Diathesis and Stress

Lecture 40
Origins of Mental Illness

• Somatogenic
  – “Plagues and Tangles” in Alzheimer’s Disease
  – Dopamine Hypothesis of Schizophrenia
  – Monoamine Hypothesis of Depression
    • Norepinephrine, Serotonin

• Psychogenic
  – Post-Traumatic Stress Disorder
  – Phobias as Acquired Fear
  – Compulsions as Avoidance Learning
  – Learned Helplessness in Depression
# The Nature of Psychopathology

**Psychological Deficits**
- Schizophrenia
- Childhood Autism
- Depression
- Attention-Deficit Disorder

**Maladaptive Social Learning**
- Phobias
- Obsessive-Compulsive Disorder
- Depression
- Psychophysiological Disorders
Diathesis-Stress Model of the Etiology of Mental Illness

Meehl (1962); Rosenthal (1963)
Monroe & Simons (1991); Belsky & Pleuss (2009)

• Diathesis
  – Predisposition
  – Vulnerability ("At Risk")
  – Adaptation
    • “Good” vs. “Poor” Premorbid Adjustment

• Stress
  – Challenge to Current Level of Adaptation
  – Precipitates Acute Episode
    • But Only in Vulnerable Individuals
Diathesis-Stress Independence (Additive Model)
Diathesis-Stress Interaction (Multiplicative Model)
Patterns of Diathesis and Stress

• Substantial Diathesis: “High Risk”
  – Little Stress Required for Acute Episode
  – Poor Premorbid Personality

• Catastrophic Stress
  – Acute Episode Even in “Low-Risk” Individuals
  – Good Premorbid Personality

• Diathesis Within Normal Limits
  – Episode a Function of Stress

• Stress Within Normal Limits
  – Episode a Function of Diathesis

Diathesis is a Specific Predisposition
Concordance Rates for Psychopathology

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>MZ</th>
<th>DZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>38%</td>
<td>14%</td>
</tr>
<tr>
<td>Bipolar Affective Disorder</td>
<td>72%</td>
<td>28%</td>
</tr>
<tr>
<td>Unipolar Affective Disorder</td>
<td>40%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Genetic Endowment = “At Risk” But Not Decisive
The Genain Quadruplets
Rosenthal (1963)

- "Dire Birth"
  - Nora
  - Iris
  - Myra
  - Hester
Environmental Contributions to Schizophrenia

• Socioeconomic Status
  – *Social Drift*, not Sociogenesis

• Coping Failures
  – Loss, Frustration

• Family Maladjustment
  – Adoption of “At Risk” Probands
Finnish Adoptive Family Study of Schizophrenia
Wahlberg, Wynn, et al. (1997)

- 167 Women Hospitalized for Schizophrenia
  – 183 Probands Given Up for Adoption
- 202 Women Hospitalized for Other Illnesses
  – 204 Probands Given Up for Adoption
- Psychological Testing of Adoptive Families
  – “Communication Deviance”
- Psychological Testing of Adoptees
  – Index of Thought Disorder
Communication Disorder and Thought Disorder

Wahlberg, Wynne, et al. (1997)

![Graph showing the relationship between Communication Deviance and Thought Disorder for High Risk and Controls groups.](image-url)
Diathesis and Stress in Adolescent Conduct Disorder

Dunedin Multidisciplinary Health and Development Study
Caspi et al. (2002)

• Adolescent Conduct Disorder in Boys
  – Aggression, Antisocial Behavior

• Diathesis: MAOA Gene
  – Promotes Monoamine Oxidase - A
    • Located on X Chromosome
    • Metabolizes Many Neurotransmitters
    • Linked to Aggression in Mice, Humans

• Stress: History of Maltreatment
  – Initiates “Cycle of Violence”
MAO-A, Maltreatment, and Adolescent Conduct Disorder

Caspi et al. (2002)
Diathesis and Stress in Depression
Dunedin Multidisciplinary Health and Development Study
Caspi et al. (2003)

• Major Depressive Illness

• Diathesis: 5-HTT Gene
  – Located on Chromosome 17
    • 2 Alleles, “Short” and “Long”
      – 4 Genotypes: SS, SL or LS, and LL
  – Serotonin Transporter
    • Serotonin Linked to Depression in Humans
    • Efficacy of SSRIs like Prozac, Zoloft

• Stress: Stressful Life Events
  – Occurring Between Age 21-26
5-HTT, Life Stress, and Depression
Caspi et al. (2003)

% of Subjects

Stress Events

None
1
2
3
4+

"Short"
"Long"

5-HTT Genotype

0 5 10 15 20 25 30 35

Caspi et al. (2003)
Diathesis and Stress in Psychosis
Dunedin Multidisciplinary Health and Development Study
Caspi et al. (2005)

