An Integrative Approach to Psychopathology II
Neuroscience: Neurotransmitters

• Production
• Reuptake
• Functions
  – Agonists
  • Inverse agonists
  – Antagonists

Mechanisms

Some drugs directly inhibit, or block, the production of a neurotransmitter.

Others increase production of competing biochemical substances that may deactivate the neurotransmitter.

Other drugs do not affect the neurotransmitters directly, but rather, prevent chemicals from reaching the next neuron by closing down or occurring the receptors of that neuron.

Finally, some drugs work by blocking the reuptake process, thereby causing continued stimulation along the brain circuit.
**Neurotransmitters**

- **Glutamate & Gamma aminobutyric acid (GABA)**
  - Glutamate — **excitatory**
  - GABA — **inhibitory**
  - Fast acting
  - Chemical Brothers working in tandem to balance functioning in the brain.
  - Implicated in anxiety
  - **Benzodiazepines**
    - Makes it easier for molecules to attach themselves to the receptors of specialized neurons. — the more GABA that becomes attached, the calmer we feel.
  - **Similar to alcohol** - another CNS depressant that slows the central nervous system
Neurotransmitters

• **Norepinephrine**
  – Stimulation of alpha- and beta-adrenergic receptors
  – Respiration, reactions, alarm response
  – Beta Blockers: drugs that block the beta-receptors so that their response to a surge of norepinephrine is reduced, which keeps blood pressure and heart down.
    – Panic example
Neurotransmitters

- **Dopamine (DA)**
  - “Switch” function in brain circuits
  - Interacts with other neurotransmitters
    - Because both DA and Serotonin circuits cross and merge, they can often balance one another out.
      - DA is associated with exploratory, outgoing and pleasure seeking behaviors whereas Serotonin is responsible for inhibition and constraint.
    - Implicated in schizophrenia: Hyper vs. Hypo
    - Parkinson’s disease
Movement Abnormalities and Psychosis

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Representative Disease</th>
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<tbody>
<tr>
<td><strong>Hypokinesia</strong> (associated with decreased DA activity in striatal pathways)</td>
<td>Parkinson’s Disease</td>
</tr>
<tr>
<td><em>Akinesia</em> – poverty of movement and movement initiation.</td>
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<td><em>Bradykinesia</em> – slowness of movement.</td>
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<td><em>Rigidity</em> – uniform increase in resistance to passive movements about individual joints.</td>
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<td><em>Tremor</em> – rhythmic, involuntary muscular contraction characterized by oscillations of a part of the body.</td>
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<tr>
<td><strong>Hyperkinesia</strong> (associated with increased DA activity in striatal pathways)</td>
<td>Huntington’s disease</td>
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<tr>
<td><em>Choreoathetosis</em> – brief, irregular contractions that are not repetitive or rhythmic, but appear to flow from one muscle to the next.</td>
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<td><em>Ballistic movements</em> – violent or flinging movement.</td>
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<td><em>Dystonia</em> – sustained muscle contractions cause twisting and repetitive movements or abnormal postures.</td>
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<td><em>Stereotypy</em> – Movements of frequent repetition that serve no obvious purpose.</td>
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Low Striatal DA Activity

**Hypokinesia**

Slow Movements
Characteristic of Parkinson’s

Antipsychotic meds lower DA and can cause these movements (tardive dyskinesia).

High Striatal DA Activity

**Hyperkinesia and Psychotic Symptoms**

Spontaneous, Violent, Jerking, Non-instrumental Involuntary Movements Characteristic of Huntington’s or Schizophrenia

DA agonists used to treat Parkinson’s (levodopa) can result in drug induced hyperkinesias and in extreme cases, psychotic symptoms (Papapetropoulos & Mash, 2005).
Neurotransmitters

- **Serotonin (5HT)**
  - Monamine class
  - Widespread, complex circuits
  - Regulates behavior, moods, thought processes
  - Low levels and vulnerabilities
    - Instability, impulsivity, aggression
    - This may not be directly a result of low 5HT but rather other areas in the brain may be compensating and causing this as a result!
  - High Levels
    - Interact with GABA to counteract glutamate
  - Multiple receptors (at least 15!):
    - Has different effects depending on type or subtype involved
  - Implicated in several psychopathologies
Behavioral and Cognitive Sciences

- **Learned helplessness**
  - **Perceptions of control**
    - People who are faced with uncontrollable stress in their lives become depressed, even if it seems to others that there is something they could do.
  - **Implicated in depression**
    - Negative attributions
    - *All of this set the background for one of our most useful therapeutic tools: CBT*
  - “Learned optimism”
Behavioral and Cognitive Sciences

- Social learning
  - Albert Bandura
  - Modeling
  - Observational learning
  - Interactive and contingent on perceptions of similarity
  - “a symbolic integration of the experiences of others with judgments of what might happened to oneself”
• Prepared learning
  – Evolutionary basis
    • We learn to fear some objects more easily than others? An evolutionary susceptibility?
  – Increases survival
  – “One-trial” learning
    • Garcia Effect
Cognitive Science and the Unconscious

- **Implicit learning**: When someone clearly acts on the basis of things that have happened in the past, but cannot remember these events.

