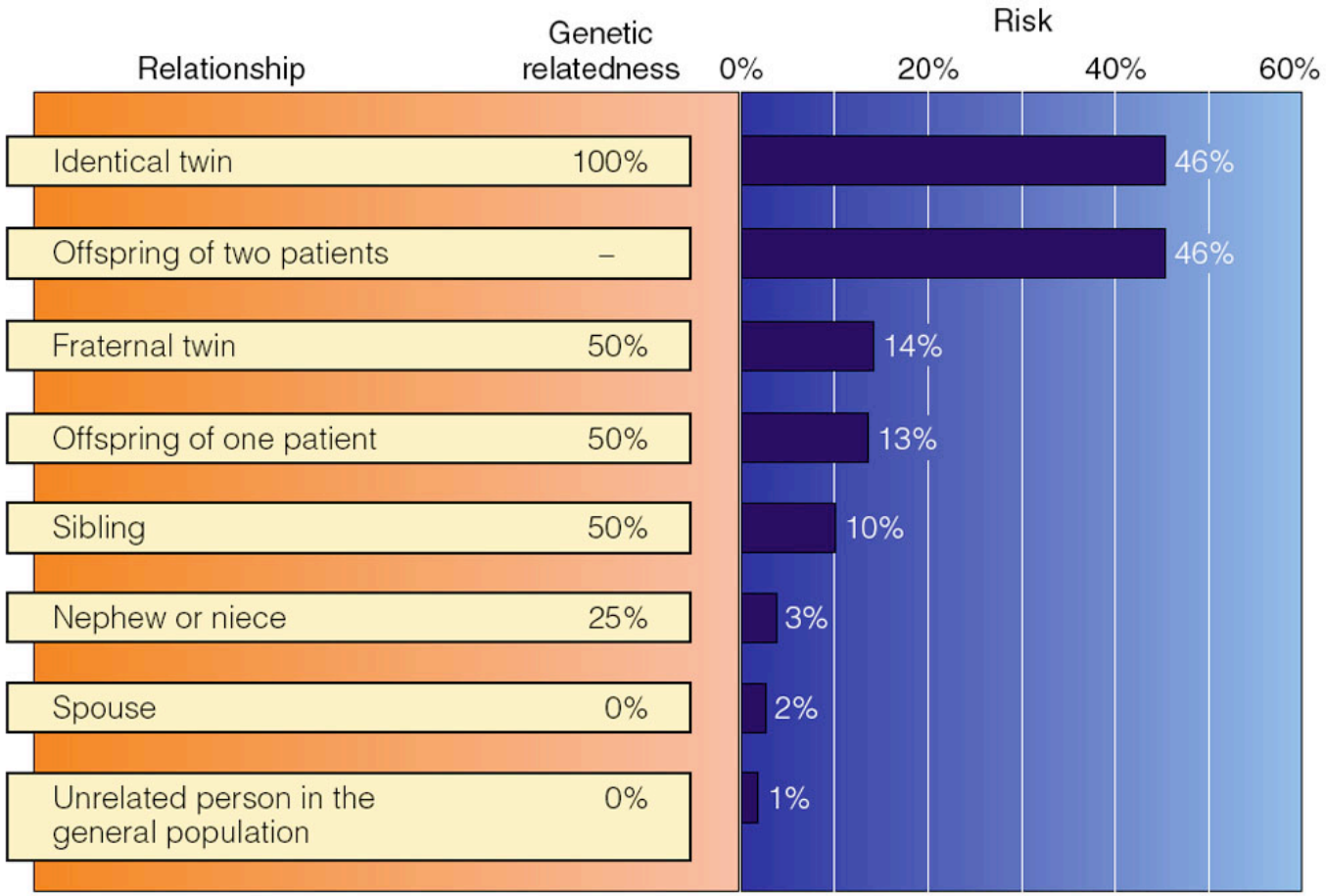
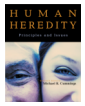


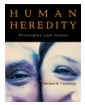
Fig. 18.13



Genetics and Social Behavior

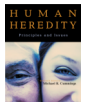
Genetic control of

- Tourette syndrome
- Alzheimer disease
- Alcoholism
- Sexual orientation



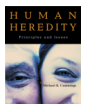
Tourette Syndrome

- Motor and behavioral disorder
- Family studies indicate genetic components
- Inheritance involves a major gene, a number of minor genes, and environmental contributions
- DNA markers in genetically isolated populations have been used to identify regions of importance on chromosome 2p, 8q, 11q, 20q, and 21q



