Integrated Approach to Psychopathology
What causes X?

- Elizabeth Cooper (aged 27): arrested after crashing her car into a house - police discovered she had set 15 fires during the past 2 weeks, she also stole car owners manuals, a bowling ball, and tulips (Columbus Dispatch, April 15, 2000)
- Cooper is a middle school teacher with no criminal hx - “Miss Cooper is like so innocent… She doesn’t seem like the kind of person who would do something wrong” - student in her class
- What happened to cause this?
- Recently settled a civil lawsuit against a car dealership
- Reports that she had been attacked in recent past
- Reports that she had started taking Paxil and felt worse
- Probably no single pathway can account for this behavior
One-Dimensional vs. Multidimensional Models

• One-Dimensional Models
  – Single paradigm or conceptual approach
  – Problems occur when information from other areas is ignored

• Multidimensional Models
  – Interdisciplinary, integrative
  – “System” of influences that cause and maintain suffering
  – View abnormal behavior as multiply determined
Multidimensional Models of Abnormal Behavior

- Biological Influences (Physiological/Developmental, Genetic)

- Environmental Influences (Behavioral, Social, Emotional)
Case Example: Judy - Blood Injury/injection Phobia

- *Presentation at age 16 (Chapter 1)*
- *Viewed graphic film - frog dissection*
- *Experienced syncope, avoidance of blood/injury stimuli*
Figure 2.1
Judy’s case: one-dimensional or multidimensional models
Physiological Approaches to Psychopathology

- **Three Main Pathways to Disease**
  - Pathological Sequelae from a Biological Agent
    - *EX. Virus invades the brain*
  - Genetic Flaw
    - *EX. Trisomy 21 (Down’s Syndrome)*
  - Interaction between Genetic Predisposition and E
    - *Diathesis - Stress Model (Integrated Model)*

![Diagram with an illustration of a glass and text indicating Threshold, E Stressor, Genetic Contribution.](image-url)
Behavior Genetics

• **Terminology:**
  – **Chromosomes (23 pairs)** - each parent contributes one member to the pair
  – **Genes** - long molecules of DNA
    • **Beads on String (Genes on Chromosome)**
  – **Allele** - different form of a gene
  – **Genotype** - overall genetic makeup
  – **Phenotype** - What we see
  – **Expression** - end-product of gene, involves gene-gene and gene-E interactions
Genetic Problems resulting in Psychopathology

- **Chromosome Abnormality**
  - Bad news bc many genes are affected
  - Trisomy 21 - results in dramatic behavioral problems, low IQ, learning disabilities

- **Gene Mutations/Polymorphisms**
  - When a gene mutates into a rare form and it causes malfunction = mutation
  - When a gene mutates and is relatively common = polymorphism
  - Single gene mutates creating some dysfunction
  - Multiple genes (alleles) in the right combination create a dysfunction
Inheritance Patterns

Dominant Inheritance: if you pass on the abnormal gene, the disorder will emerge (Ex. Huntington’s Disease)
Inheritance Patterns

Recessive Inheritance: two copies of the abnormal gene are required for the disorder to emerge (Ex. Cystic fibrosis, PKU)
However, most psychiatric conditions do not follow Mendelian inheritance -
why not?

- **Incomplete penetrance**

Dominant gene for RED is not completely penetrant

Other factors (G or E) can cancel effects (e.g., PKU)
Mulitfactorial Inheritance

Polygenic inheritance of skin color (3 genes/2 alleles)

Liability Threshold
What does it mean to say that something is inherited?

- **Heritability** = *degree to which genetic differences account for phenotypic differences*
- **Range** = 0 - 1.0
- **Derived from correlations (continuous traits) or concordances (dichotomous trait)**
## Heritability of IQ (Correlational Example)

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Genetic Relatedness</th>
<th>Rearing: Together</th>
<th>Rearing: Apart</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZ Twins</td>
<td>1.0</td>
<td>.85</td>
<td>.67</td>
</tr>
<tr>
<td>DZ Twins</td>
<td>.50</td>
<td>.58</td>
<td>.45</td>
</tr>
<tr>
<td>Sibs</td>
<td>.50</td>
<td>.45</td>
<td>.24</td>
</tr>
<tr>
<td>Parent - kids</td>
<td>.50</td>
<td>.39</td>
<td>.22</td>
</tr>
<tr>
<td>Half-sibs</td>
<td>.25</td>
<td>.35</td>
<td>.22</td>
</tr>
<tr>
<td>Unrelated Children</td>
<td>.00</td>
<td>.30</td>
<td>.00</td>
</tr>
<tr>
<td>Adoptive Parent - Child</td>
<td>.00</td>
<td>.18</td>
<td></td>
</tr>
</tbody>
</table>
Concordance:
Heritability = 2(MZ concordance - DZ concordance)

EX. H2 (ETOH) = 2 (.3 - .2)
Is something that is highly/completely heritable fixed or determined?