- The black box

- We simply seem able to process and store information, and act on it, without having the slightest awareness of what the information is, or why we are acting on it. : Blind sight and hypnosis
Was Dr. Freud really on to something after all?: *Stroop*

<table>
<thead>
<tr>
<th>1. RED</th>
<th>6. GREEN</th>
<th>11. BLUE</th>
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<tbody>
<tr>
<td>2. PURPLE</td>
<td>7. PURPLE</td>
<td>12. PURPLE</td>
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<tr>
<td>3. GREEN</td>
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<td>13. BROWN</td>
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<td>4. BLUE</td>
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*Color naming is delayed when the meaning of the word attracts the subject’s attention.*
The Role of Emotion in Psychopathology

- **The Nature of Emotion**
  - *Fight or flight response* (an evolutionarily viable trait is also tied into mental illness)
  - Fear response
    - **Cardiovascular**
      - Vessels constrict and redirect blood from extremities to vital organs that may be needed in an emergency
      - White with fear (decreased BF to skin)
      - Trembling with fear/hair standing up (reaction to conserve heat when vessels are constricted.)
    - **Cortical**
      - Emotional response is terror, motivation for action
      - Short-lived, temporary states
  - Different from mood or affect
Emotion and Physiology

- Hostility and anger are risk factors for heart disease
  - Cardiovascular efficiency ↓
    - Different than response to stress or exercise

- Lazarus (1968)- changes in a person’s environment are appraised in terms of their potential impact on that person. The type of appraisal you make determines the emotion you experience:
  - Example of gun.

- Discussion: How would this tie into mental illness?
  - An appropriate response at the wrong time?
  - Error in appraisal? (CBT)
  - Starting a cascade or cycle? (Stress)
Cultural, Social, and Interpersonal Factors

- Cultural Factors
  - Influence form and expression of behavior
  - Culturally-bound “fright disorders”
    - Susto
    - Voodoo Death

- Social Environment
  - Individualist vs collectivist cultures
  - Urbanicity example
  - Spanking and EE examples

- Interaction with physiology
Cultural, Social, and Interpersonal Factors

• Gender Effects and Roles
  • Phobia, Alcohol, Bulimia
    – Moderating effects: gender doesn’t cause psychopathology, but it can influence its effects (larger or smaller).
    – Related to cultural imperatives
    – Influence across several dimensions
      • Type and prevalence of fears
      • Fear behaviors
      • Responses
      • Coping strategies
Cultural, Social, and Interpersonal Factors

• Social Effects on Health and Behavior
  – Frequency and quality are critical
  – Low social contacts
    • Higher mortality
    • Higher psychopathology
    • Lower life expectancy

  – Mediated by meaning and perception
  – Urbanicity: 38% higher rate of schizophrenia in men raised in cities.
Cultural, Social, and Interpersonal Factors

• Stigma of Psychopathology
  – Influences the expression of distress
  – Limits help-seeking behaviors
  – Helps maintain the cycle of pathology

Pathways to care
http://www.namibouldercounty.org/
Are Psychological Disorders Universal?

- Global Incidence of Psychological Disorders
  - Disorders are common across cultures
  - Rates and expression varies
  - Prevalence and incidence influenced by:
    - Poverty
    - Political unrest
    - Technological disparities
  - Treatment depends on views and provider availability
Life-Span Developmental

• Change over time
  – Biological maturation
  – Psychological development
  – Social complexity
  – Roles and demands
  – Expression of disorders
  – Treatment response
Life-Span Developmental

• The Principle of **Equifinality**
  – Several paths to a given outcome
  – Paths vary by developmental stage
    • Example: Delirium
  – Interaction with other dimensions
    • Social support

*Given this principle is true, how should be modify our conceptualizations of treatment?*
Review: Components of Multidimensional Models

• 1) Biological Factors
   – Genetics
   – Physiology
   – Neurobiology
• 2) Behavioral Factors
• 3) Emotional Influences
• 4) Social Factors
• 5) Developmental Factors

How do we put them all together?
Application to Schizophrenia

• 1. Biological
  – Genetics: COMT
  – Neurotransmitters: D2 Receptors and Dopamine
  – Cerebral: Hippocampal irregularity, poor connectivity between frontal and subcortical regions
  – Endocrinological: heightened cortisol

• 2. Behavioral and Cognitive
  – Learned helplessness
    • Poor stress coping
    • Neuropsychological deficits
Application to Schizophrenia

• 3. Emotional
  – Reading others, experiencing emotion is confused
  – hopelessness
  – Questionable Support as family doesn’t know how to respond
  – Engagement in life is less (social anhedonia)
  – Spirituality

• 4. Social
  – Life events
  – Expressed emotion
  – Cultural effects
    • Pathways to care
    • Stigma
Application to Schizophrenia

• 5. Lifespan/Developmental
  – Onset and course: At the end of adolescence
  – Equifinality
    • Many roads to the same outcome
Risk Markers and the Neurodevelopmental Pathogenesis of Psychosis

OC Hypoxia example:

- Prenatal Insults
- Inherited Genetic Factors
- Genetic Mutations

Congenital Vulnerability (DA Fontal-striatal Circuitry) → Adolescent Neuromaturation → Neuropathological Process → PSYCHOSIS

Stress
- Cognitive & Role Dysfunction
- DA Hyperactivity
- HPA hyperactivity
- Gene Expression

Brain Degenerative Processes

Gene Expression

Brain Development

HPA & HPG activation