• “Psychotic” Symptoms at Age 26
  – “Schizophreniform” Hallucinations/Delusions

• Diathesis: COMT Gene
  – Located on Chromosome 22
    • 2 Alleles, “MET” (Methionine) and “Val” (Valine)
      – 4 Genotypes: MetMet, MetVal or ValMet, ValVal
  – Involved in Metabolism of Dopamine
    • MetMet, Fastest Breakdown; ValVal, Slowest Breakdown
  – Linked to Schizophrenia

• Stress: Adolescent Marijuana Use
  – At Least Once Per Month Prior to Age 18
COMT, Marijuana Use, and Psychosis
Caspi et al. (2005)

![Bar graph showing the percentage of subjects with different COMT genotypes (MetMet, Met/Val, ValVal) with and without drug use. The graph indicates a higher percentage of subjects with the ValVal genotype who used drugs compared to those who did not.]
5-HTT and Depression: Current Status
Caspi et al. (2010); Karg et al. (2011)

• Gene x Environment Interaction Controversial
  – Some Studies Failed to Replicate
  – Assessment of Stress

• 56 Published Studies ($N = 40,749$)
  – Overall Confirmation of Interaction ($p = .00002$)
    • Short Allele More Sensitive (42/56)
    • Long Allele More Sensitive (6/56)
    • No Difference (8/56)

  – Nature of Stress
    • Stressful Life Events
    • Childhood Maltreatment
    • Life-Threatening/Chronic Medical Conditions
Examples of Diathesis and Stress

• Schizophrenia and Unipolar Affective Disorder
  – Genetic Component
  – Nonshared Environment – Communication Deviance

• Adolescent Conduct Disorder
  – MAOA Activity
  – History of Maltreatment

• Depression
  – 5-HTT Allele (Short)
  – Stressful Events

• Pathological Shyness
  – 5-HTT Allele (Short)
  – Social Support
Diathesis and Stress in Psychosomatic Ulcers


• Diathesis
  – Bacterial Infection
    • *Helicobacter pylori*

• Stress
  – Prolonged Emotional Stress
    • Autonomic Nervous System activation

• Laboratory Model in Rats
  – *H. pylori* Infection
  – Unpredictable, Uncontrollable Shock
Diathesis and Stress in Phobias
Mineka & Zinbarg (2006)

• Stress
  – Fear Conditioning, But…
    • History Not Always Positive
    • Phobias are Not Arbitrary

• Laboratory Model in Monkeys
  – Observational Fear Conditioning
    • Exposure to Snakes but not to Flowers

• Preparedness Argument
  – Evolved Predisposition as Diathesis
    • Fear Dark, Heights, Open Spaces, Certain Animals
Diathesis often Biological, and Stress often Psychological, *but* Stress Can Be Biological

• Birth Complications in Schizophrenia
  – Prenatal
    • Exposure to Viruses
    • Malnutrition
    • Short Gestation, Low Birth Weight
  – Perinatal
    • Birth Complications

But These Factors Do Not Inevitably Give Rise to Mental Illness
Nor Are They Specific to Schizophrenia
Diathesis often Biological, and Stress often Psychological, but Diathesis Can Be Psychological

Cognitive Theory of Depression
Beck (1967)

• Depressogenic Schemata
  – Negative View of Self
  – Negative View of the World
  – Negative View of the Future

“I’m no good, the world is hostile, and the future is bleak.”
Diathesis often Biological, and Stress often Psychological, *but* Diathesis Can Be Psychological

**Hopelessness Theory of Depression**

Abramson & Alloy (1989)

- Learned Helplessness Theory of Depression
- Depressive Attributional Style
  - Stable vs. Variable
  - Internal vs. External
  - Global vs. Specific

“I’m always responsible for all the bad things that happen to me”
Diathesis and Stress in Depression

• Biological Stress
  – Sudden Changes in Hormonal Environment
    • e.g., Pregnancy, Parturition, Menopause
  – Behavioral Consequences
    • Altered Mood State
    • Reduction in Activity Levels

• Psychological Diathesis
  – Depressogenic Schemata, Attributional Style
    • Affect Interpretation of Changes in Mood, Activity
    • Hormonal Changes, Interpretation of Effects
Can Combine to Cause Episode of Depression
Diathesis and Stress as Person-Situation Interaction

• Diatheses are Internal, Personal Factors
  – Origins in Genetic Endowment
  – Origins in History of Social Learning

• Stressors are Features of the Environment
  – Biological in Nature
  – Psychosocial in Nature

Episodes of Mental Illness Emerge from the Interaction of the Person and the Environment