Psychological Disorders

Schizophrenia
Affective disorders
Anxiety disorders
Psychological Disorders
Figure 14.1: Psychological Disorders Impair a Person’s Ability to Cope

- 25% of adults in U.S. suffer from diagnosable mental illness
- 46% fall victim during lifetime
- Cost estimated at $317 billion a year in U.S.
- The economic burden of treating schizophrenia represents 50% of the costs of treating all other psychological disorders combined.
Schizophrenia

- **Schizophrenia**: “Split mind”
- **Psychosis** characterized by
  - Perceptual, emotional, and intellectual deficits
  - Loss of contact with reality
  - Inability to function in life
- NOT Dissociative Identity Disorder (multiple personality)
- The most severe or debilitating mental illness
Psychological Disorders

Figure 14.4: Philippe Pinel Freeing Mental Patients From Their Chains

SOURCE: © Rapho Agence/Photo Researchers.
Schizophrenia

Figure 14.2: Eugen Bleuler (1857-1939).

- 1% of men and women.
  - Men show first symptoms during teens / twenties,
  - Onset for women ordinarily comes a decade later.
  - *Prevalence (# of diagnoses) is stable or declining slightly

- **Acute** symptoms
  - Develop suddenly
  - More responsive to treatment.
  - Prognosis reasonably good

- **Chronic** symptoms: less responsive to treatment
  - Symptoms develop gradually and persist for a long time
  - Poor prognosis. 20 years after 1\textsuperscript{st} diagnosis only 22% are fully recovered

SOURCE: © Bettmann/Corbis.
Schizophrenia

Figure 14.3: Age of Risk for Schizophrenia

- Familial disorder—incidence is higher among the relatives of schizophrenics.
  - Heritability estimated between .60 and .90.
  - Identical twins 3X likely as fraternal twins
  - Multiple genes are involved, each contributing only a small effect.
  - Some researchers include spectrum disorders, and others don’t, so it makes specific genetic influences tough to isolate or pin down.

SOURCE: Data from Huber et al. (1980).
Schizophrenia

Figure 14.5: Concordances for Schizophrenia Among Relatives

<table>
<thead>
<tr>
<th>Genetic Relatedness</th>
<th>Relationship</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>Identical twin</td>
<td>48%</td>
</tr>
<tr>
<td>—</td>
<td>Offspring of two patients</td>
<td>46%</td>
</tr>
<tr>
<td>50%</td>
<td>Fraternal twin</td>
<td>17%</td>
</tr>
<tr>
<td>50%</td>
<td>Offspring of one patient</td>
<td>17%</td>
</tr>
<tr>
<td>50%</td>
<td>Sibling</td>
<td>9%</td>
</tr>
<tr>
<td>25%</td>
<td>Nephew or niece</td>
<td>4%</td>
</tr>
<tr>
<td>0%</td>
<td>Spouse</td>
<td>2%</td>
</tr>
<tr>
<td>0%</td>
<td>Unrelated person in the general population</td>
<td>1%</td>
</tr>
</tbody>
</table>

Schizophrenia

Figure 14.6: Risk of Schizophrenia in the Offspring of Normal and Schizophrenic Twins

SOURCE: Based on data from Gottesman and Bertelsen (1989).
Schizophrenia

• The **Vulnerability Model**
  • Some threshold of causal forces must be exceeded in order for the illness to occur.
  • Environmental challenges combine with a person’s genetic vulnerability to exceed that threshold.

• Environmental influences work in part by epigenetic means
  • Up-regulating and down-regulating gene functioning.
### Schizophrenia

**Table 14.2: Crow defined Type I and Type II schizophrenia based on Positive Versus Negative types of symptoms**

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Type I (Positive)</th>
<th>Type II (Negative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic symptoms</td>
<td>Delusions, hallucinations, etc.</td>
<td>Poverty of speech, lack of affect</td>
</tr>
<tr>
<td>Response to anti-dopaminergic drugs</td>
<td>Good</td>
<td>Poor</td>
</tr>
<tr>
<td>Symptom outcome</td>
<td>Potentially reversible</td>
<td>Irreversible?</td>
</tr>
<tr>
<td>Intellectual impairment</td>
<td>Absent</td>
<td>Sometimes present</td>
</tr>
<tr>
<td>Suggested pathological process</td>
<td>Increased $D_2$ dopamine receptors</td>
<td>Cell loss in temporal lobes</td>
</tr>
</tbody>
</table>

