Boards & Beyond:
Psychiatry Slides

Color slides for USMLE Step 1 preparation from the Boards and Beyond Website

Jason Ryan, MD, MPH

2020 Edition

Boards & Beyond provides a virtual medical school curriculm used by students around the globe to supplement their education and prepare for board exams such as USMLE Step 1.

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Conditioning and Transference

Conditioning and Transference

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Behavioral Therapy

- Seeks to modify unwanted behavior (i.e. anxiety)
- Goal: change patient's response to environment
- **Conditioning** and **reinforcement** → behavior
- Therapy aims to alter conditioning/reinforcements

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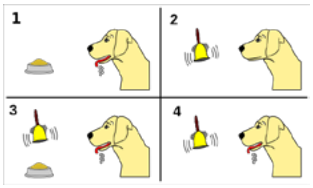
Conditioning

- Linking of **stimulus** to **response**
  - Pavlov's dog
  - Stimulus: Ringing of a bell
  - Response: Salivation
- Classical
- Operant



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Classical Conditioning

- Unconditioned stimulus and response
  - Natural stimulus for a particular response
  - Food and salivation
- Conditioned stimulus and response
  - *Unnatural* stimulus for a particular response
  - Bell and salivation
- Often response is **involuntary**
  - Salivation
  - Fear

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Classical Conditioning

- Clinical example: **Enuresis alarms**
  - Treatment for bed wetting (enuresis)
  - Water-sensitive pad under child's sheet
  - Alarm awakens child
  - Over time, child awakens from sensation to urinate
- Unconditioned stimulus and response
  - Alarm → awakening
- Conditioned stimulus and response
  - Urinary fullness → awakening

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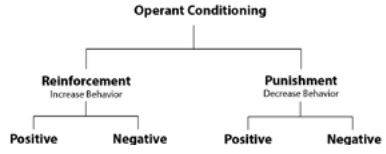
Operant Conditioning

- Behavior from reward or punishment
- Reinforces or decreases voluntary behaviors
- Often deals with **voluntary behavior**



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Operant Conditioning

- Reinforcement: ↑ **frequency** of behavior (response)
- **Positive** reinforcement
  - Behavior → reward → ↑ frequency
  - Child rewarded for good behavior → ↑ good behavior

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Operant Conditioning

- **Negative** reinforcement
  - Behavior → removal of aversive stimulus
- "Negative reinforcer"
  - Something you don't want
  - Changes behavior
- Wearing sunscreen to avoid sunburn
- Child cleans room to avoid parent yelling
- Different from punishment
  - Behavior *increases* from stimulus (sunburn, yelling)
  - Punishment → less behavior

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Operant Conditioning

- Punishment: ↓ frequency of behavior
- **Positive** punishment
  - Behavior → aversive stimulus → ↓ frequency
- **Negative** punishment
  - Behavior → removal of desired stimulus → ↓ frequency

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Operant Condition Quadrants

	Increase Behavior	Decrease Behavior
Add Stimulus	Positive Reinforcement	Positive Punishment
Remove Stimulus	Negative Reinforcement	Negative Punishment

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Extinction

- Gradual weakening of conditioned response
- Classical conditioning:
  - Conditioned and unconditioned stimuli no longer linked
- Operant conditioning
  - Behavior no longer reinforced
  - Remove reward/punishment

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Other Learning Processes

- **Habituation**
  - Repeated exposure → less response
  - Child becomes accustomed to MD visits → less anxiety
- **Sensitization**
  - Repeated exposure → more response
  - More MD visits for child → more anxiety

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Transference

- **Unconscious** projection by patient onto others
- Often feelings associated with patient's past
- Patient responds to clinician as a parent
  - Example: Patient angry with therapist behavior
- Patient responds to spouse as a parent

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Countertransference

- **Clinician** projects onto patient
- Clinician treats patient as son/daughter

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Ego Defenses

Ego Defenses

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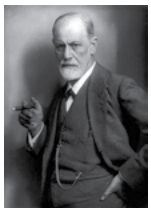
Freudian Psychology