- **No - difference bw heritability and fixity**
- **Highly heritable traits can be dramatically influenced by E**
  - Examples
  - Phenylketonuria (PKU)
  - twins w Huntington’s disease may have different onset/course
  - Diet/malnutrition may influence height
  - Suomi (1999) genetically “emotional” monkeys reared by “calm” mothers - non-reactive as adults - calm E seems to counteract genetic liability
- **Bottom Line: heritability estimates may underestimate the role of E in the expression of psychopathology**
Additional Complexity: Sometimes genes “enhance” E

- **Gene - E reciprocity:** idea that genes can increase the likelihood that the person will experience the necessary E that creates the expression of the disease

  Rende & Plomin, 1992

- **Examples?**
  - Some people with a genetic risk for depression may also have traits that contribute to the development of depression (e.g., tend to have difficult interpersonal relationships)
  - People with a genetic risk for alcoholism might also have other traits like antisocial PD that contributes to ETOH
Main Methods for Evaluating Genetic Contributions to Psychopathology

- **Step 1: Determination of the level of gene influence**
  - *Family, Twin, Adoption studies*

- **Step 2: Determination of the location and function of the relevant gene(s)**
  - *Linkage and Association Studies*
Research Designs: Family Studies

- Assess within large families the relative risk of the disorder (compared to the population)
- Problems?
- G and E confounded
Research Designs: Twin Studies

- *Comparing Concordance bw MZ and DZ twins*
- *Problems?*
- *Assumption that E is same between MZ and DZ twins*
• *Adopted away children can be compared to Adopted and biological Parents*

- Adoptive Parents
  - Share 0% of genes

- Biological Parents
  - Share 50% of genes
Research Designs: Cross Fostering Design

- Adopted away children can be compared to Adopted and biological Parents

Examine the rates of SZ in kids relative to general population (or biological parents)
Molecular Biology approaches

- If twin, adoption studies suggest heritability - use these approaches to find the genes responsible for psychopathology
- Linkage and association studies are about “gene finding”
- Basic premise: compare genetic Maps between affected and unaffected individuals to find location
Linkage Studies

- Collect blood/tissue in large families affected by disorder of interest
- Examine the correspondence between presence of gene and presence of disorder (remember: never perfect agreement)
- Provides a statistic (LOD ratio) suggesting whether this linkage is not just a random effect
- Problem: remarkable INCONSISTENCY
- Why? Linkage studies work best with single gene disorders (remember: this is not the case with psychopathology)
Association/Candidate Gene Studies

- **Candidate Genes are genes with known function**
- **Test the Association bw the disorder/phenotype and the gene of interest (alleles)**

<table>
<thead>
<tr>
<th>Genotype: 5-HTT</th>
<th>Personality Trait (NEO)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neuroticism</td>
</tr>
<tr>
<td>Long/Long</td>
<td>53.4</td>
</tr>
<tr>
<td>Long/Short</td>
<td>57.8</td>
</tr>
<tr>
<td>Short/Short</td>
<td>58.9</td>
</tr>
</tbody>
</table>

Candidate gene studies can assess subtle effects
Limitations of All Genetics Studies

- Reliability of Diagnoses
  - Need a clear definition of disorder
- Variable Penetrance
  - Difficult to account for
- Accurate knowledge of Baserates
  - Need for Comparison
- Adequacy of Typical Genetic Models
  - Most are single gene models
- Phenocopies
  - Cannot test theory
Neuroscience Contributions to Psychopathology

- The Field of Neuroscience
  - The role of the nervous system in disease and behavior
  - Two main influences:
    - Role of neurotransmitters on psychopathology
    - Role of brain regions on psychopathology
Neuroscience Basics

Figure 2.4

Divisions of the nervous system (from Goldstein, 1994)
Figure 2.5

Neural Transmission of information
Neuroscience and Major Neurotransmitters in Psychopathology

• Norepinephrine (or noradrenaline) (NE)
• Serotonin (5-HT)
• Dopamine (DA)
• Gamma Aminobutyric Acid (GABA)

• Excess/Deficit Models of Psychopathology (e.g., SZ = excess DA) - too simplistic
Neuroscience and the Divisions of the Brain

- **Hindbrain (ancient part - basic functions)**
  - Medulla – Heart rate, blood pressure, respiration
  - Pons – Regulates sleep stages
  - Cerebellum – Involved in physical coordination

- **Forebrain (More evolved - Cerebral Cortex)**
  - Location of emotional and cognitive processing
Neuroscience and Structures Directly Related to Psychopathology

**Limbic System** [“border” - between forebrain and ancient structures]
- regulates emotions, learning, impulses, also sex and aggression