*SOURCE: Crow (1985)*
Schizophrenia

• Dopamine hypothesis
  • Excessive dopamine activity in the brain
    • Higher activity in the striatum
    • However, anti-dopamine drugs don’t help 30% to 40%
  • 1st Generation antipsychotics, though effective, often produce tardive dyskinesia (involuntary motor movements)
• Atypical antipsychotics
  • Target D$_2$ receptors less and less likely to produce tardive dyskinesia
  • Equal to or more effective than anti-dopamine drugs
  • Help resistant cases through *action on serotonin synapses and glutamate levels.
Schizophrenia

Figure 14.7: Relationship Between Receptor Blocking and Clinical Effectiveness of Schizophrenia Drugs.

Schizophrenia

• **Disordered Connections Theory**
  • Activity in the prefrontal area and the hippocampus is not coordinated.
  • Cells in the hippocampus show unusually disorganized structural patterns.

• **Glutamate Theory**
  • Too little glutamate to slow down brain activity
  • PCP mimics schizophrenia by inhibiting NMDA receptors
  • Increasing glutamate amounts through direct administration of glycine also decreases positive and negative symptoms
Schizophrenia
Figure 14.8: Ventricle Size in Normals and People with Schizophrenia

- **Brain Anomalies**
  - Reduced gray matter and limbic area volume, sometimes resulting in increased ventricular size.
  - Hypofrontality, indicated by brain scans and the **Wisconsin Card Sorting Test**, is due to disrupted communication between the hippocampus and the prefrontal cortex.

**SOURCES:** (a) From “Lateral Cerebral Ventricular Enlargement in Chronic Schizophrenia,” by D. R. Weinberger et al., Archives of General Psychiatry, 36, pp. 735–739. Copyright 1979 American Medical Association. Reprinted with permission; (b) Copyright 1990 Massachusetts Medical Society. All rights reserved.
Schizophrenia

Figure 14.9: Blood Flow in Normal and Schizophrenic Brains During Card Sorting Test.

Schizophrenia

Figure 14.10: Brain Activation During Visual and Auditory Hallucinations in a Schizophrenic

- Neural connections and synchrony
  - Decreased between brain areas
    - Reduced white matter
    - Environmental stimuli are sometimes perceived as threatening.
  - Impaired auditory gating
- Increased within smaller areas
  - Hallucinations due to hyper-excitability in sensory areas
- Nicotine
  - Normalizes auditory gating and improves negative symptoms
  - 80% of schizophrenia patients smoke.
  - Gene for nicotinic acetylcholine receptor implicated in reduced activity of the receptor and symptoms.

Schizophrenia

Figure 14.11: Interleukin-1β Levels in Schizophrenics and Controls.

- Environmental Origins and Transmitter Anomalies
  - Direct brain damage or injury during early years
  - Prenatal complications, stress, immune responses, and starvation during pregnancy

Schizophrenia

Figure 14.12: Relationship of Schizophrenic Births to Season and Influenza Epidemics in England and Wales (1939–1960).

• Environmental Origins and Transmitter Anomalies
  • Direct brain damage or injury during early years
  • Prenatal complications, stress, immune responses, and starvation during pregnancy
  • Winter birth effect
  • Neurodevelopmental problems during neuron migration (Reelin)
Adolescence as a significant period (onset timing)

• Brain maturation is affecting connections between the temporal and limbic areas.
• Extensive frontal lobe myelination is happening during this period
• Circuit pruning is a major developmental event during this time.
Affective Disorders

• **Mood disorders: popular** (30% will suffer with one some time during their lifetime)...the most common one being...

• **Depression** is an intense feeling of sadness
  • **Major depression** lasts for weeks to months at a time
  • Symptoms include sadness to the point of hopelessness, loss of enjoyment of life, lack of energy, sleep disturbance, and slowness of thought
  • Annual cost for all mood disorders range from $24B to $234B annually.
Affective Disorders

• Forms
  • **Unipolar depression.**
    • Females are three times more likely to be depressed than males.
    • Risk for men increases with age; women are most vulnerable between the ages of 35 and 45.
  • **Bipolar disorder**
    • Alternate between periods of depression and **Mania**
      • Excess energy, decreased need for sleep and increased sex drive and (often) drug use
      • In some cases, a period of agitation replaces mania
Affective Disorders

Figure 14.15: The Role of Stress and the Serotonin Transporter Gene in Depression

• Heredity
  • Affective disorders are partially inheritable, with bipolar disorder more heritable than depression.
  • Heritability is 29% in men, 42% in women: genes implicated tend to be gender-specific.