- Id - desire
- Superego – societal rules, morality
- Ego - mediator between id and superego



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Ego Defenses

- Adjustments in reality perception
- Mostly **unconscious**
- Resolve/manage conflict between id and superego
- Minimize anxiety
- Adaptation to stressful circumstances

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Acting Out

- Avoiding emotions by **bad behavior**
- Attention seeking, socially inappropriate behavior
- Examples:
  - Child with sick parents misbehaves at school
  - Adolescent engages in promiscuous sex during parents' divorce

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Denial

- **Refusing to accept** unpleasant reality
- Examples:
  - Patient thinks doctor is wrong about diagnosis
  - Heavy drinker believes she drinks socially

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Displacement

- Directing emotions to another person
- Example: Patient angry at doctor after injury

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Dissociation

- Detachment from reality
- Often sudden onset after triggering event (i.e. rape)
- Patient may appear detached with flat affect
- Patient may lose track of time

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Repression

- "Motivated forgetting"
- Usually **forgetting** one particular memory/fact
- Often something that happened long ago
  - Example: difficult period of childhood
- First defense mechanism described by Freud
- Thoughts repressed to avoid guilt

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Fixation

- Failure to develop beyond a childhood growth stage
- Oral fixation
  - Stuck in oral phase
  - Thumb sucking, eating, chewing pencils
- Adult lives with mother and depends on her

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Idealization

- Emphasizing positive thoughts/memories
- De-emphasizing negative thoughts/memories
- Classically done with childhood events
- "Our family vacations were always amazing!"

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Identification

- **Mimicking behavior** of someone else
- Can be positive or negative
- Child behaves like school bully with little sister
- Child behaves like other child in new school

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Intellectualization

- Avoiding emotions through reasoning
- Spouse going through divorce cites divorce statistics to friends to avoid admitting sadness

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Isolation

- Isolating a distressing memory/event
- Failing to experience emotions of event
- Person describes rape without expressing sadness

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Passive Aggression

- Conflict with others in non-confrontational manner
- Husband uncooperative with wife because he is mad

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Projection

- Attributing feelings/emotions to others
- A cheater accuses a classmate of cheating off him
- Man with homosexual impulses accuses another man of being attracted to him

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Rationalization

- Distorting events so outcome is positive
- "I'm glad I got fired, I needed a change."

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Reaction Formation

- Opposite behavior (reaction) to unwanted feelings
- Man who craves alcohol preaches abstinence
- Woman despises mother, throws birthday party
- Parent despises child shows extreme love/affection

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Regression

- Reverting to behavior of younger person/child
- Stressed adult watches cartoons from childhood
- Sick adult wants parent to stay in hospital with them

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Splitting

- Categorizing others at extremes
- "Wonderful" or "horrible" people
- Patient likes her doctor but hates nurse
- Common in borderline personality disorder

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Sublimation

- Using negative emotions in a positive way
- Anxious person becomes a security guard
- Aggressive person becomes a boxer

Altruism

- Practice of concern for others
- Caring for others to reduce stress/anxiety
- Cancer survivors help others with same disease

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Suppression

- **Conscious** defense mechanism
- Done intentionally to relive stress/anxiety
- Ignoring stressful thoughts/feelings to cope
- "I'm not going to think about that now."

Humor

- Relief of anxiety with jokes/laughter
- Medical student jokes about board studying

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Mature Defenses

- Sublimation
- Altruism
- Suppression
- Humor

Child Abuse and Neglect

Child Abuse and Neglect

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Infant Deprivation

- Normal development requires human interaction
- **Attachment**
  - Child is repeatedly comforted, cared for
  - Caregiver consistently meets child's needs
  - Warm, consistent loving attention

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Infant Deprivation

- Lack of attachment → adverse effects on child
- Failure to thrive
- Poor development
- Lack of social skills
- Death

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RAD

Reactive Attachment Disorder

- DSM-V disorder of attachment
- Some similarities to autism spectrum disorders
- Associated with severe early deprivation
- Detached child
- Unresponsive to comforting
- Inhibited (does not show emotions)
- Withdrawn/avoidant