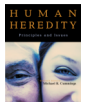
Genetics of Alzheimer Disease (AD) Are Complex

- Gene *AD1* encoding amyloid beta-protein is located on long arm of Chromosome 21
- Mutations of *AD1* responsible for early onset AD - autosomal dominant
- *ApOE* gene - sporadic
- Other genes on chromosome 1, 14, and possibly others including mitochondrial DNA



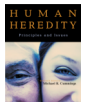
Environmental Factors in AD

- Factors that increase the rate of the disease
  - Free radicals production
  - Calcium uptake
  - Beta amyloid toxicity to nerve cells
- Intellectually stimulating jobs, moderate exercise, diets low in cholesterol, and saturated fats may help decrease risk of AD



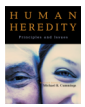
Components of Alcoholism

- Two components of excessive alcohol consumption
  - Damage to nervous system and other organs results in altered behavior, hallucinations, and loss of memory
  - Behavior patterns that lead to alcohol abuse and loss of ability to function



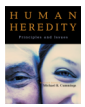
Genetics of Alcoholism

- Alcohol preference can be selected for in mice
- 25–50% risk of alcoholism in sons and brothers of an alcoholic family member
- 55% concordance in MZ twins and 28% concordance of same sex DZ twins
- Adopted sons show rate of alcoholism closer to their biological fathers
- No genes have been identified; is probably multifactorial (DRD2 - A1?)



Sexual Orientation

- Studies suggest a genetic component
- One study suggests
  - Concordance for homosexuality in males is 52% for MZ twins, 22% for DZ twins, and 11% for adopted unrelated siblings
  - Heritability between 31–74%
- Another study in women
  - Heritability 27–76%



Genes for Sexual Orientation?

- Genes in Xq28 region possibly associated with homosexual behavior??

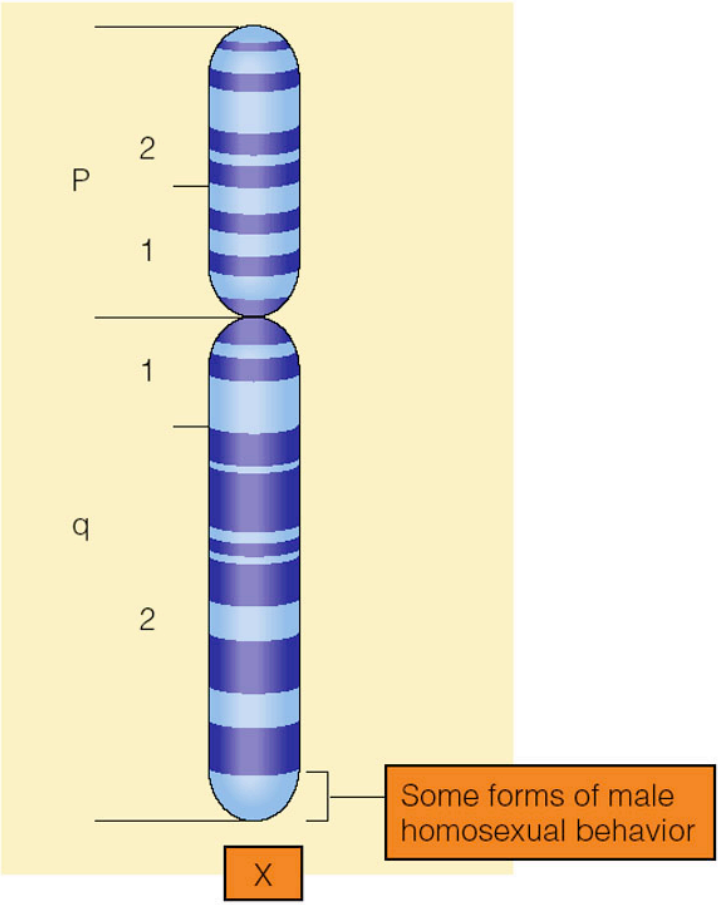


Fig. 18.17

Current Status

- Evidence for genetic control of complex behaviors is indirect
- Some progress and possible linkages have been found on some chromosomes
- At present no genes have been discovered
- Human Genome Project, along with other methods of study, may lead to identification of genes involved in behavior