![Graph showing the role of stress and the serotonin transporter gene in depression](image)

Affective Disorders

- **Heredity**
  - Candidate genes include the 5-HTTLPR serotonin transporter gene.
  - VAL66MET allele of the gene for **brain-derived neurotrophic factor (BDNF)**
    - BDNF encourages neuron growth and survival
    - VAL66MET protects against effects of the 5-HTTLPR gene through epistasis.
- **Other genes implicated**
  - Calcium channels at myelin nodes
  - Genes shared with several other mental disorders.
Affective Disorders

• **Monoamine Hypothesis** of Depression
  • Depression involves reduced activity at norepinephrine and serotonin synapses
  • Effective antidepressant drugs increase the activity of NE and/or S, but usually take a few weeks to work
    • Antidepressant classes
      1. Monoamine oxidase inhibitors (MAOI) block enzymatic destruction of neurotransmitters.
      2. Tricyclic antidepressants block reuptake (like SSRIs).
      3. Atypical (second generation) antidepressants target a specific neurotransmitter.
  • Smoking: Ingredients in tobacco act as an MAOI
    • 80% of affected individuals self-treat with tobacco.
Affective Disorders

Figure 14.16: Monoamine Oxidase Levels in the Body of a Nonsmoker and a Smoker

Affective Disorders

- Monoamine Hypothesis of Depression
  - NMDA receptors
    - Also play a role if hyperactive
    - Ketamine (animal tranquilizer and potent dissociative) is an NMDA receptor antagonist, produces almost immediate improvement
  - Cognitive Behavior Therapy (CBT)
    - Drugs can be more effective if paired with Cognitive Behavioral Therapy
Affective Disorders

- **Electroconvulsive Therapy (ECT)**
  - Reduces depression by inducing a seizure
  - Can be more effective than antidepressant drugs
  - Generally also works faster than antidepressant drugs
  - Effects are often relatively short lived (less than 1 year)
  - Increases synchrony over large brain areas
  - Side effects (retrograde amnesia in particular) are still an issue, but have been diminished by using lower voltage shocks to initiate the seizure.
  - Still considered a ‘last resort’ treatment for many
Affective Disorders
APPLICATION: Electrical Stimulation for Depression

• Other techniques
  a. Transcranial magnetic stimulation (TMS; applying magnets to the scalp)
  b. Deep Brain Stimulation (electrodes placed in the brain directly)

SOURCES: (a) Courtesy of National Institute of Health; (b) Courtesy of Helen Mayberg.
Affective Disorders

• Rhythms and Affective Disorders
  • Circadian Rhythms and Antidepressant Therapy
    • The circadian rhythm is a daily biological rhythm
    • Readjusting a person’s circadian rhythm can relieve depression
    • Reducing the amount of a person’s rapid eye movement (REM) sleep can also reduce depression
  • Seasonal Affective Disorder
    • In Seasonal Affective Disorder (SAD), depression varies with the seasons
    • Phototherapy (exposure to high intensity lights) is a treatment for winter depression. It works because it resets the person’s circadian rhythms.
Affective Disorders

Figure 14.18: Increased Neurogenesis in the Hippocampus During Antidepressant Treatment.

• Antidepressants, ECT, and Neural Plasticity
  • Have been used to treat depression for more than half a century, though not sure how they work
  • Cell turnover (neurogenesis) may play a role, though the key factor may be increased plasticity in the hippocampus

Affective Disorders

• In bipolar disorder, periods of depression typically last longer than mania.
• Cycling is regular in some and unpredictable in others; cycle length varies from 48 hours to months.
• Lithium is the drug of choice for bipolar disorder, and usually works best in the manic phase.
  • The belief has been that lithium works by stabilizing many transmitters.
  • Recent evidence is that lithium and valproate inhibit protein kinase C, an enzyme that regulates neuron excitability.
Affective Disorders

See Figure 14.20: Decreased Frontal Activity in Depression

• Brain Anomalies in Affective Disorder
  • Volume deficits and decreased activity in prefrontal areas, especially the dorsolateral cortex.
  • Also loss in hippocampus
Affective Disorders

Figure 14.21: Increased Activity in the Ventral Prefrontal Cortex (PFC) and Amygdala in Depression.

• Brain Anomalies in Affective Disorder
  • Increased activity in ventral prefrontal cortex
  • Increased volume and activity of amygdala

Affective Disorders

Figure 14.22: Glucose Metabolism Increase During Mania in a Rapid-Cycling Bipolar Patient.