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DSED

Disinhibited social engagement disorder

- DSM-V disorder of attachment
- Associated with severe early deprivation
- Little/no reluctance to interact with adults
- Hugging strangers
- Sitting on lap of stranger

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Child Maltreatment

- Child (physical) abuse
- Sexual abuse
- Emotional abuse
- Child neglect

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Child Abuse

- Injury to a child by parent or caregiver
- Commonly affects **children < 1 year of age**
- Perpetrator usually closest family member (mother)
- Often identified by healthcare providers

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Child Abuse Injuries

History

- Reported minor trauma → major injury
- Caregiver history changes over time
- Severe injury blamed on siblings/pets

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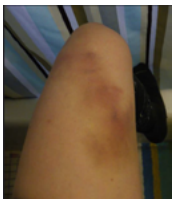
Child Abuse Injuries

Bruising

- **Most common abuse injury**
- Multiple bruises
- Buttocks, trunk, ear, neck



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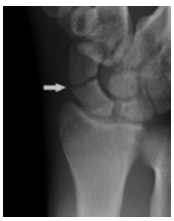
Child Abuse Injuries

Fractures

- Often identified by skeletal survey
  - X-rays of all bones
- **Multiple fractures** in **different healing stages**
- Rib fractures
- Long bone fractures in baby



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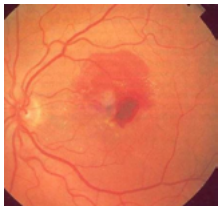
Child Abuse Injuries

Head Trauma

- "Abusive head trauma"
- "Shaken baby syndrome"
- Retinal hemorrhages
- Subdural hematoma



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Child Abuse

Selected Risk Factors

- Parent factors
  - Single, young parents
  - Lower parental level of education
  - Parental substance or alcohol abuse
  - Parental psychiatric illness
- Child factors
  - Unplanned pregnancy
  - Unwanted child
  - Learning disabilities, behavioral problems

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Child Sexual Abuse

- Most common **pre-puberty (9-12 years old)**
- Perpetrator usually **male** known to child
- Trauma to mouth, anus, genitals
- Sexually transmitted infection

Emotional Abuse

Psychological Abuse

- Child feels worthless, unloved
- Verbal abuse
- Criticism
- Intimidation (scaring child)
- Humiliation
- Confinement for prolonged periods as punishment

Child Neglect

- Common form of child maltreatment
- 50% cases reported to child protection services
- Inadequate food, shelter, supervision, affection
- Poor clothing and hygiene
- Underweight or malnourished
- **Must be reported to protective services**
- All 50 states have laws requiring physician reporting

Vulnerable Child Syndrome

- Problem of **parental reactions to child**
- Parents believe child highly susceptible to disease
- Child illness may be real or perceived
- Risk factors
  - Parents with difficult conception
  - Difficult pregnancy or post-natal period
  - Parental anxiety/depression
- Multiple visits to providers, emergency room
- Often numerous, minor complaints

Childhood Disorders

Childhood Disorders

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Rett Syndrome

- Neurodevelopmental disorder of **females**
  - Contrast with autism: 4x more common in males
- Initially normal development
- Slow symptom onset 1-2 years of age
- Hallmark: **regression** of cognitive/motor skills
  - Diagnostic criteria for disorder

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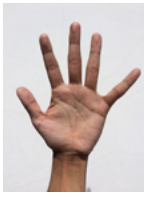
Rett Syndrome

- Deceleration of head growth
- *Loss* of motor, intellectual, speech abilities
- *Loss* of balance (ataxia)
- **Repetitive hand movements**
  - Hand-to-mouth licking
  - Grabbing of clothing or hair
  - Hand wringing



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Rett Syndrome

Genetics

- **X-linked disorder**
  - X-linked dominant: 1 abnormal gene → disease
- 99% cases: sporadic gene mutation
- MECP2 gene mutations (X chromosome)
  - Significant expression in brain