**Structures:**
- Amygdala (fear)
- Hippocampus (trauma/PTSD)
- Basal ganglia (OCD)
- Thalamus – Receives and integrates sensory information
- Hypothalamus – Controls eating, drinking, aggression, sexual activity
The Endocrine System

- Part of the Peripheral Nervous System
- Uses Hormones
  - EX: Adrenal glands release epinephrine (adrenaline) in response to stress; leads to activation or “alarm” response
- The Hypothalamic-Pituitary-Adrenal Cortical Axis (HYPAC or HPA axis)
  - Integration of endocrine and nervous system function
  - Activation of HYPAC also produces cortisol (another stress hormone)
  - Cortisol implicated in different diseases (Health Psychology)
Neuroscience: Functions of Main Types of Neurotransmitters

- Affecting the activity of Neurotransmitters
  - Agonists (Increase Neurotransmission)
  - Antagonists (Decrease Neurotransmission)
  - inverse agonists (Produce effects that are opposite of what the neurotransmitter does)
  - Most drugs are either agnostic or antagonistic
  - Four Neurotransmitter Systems most frequently cited as involved with Psychopathology
5-HT: 6 Major pathways in the brain

Widespread 5-HT circuits: suggest wide influence on behavior

Implicated in Anxiety, Depression, Eating Disorders
Manipulating 5-HT in the Brain

How Serotonin Drugs Work
Prozac enhances serotonin’s effects by preventing it from being absorbed. Redux and fenfluramine (anti-obesity drugs) cause the release of extra serotonin into the synapse.

Receptor Variation
There are at least 15 different serotonin receptors, each associated with a different function.

Complex System - 5-HT receptor differences
Other Neurotransmitter Systems

- **GABA**
  - Tends to reduce activity/inhibit behavior
  - Benzodiazepines act on this system
  - GABA activation REDUCES anxiety, aggression

- **NE**
  - stimulates Alpha-adrenergic and beta-adrenergic pathways
  - Beta-Blockers - block beta pathways
  - used for hypertension and social anxiety

- **Dopamine**
  - Activity associated with pleasure
  - Implicated in addictions, SZ
Implications of Neuroscience for Psychopathology

• Relations Between Brain and Abnormal Behavior
  – Example: Obsessive compulsive disorder (OCD)
    • Increased activation in certain brain regions (regions w high concentrations of 5-HT)
    • Disruption of 5-HT circuits may create disinhibited behavior (act on every impulse/thought)
    • TX by surgery at activation sites, SSRIs, and psychosocial tx - changes activation

• Experience/psychosocial Tx Can Change Brain Structure and Function
  – Effective Tx does not imply etiology (e.g., pain relief from Aspirin not due to Aspirin deficiency)
E can Interact with Brain Structure/Function

- **Insell et al. (1988) - Monkey control Study**
  - Two groups of monkeys
  - Raised identically except: one had control over the E (toys & food) and the other did not
  - Administered a benzodiazepine inverse agonist
  - Monkeys with no control - reacted with panic
  - Monkeys with control - reacted with anger

- **Suggests that E (psychosocial development) can dramatically affect how neurotransmitter systems develop and function**
What about the other direction? How does E contribute to psychopathology?

- **Ecopathology** - the assumption (underlying most psychological models) that Adverse Environments cause psychopathology
  - Two components: E plays a causal role; the level of association between E and psychopathology is High

- **First Assumption: Causality**
  - EX. Children abused (locked in closets, malnourished) exhibit developmental delays, behavior problems (Money, 1992)
  - Soldier exposed to terrible events develops flashbacks, withdrawal, hypervigilance (PTSD)
Alternative Models

- **Proactive Model**: E (environment) causes P (psychopathology)

- **Reactive Model**: P causes E
  - EX. Autistic child elicits parental abuse

- **Transactive Model**: E and P cause each other
  - EX. Depressives create social rejection, isolation increases depression

- **Expressive Model**: E and P created by underlying cause
  - EX. Genetic vulnerability creates strange behavior in parent and clinical SZ in child

- **Selective Model**: E is sought out as best fit for P
  - EX. Psychopaths gravitate to noxious E

- **Bottom Line**: if you see bad E and psychopathology - you cannot assume E caused P
Assumption 2: High Association between E and Psychopathology

• *Except in certain situations (severe trauma) - environmental factors are not highly associated with psychopathology*

• *Why not?*
  – *Complexity - causality is determined by multiple factors and interaction among factors (diathesis-stress)*
  – *Moreover, sometimes these interactions are subtle*
  – “It’s not the large things that send a man to the madhouse... No, it’s the continuing series of small tragedies... not the death of his love but the shoelace that snaps with no time left” (Bukowski)
  – *Events that are insignificant in isolation may combine in important ways*

• *At present, our understanding of the E contributions to psychopathology is far from complete*
Summary of the Multidimensional Perspective of Psychopathology

• Multiple Causation
  – Is the rule, not the exception in explaining normal and abnormal behavior