**Bipolar Disorder**

- Cycling varies in length from as little as 48 hours to months
- Cycling can be regular or unpredictable
- Stress can trigger manic episodes
- Lithium (the go-to drug) stabilizes neurotransmitter and receptor systems to prevent large mood swings

Affective Disorders

Figure 14.23: Activity in the Subgenual Prefrontal Cortex in Depression and Mania.

• **Brain Anomalies in Affective Disorder**
  - Anomalies in functional brain connectivity between cortex, corpus callosum, and thalamus in bipolar disorder patients.
  - Brain activity increases during manic episodes by 4% to 36%
  - The ventral prefrontal cortex may be a “depression switch” and the subgenual prefrontal cortex may be a “bipolar switch”

Affective Disorders

Figure 14.24: Suicide Rates for Three Disorders in Men and Women.

• Suicide
  • High among people with affective disorders, especially bipolar disorder (20%)

Affective Disorders

Figure 14.25: Serotonin Levels and Suicide.

• Suicide
  • High among people with affective disorders, especially bipolar disorder (20%)
  • Serotonin activity is low, particularly in repeat attempters
  • Impulsivity and aggression linked to serotonin and BDNF genes
  • Lower levels of 5-HIAA also associated with higher suicide rates

Anxiety Disorders

• Generalized Anxiety, Panic Disorder, and Phobia
  • Phobias are the most common, hitting about 13% of the population.
  • Neurotransmitters
    • GABA (increased sensitivity)
    • Serotonin (too little)
  • Drugs
    • Benzodiazepines- increase sensitivity of receptors to GABA, but are highly addictive
    • SSRIs are now the drug of choice as a result.
Anxiety Disorders

Figure 14.26: Hippocampal Volume Is Reduced in Combat Veterans and Their Twins.

- **Posttraumatic Stress Disorder (PTSD)**
  - Prolonged stress reaction to traumatic event, including nightmares, hyper-reactivity to environmental stimulation, flashbacks, & trouble concentrating.
  - Heritability is about 30%, and unrelated to severity or reaction to a traumatic event

- Treatment
  - Exposure therapy is a promising alternative to drugs and psychotherapy
  - Virtual reality and fear erasure are also possibilities
  - New treatment, D-cycloserine combined with virtual reality therapy, has been shown to reduce PTSD remission by 50% after 6 months.
Anxiety Disorders

Figure 14.26: Hippocampal Volume Is Reduced in Combat Veterans and Their Twins.

- Brain changes due to PTSD
  - Hippocampal volume is reduced
  - May be a predisposing factor rather than a result
  - Decreased medial prefrontal cortex activity, maybe hippocampus
  - Hyperactive amygdala, anterior cingulate, insular cortex

Anxiety Disorders

Figure 14.27: Networks Involved in Anxiety

- Circuits contributing to anxiety
  - Ventral attention network
    - Contributes to excessive stimulus-driven attention
  - Salience network
    - Error detection between intended and appropriate responses
  - Frontoparietal network
    - Executive control
  - Default mode network
    - Self-monitoring, planning, and emotional regulation

Anxiety Disorders

Figure 14.28: Brain Structures Involved in Obsessive-Compulsive Disorder

- **Obsessive-Compulsive Disorder (OCD)**
  - Obsessions (recurring thoughts) and compulsions (irresistible impulses to act)
  - Abnormally high activity in the orbital frontal cortex and the caudate nuclei, and low activity in basal ganglion
  - Genetic association with related anxiety disorders involving imbalanced levels of serotonin (high) and dopamine. Most effective current pharmacological treatment is SSRIs (cause a compensatory reduction in activity)
Anxiety Disorders

Figure 14.31: Increased Dopamine Activity in the Caudate Nuclei in Tourette’s Syndrome

• Disorders related to OCD
  • Acral Lick Syndrome (excessive grooming) and lack of the sapap 3 gene.
  • Hoarding
  • Tourette syndrome (motor/sound tics, high dopamine activity in the basal ganglia). Think of it as “reverse OCD”.

Anxiety Disorders

**Anxiety Disorders and Heredity**
- Heritability ranges between 20% and 47% (twin studies)
- Over 90% of individuals with anxiety disorders have a history of other psychiatric problems
  - Major depression in 50%-60% of individuals with anxiety disorder
  - Panic disorder in 16% of bipolar patients