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Rett Syndrome

Genetics

- **Females**
  - One normal MECP2 gene, one abnormal
  - Random X inactivation → some cells with normal gene
  - Result: survival with symptoms
- **Males**
  - All abnormal MECP2 genes (one X chromosome)
  - Lethal

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Conduct Disorder

- Childhood behavioral disorder
- Repeated pattern of violating rights of others
- **Aggression** to people/animals
- **Destruction** of property
- Lying or stealing
- Adult version: Antisocial personality disorder

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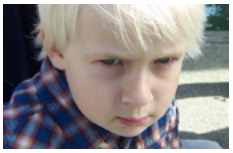
Oppositional Defiant Disorder

- Angry, irritable child
- Argues with authority figures
- Defiant
- Vindictive toward parents/teachers



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Oppositional Defiant Disorder

Diagnostic Criteria and Treatment

- Occurs with at least one individual who is not a sibling
- Causes problems at work, school or home
- Not caused by substance use, depression or bipolar
- Lasts at least six months
- Treatment: Cognitive behavioral therapy
- Resolves in most children

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DMDD

Disruptive mood dysregulation disorder

- New disorder
- Added to DSM-V in 2013
- Controversial
- Some symptoms (irritability) common
- Similarities to ODD
- Few established treatments

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DMDD

Disruptive mood dysregulation disorder

- Childhood mood disorder
  - Must occur before age 10
- Excessively irritable or angry behavior
- Frequent **temper outbursts**
  - At least three times per week
  - At least two settings (home, school, etc.)
- Behavior out of proportion to situation

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DMDD

Disruptive mood dysregulation disorder

- Cognitive behavioral therapy
- Anti-depressants
- Stimulants
- Anti-psychotics

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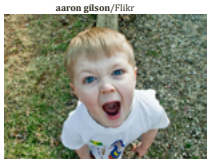

Bad Behavior

ADHD
Poor attention
Hyperactivity

ODD
Argues
Defiant

DMDD
Temper tantrums

Conduct Disorder
Property destruction
Aggression to animals

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Separation Anxiety Disorder

- Childhood anxiety disorder
- Distress when separating home/parents
  - Refusal to leave home
  - Refusal to go to school
- Worry about losing major attachment figures
- Persistent reluctance/refusal to go out

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Separation Anxiety Disorder

- Nightmares about separation
- Repeated complaints of **physical symptoms**
  - Headaches, upset stomach, nausea
  - Occurs with separation or in anticipation
- Treated with therapy
  - Goal: teach children coping skills
  - Cognitive behavioral therapy
  - Parent-child interaction therapy

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Tourette Syndrome

- Neurologic disorder
- Occurs in children
- Hallmark: **recurrent tics**
- Sudden, quick repetitive movements or speech
- Commonly co-occurs with other disorders
  - Attention deficit hyperactivity disorder (ADHD) – 60%
  - Obsessive-compulsive disorder (OCD) – 30%

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Tourette Syndrome

- Motor tics
  - Sudden, quick movements
  - Eye blink
  - Head jerk
  - Grimace
- Speech (phonic) tics
  - Sudden, quick speech, usually few words
  - Coprolalia: obscene language

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Tourette Syndrome

Diagnostic Criteria

- Based on clinical criteria
- **Tics for at least one year**
- Onset before 18 years (DSM-5 criteria)
- Multiple motor tics
- One or more phonic tics
- Tics occur many times a day
- Tics not be explained by another cause

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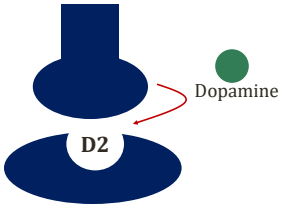
Tourette Syndrome

Treatment

- Behavioral therapy (especially if OCD, ADHD)
- **Dopamine blockade (high potency neuroleptics)**
  - Fluphenazine, Risperidone, Haloperidol, Pimozide
  - Block postsynaptic D_2 receptors



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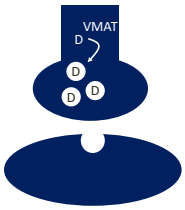
Tourette Syndrome

