Biological Basis for Understanding Psychiatric Disorders and Treatments

CHAPTER 3

Psychotropic Drugs

• Psychiatric illness is related to a number of factors (e.g., genetics, neurodevelopmental factors, drugs, infection, psychosocial experience).
• Psychiatric illness results in an alteration in neurotransmitters.
• These alterations are the targets of psychotropic drugs.

Psychotropic Drugs

Function and Activities of the Brain

• Maintenance of homeostasis
• Regulation of autonomic nervous system (ANS) and hormones
• Control of biological drives and behavior
• Cycle of sleep and wakefulness

Function of the Brain (continued)

• Circadian rhythms
• Conscious mental activity
• Memory
• Social skills

Cellular Composition of the Brain

• Neurons
• Respond to stimuli
• Conduct electrical impulses
• Release chemicals
• Neurotransmitters

Cellular Composition of the Brain (continued)

• Presynaptic neuron → synapse → postsynaptic neuron
Neurotransmitter Destruction
- Enzymes
  - (MAO)
- Reuptake

Organization of the Brain
Brainstem
- Cerebellum
- Cerebrum

Function of Brainstem
- Core – Regulates internal organs and vital functions
- Hypothalamus – Basic drives and link between thought and emotion and function of internal organs
- Brainstem – Processing center for sensory information

Function of Cerebellum
- Regulates skeletal muscle
- Coordination and contraction
- Maintains equilibrium

Function of Cerebrum
- Parietal cortex: sensory and motor, reading/math
- Temporal cortex: sound
- Occipital cortex: vision
- Frontal lobe: thought processes
- Basal ganglia: regulation of movement
- Amygdala and hippocampus: emotions, learning, memory, basic drives

Limbic System
- Many structures of the brain that interconnect (such as the amygdala, hippocampus, prefrontal cortex, anterior cingulate, ventral striatum, insula, olfactory bulb) and primarily support emotion
- This is the target of most psychotropic drugs
Audience Response Questions
Which part of the brain is most responsible for difficulty with recalling the three words at the test of memory?

A. Brainstem
B. Cerebrum
C. Cerebellum
D. Hypothalamus

Visualizing the Brain
- Structured imaging techniques
  - Computed tomography (CT)
  - Magnetic resonance imaging (MRI)
- Functional imaging techniques
  - Positron emission tomography (PET)
  - Single photon emission computed tomography (SPECT)

PET Scans
Identical Twins (31-year-old men)
Note reduced brain activity in frontal lobe

Disturbances of Mental Function
- External: drugs, infection, hormones, trauma
- Genetics
- Altered neurotransmitters
  - Norepinephrine
  - Serotonin
  - Dopamine
  - Glutamate
  - γ-aminobutyric acid (GABA)
- Neuropeptides
- Acetylcholine

Mental Dysfunction and Altered Activity of Neurons
- Depression
  - Deficiency of norepinephrine
  - Deficiency of serotonin
  - Dysregulation of dopamine, acetylcholine and GABA are also believed to be involved
Mental Dysfunction and Altered Activity of Neurons – (continued)

- Schizophrenia
- Excess transmission of dopamine
- Dysregulation of serotonin and glutamate
- Anxiety
  - Deficiency of γ-aminobutyric acid (GABA)
  - Deficiency of serotonin/excess in norepinephrine

Action of Psychotropic Drugs

- Pharmacodynamics
  - What drugs do and how they do it
  - Drug action and drug responses
  - Some drugs, foods and smoking induce or inhibit actions of drugs in the body
- Pharmacokinetics (Hint: “ADME”)
  - Absorption
  - Distribution
  - Metabolism – genetic variants also affect one’s ability to metabolize drugs
  - Excretion
- Pharmacogenetics
  - Effects of genetic variation on drug responses

Pharmacogenetics

- The study of genetic differences in metabolic pathways which can affect individual responses to drugs both therapeutic and adverse effects
- CYP450 enzyme system
  - Extensive metabolizers (normal)
  - Poor metabolizers
  - Intermediate metabolizers
  - Ultrarapid metabolizers
- Ethnopharmacology
  - Future prescribing practices may be tailored to genetic codes

Many CYP450 Systems in the Liver

CYP450 Enzyme System – Ex: 3 enzymes metabolize different SSRIs
- CYP450 2D6 - 15% Caucasians are poor metabolizers (Prozac - fluoxetine)
- CYP450 2C19 – 20-30% of Asians are poor metabolizers (citalopram)
- Lithium (anti-manic drug)
  - Same dose, but plasma concentrations 50% higher in Asians than in whites
  - Less efficient lithium-sodium countertransport ability at the cell membrane
  - Lower effective doses in African Americans due to a higher red blood cell to plasma ratio of lithium
- Clozapine (antipsychotic)
  - Life-threatening side effect, agranulocytosis, more prevalent in Ashkenazi Jews than in other ethnic groups
Anxiolytics/Antianxiety Medications

- Benzodiazepines
- Non-benzodiazepines: BuSpar
- Sedative-Hypnotics
- Melatonin Receptor Agonists

Antidepressants

- Tricyclic Antidepressants (TCA)
- Selective Serotonin Reuptake Inhibitors (SSRI)
- Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)
- Serotonin-Norepinephrine Disinhibitors (SNDI)
- Monoamine Oxidase Inhibitors (MOAI)
- Norepinephrine Dopamine Reuptake Inhibitor (NDRI)
- Serotonin Antagonist and Reuptake Inhibitor (SARI)
- More....

Mood Stabilizers

- Lithium (Eskalith, Lithobid)
- Anticonvulsant drugs
  - Valproate (Depakote, Depakene)
  - Carbamazepine (Equetro, Tegretol)
  - Lamotrigine (Lamictal)
  - Gabapentin (Neurontin)
- More.....

Antipsychotic Drugs

- Conventional Antipsychotics (also called typical or standard)
  - Haldol (haloperidol)
  - Thorazine (chlorpromazine)
  - Prolixin (fluphenazine)
  - Orap (pimozide)
- Atypical Antipsychotics (second generation antipsychotics)
  - Clozaril (clozapine)
  - Risperdal (risperidone)
  - Saphris (asenapine)
  - Seroquel (quetiapine)
  - Zyprexa (olanzapine)
- Third Generation Antipsychotic
  - Abilify (aripiprazole)

Herbal Medicine

- Major concerns
  - Potential long-term effects
    - Nerve damage
    - Kidney damage
    - Liver damage
  - Possibility of adverse chemical reactions
    - With other substances
    - With conventional medications
Audience Response Questions
If a person has decreased circulating levels of GABA, which health problem would be expected?
A. Major Depressive disorder  
B. Schizophrenia  
C. Anxiety disorders  
D. Bipolar disorder

Audience Response Questions
Which neuroimaging technique would reveal problems in the anatomical structure of the brain but not problems in function?
A. CT  
B. PET  
C. SPECT  
D. Functional MRI

Audience Response Questions
Genetics play which role in response to psychotropic drugs?
A. Different ethnic groups have different responses.  
B. Genetics are not associated with drug response.  
C. Response to psychotropic drugs may be related to genetics.  
D. Genetics are related to the disease process and not the drug response.

Audience Response Questions
Psychogenetics may one day lead to which of the following? (Select all that apply.)
A. Personalized medications  
B. Safer drugs  
C. Targeted pharmacologic therapies determined by genetically inherited factors  
D. Increased number of receptors