Treatment

- **Tetrabenazine** ("dopamine depletion")
  - Inhibits VMAT-2 (vesicular monamine transporter type 2)
  - Blocks uptake of dopamine synaptic vesicles (pre-synapse)
  - Less dopamine storage/release



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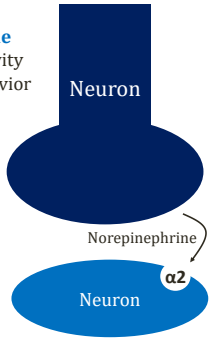
Alpha 2 Agonists

Clonidine, Guanfacine
↑ prefrontal cortex activity
Regulate attention/behavior
Also used in ADHD



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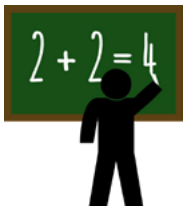
Learning Disability

- Difficulty acquiring, retrieving, and using information
- Often specific problems with math, reading, writing



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ADHD and Autism

ADHD and Autism

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ADHD

Attention deficit hyperactivity disorder

- Exact cause unknown
- Limited attention
- Hyperactivity
- Poor impulse control
- Normal intelligence on testing
  - But may have difficulty in school

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ADHD

Diagnostic Criteria

- Frequent symptoms of hyperactivity/impulsivity
- **Present in more than one setting (school/home)**
- Persist for **at least six months**
- **Present before age of 12**
- Impairs social/school functioning
- Excessive for developmental level of the child

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ADHD

Epidemiology

- Four times more common in **males**
- Most cases among children 6 to 12 years old
- Symptoms persist to adulthood up to 2/3 of cases

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ADHD

Treatment

- Behavioral interventions (rewards, time out)
- Behavioral therapy
- Stimulants
- Atomoxetine
- Alpha-2 agonists

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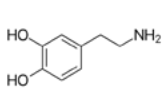
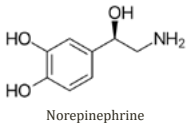
Stimulants

- Increase CNS dopamine and norepinephrine activity
- Increase **CNS levels** in synapses
- Improve ADHD symptoms
  - ADHD children stimulated by activity
  - Drugs relieve need to self-stimulate



Dopamine



Norepinephrine

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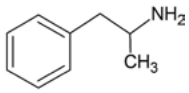
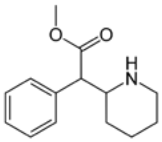
Stimulants

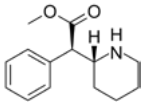
- Methylphenidate (Ritalin)
- Amphetamine (Adderall)
- Dexmethylphenidate (Focalin)



Amphetamine



Methylphenidate



Dexamethylphenidate

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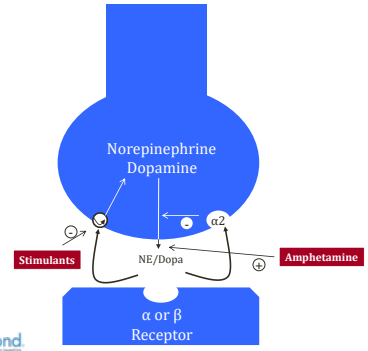
Stimulants



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Stimulants

Adverse Effects

- Loss of appetite
- Weight loss
- Insomnia
- Abuse potential


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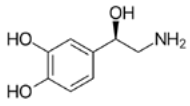
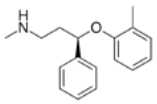
Atomoxetine

- Considered a **non-stimulant** treatment for ADHD
  - May have less insomnia, loss of appetite
- Selective **norepinephrine** re-uptake inhibitor
- No direct effects on dopamine systems in CNS
  - Dopamine effects may cause euphoria (abuse potential)



Norepinephrine



Atomoxetine

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Alpha-2 Agonists

- **Clonidine**
  - Old, rarely used hypertension drug
  - Key side effect: **sedation**
- **Guanfacine**
- Major effects: **alpha-2A receptors prefrontal cortex**
- Increases prefrontal cortical activity
- Regulate attention and behavior

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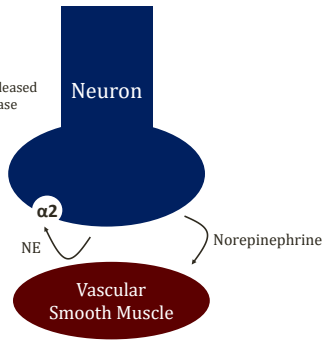
Alpha 2 Receptors

Hypertension Effects

α2 receptors
Presynaptic receptor
Feedback to nerve when NE released
Activation leads to ↓NE release



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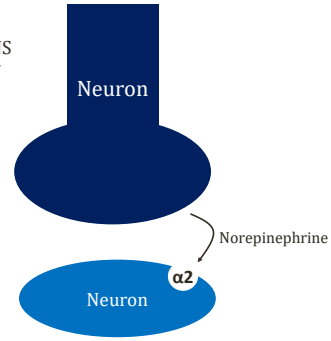
Alpha 2 Receptors

ADHD Effects

α2 receptors in CNS
Postsynaptic receptor



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Autism Spectrum Disorder

- Neurodevelopmental disorder
- Exact cause unknown
- Abnormal social skills (communication/interaction)
- Repetitive behavior patterns
- Limited interests and activities
- Clinical diagnosis

Hepingting/Flikr

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Autism Spectrum Disorder

Diagnostic Criteria

- Deficits in social interaction in multiple settings
  - Failure of back-and-forth conversation
  - Reduced sharing of interests, emotions
  - Abnormal eye contact or body language
  - Difficulty making friends
  - Lack of interest in peers

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Autism Spectrum Disorder

Diagnostic Criteria

- Restricted, repetitive patterns
  - Repetitive movements, use of objects
  - Insistence on sameness, unwavering adherence to routines
  - Preoccupation with certain objects
- Symptoms must impair function
- Symptoms must be present in early development
  - Often diagnosed about 2 years of age
  - Symptoms sometimes present earlier but unnoticed

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Autism Spectrum Disorder

Other Features

- Intellectual impairment
  - Variable
  - Some skills weak (i.e. verbal communication, reasoning)
- **Savants**
  - Some patients have special skills in one area
  - Memory, music, art, math
  - Classic example: determining day of week for given date

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Autism Spectrum Disorder

Clinical Features

- Often identified by pediatrician
- Issues with behavior, language, socialization
- Failure to reach developmental milestones
- Referral to ASD specialists for diagnosis

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Autism Spectrum Disorder

Clinical Features

- More common among **males**
  - Four times > females
- Increased head circumference
  - 25% of cases: greater than the 97th percentile

Ephert/Wikipedia

Autism Spectrum Disorder

Associated Disorders

- **Fragile X syndrome**
  - X-linked trinucleotide repeat disorder
  - Long face, big ears, large testes
- **Double Y males (XYY)**
  - Tall
  - Severe acne

Autism Spectrum Disorder

Treatment

- **Early intervention**
  - Behavioral management
  - Occupational therapy (teaching skills for daily activity)
  - Speech therapy
- No specific effective medical therapy
- Medications only for symptoms
  - Hyperactivity
  - Depression

Cognitive Disorders

Cognitive Disorders

Jason Ryan, MD, MPH

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Disorientation

- Orientation: knowledge of **name, date, and place**
  - "Patient was alert and oriented times three"
- Lost in many cognitive disorders
  - Patient becomes disoriented
- Time lost first
- Person last
- **Time → place → person**

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Loss of Orientation

Causes

- Fever/infection
- Alcohol/drugs
- Hypoglycemia
- Electrolytes
- Cognitive disorders (delirium, dementia)

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Amnesia

- Loss of memory
- Often caused by CNS injury
- **Retrograde amnesia**
  - Loss of memories in the past
  - Retained ability to make new memories
- **Anterograde amnesia**
  - Inability to make new memories
- Dissociative amnesia
  - Response to trauma/stress
  - NOT caused by CNS injury

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Wernicke-Korsakoff Syndrome

- Wernicke: Acute encephalopathy
- **Korsakoff: Permanent neurologic condition**
  - Usually a consequence of Wernicke
- Both associated with:
  - **Thiamine (B1) deficiency**
  - **Alcoholism**

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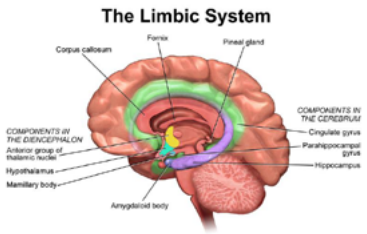
Wernicke-Korsakoff Syndrome

- Atrophy of **mammillary bodies** common finding



BruceBlaus/Wikipedia

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Korsakoff Syndrome

- Confabulation
  - Can't remember so make things up
- Apathy (lack of interest or concern)
- Personality changes
- **Amnesia**
  - **Anterograde > retrograde**

Cognition

- Mental process
- Acquiring knowledge and understanding
- Involves thought, experience, senses

Cognitive Disorders

- Inability to acquire knowledge and understand
- Disorganized thinking
- Disorientation
- Delirium
- Dementia

Dementia vs. Delirium

- Dementia
  - **Chronic, progressive** cognitive decline
  - **Usually irreversible**
- Delirium
  - **Acute**
  - **Waxing/waning**
  - Usually reversible

Delirium

- Loss of focus/attention
- Disorganized thinking
- Hallucinations (usually visual)
- Sleep-wake disturbance
  - Up at night
  - Sleeping during day

Hyperdrive/Wikimedia Commons

Delirium

Causes

- Rarely a primary disorder
- Usually secondary to another cause
- Infection
- Alcohol
- Withdrawal
- Dementia patient in unknown setting
  - Hospitalized
  - Fever, pain
- Causes **altered mental status** in hospital

EEG

Electroencephalogram

- Records voltage changes in brain
- Different leads
  - Frontal, parietal, occipital
- Characteristic patterns
- NORMAL in dementia
- ABNORMAL in delirium

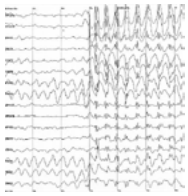

Image courtesy of Der Lange

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Delirium Treatment

- **Fix underlying cause**
  - Treat infection, withdrawal, etc.
  - Maintain O2 levels
  - Treat pain
  - Hydrate
- Calm, quiet environment
- Drugs
  - Haloperidol (vitamin H)

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Dementia

- Gradual decline in cognition
- No change level of consciousness (LOC)
- Usually irreversible (unlike delirium)
- Memory deficits
- Impaired judgment
- Personality changes

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Dementia Causes

- **Alzheimer's disease (60% of cases)**
- Multi-infarct dementia (stroke) ~20% of cases
- Lewy body dementia
- Rare disorders
  - Pick's disease
  - Normal pressure hydrocephalus (NPH)
  - Creutzfeldt-Jakob
  - HIV
  - Vitamin deficiencies
  - Wilson's disease

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Dementia

Work-up

- Extensive screening/testing is low-yield
- Certain treatable causes should be excluded
- **Depression**
  - Can present with dementia-like complaints
- **Hypothyroidism**
  - Check TSH
- Other testing if indicated
  - Neurosyphilis
  - Vitamin deficiency
  - HIV

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Psychosis

Psychosis

Jason Ryan, MD, MPH

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Psychosis

- Loss of perception of **reality**
- Occurs in medical and psychiatric disorders
  - **Delirium**
  - **Schizophrenia**
- Three main manifestations
  - Delusions
  - Disorganized thought
  - Hallucinations

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Delusions

- Strongly held **beliefs** that conflict with reality
- Expressed in **speech** by patient
- Persecutory delusions
  - Someone is after me!
- Grandiose delusions
  - I am a millionaire!
- Erotomaniac delusions
  - Brad Pitt is in love with me!

if speech conflicts w/ reality = delusion

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Delusions

- Somatic delusions
  - There are worms in my chest!
- Delusions of reference
  - The television news caster is talking about me!
- Delusions of control
  - My body is controlled by aliens!
  - I can change the sun!

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Disorganized Thought

= 2nd feature of psychosis

ie. what they say vs. HOW THEY SAY IT

- Shown by **patterns of speech**
- Alogia (speech poverty)
- Thought blocking
  - Sudden, abrupt stop while talking
- Loosening of association
  - Ideas discussed that do not follow each other
- Tangentiality
  - Diverging from topic under discussion to another

says something, then suddenly stops and shuts down

Nevit Dilmen/Wikipedia

starts talking about how they feel → then talk about how weather makes them feal → talks about how weather was yesterday

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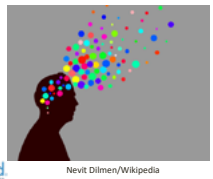
Disorganized Thought

- Clanging
  - Using **words that rhyme** but do not make sense
  - "The cow said how he had to bow"
- Word salad: incoherent words that make no sense
- Perseveration: repeating words or ideas persistently



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Hallucinations = 3rd element of psychosis

- **Sensory perceptions without external stimuli**
- Many different sub-types
- **Visual**
  - Seeing things that are not there
  - Common in hospitalized patients with **delirium**
- **Auditory**
  - Hearing voices or sounds
  - Classic feature of **schizophrenia**

eg. eldery pt in hospital who becomes delerious starst to see their dead spouse

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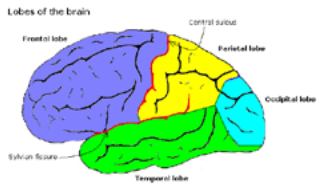
Hallucinations

Olfactory

- Smell or odor
- Classic feature of **aura in temporal lobe epilepsy**



RobinH/Wikipedia

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Hallucinations

- Gustatory (taste)
- Tactile (feeling/sensation)
  - Insects crawling on skin
  - Seen in **alcohol withdrawal**
  - **Stimulants: cocaine, amphetamines**

Wikipedia/Public Domain

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Hallucinations

- **Hypnagogic**
  - Occurs while falling asleep (hypna = sleep)
- **Hypnopompic**
  - Occurs just before waking up
- Both seen in patients with **narcolepsy**

Evgeny Galkovsky aka ZheGal

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Psychotic Disorders

Psychotic Disorders

Jason Ryan, MD, MPH

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Schizophrenia

- Chronic psychiatric syndrome
- Recurrent episodes of psychosis
- Cognitive dysfunction
- Negative symptoms

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Psychosis

- Loss of perception of **reality**
- Occurs in medical and psychiatric disorders
  - **Delirium**
  - **Schizophrenia**
- Three main manifestations
  - Delusions
  - Disorganized thought
  - Hallucinations

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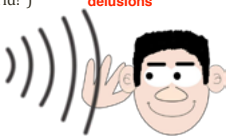
Schizophrenia

Hallucinations and delusions

- Main manifestation is **auditory hallucinations**
  - Hearing voices
  - Strange sounds
- **Delusions**
  - Fixed, false beliefs
  - Paranoid ("they are coming after me!")
  - Grandiose ("I am king of the world!")

Schizophrenia pts can have all types of delusions



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Schizophrenia

Disorganized thought

- Most commonly tangential or circumstantial speech
- **Tangential speech**
  - Changes topic frequently
  - May not answer question
- **Circumstantial speech**
  - Long, round-about answers to questions

these pts can be difficult to talk to/get history from bc it's hard for them to focus

can be hard to keep pt on topic when taking history

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Schizophrenia

Cognitive impairment

- Difficulty processing information
- Poor attention
- Poor learning and memory

Onlineassignmenthelps/Wikipedia

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Symptoms

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- **Positive symptoms** behaviors that should NOT be there but are present
  - Abnormal behaviors
  - Hallucinations, delusions, disorganized thought
- **Negative symptoms** behaviors that SHOULD be there but are not; difficult to treat
  - Absence of normal behaviors
  - Flat affect
  - Poverty of speech (alogia)
  - Cannot engage in social interactions (asociality)
  - Lack of motivation/cannot complete tasks (avolition)
  - Cannot feel pleasure (anhedonia)
  - Often persist despite therapy

(psychotic Sx may go away with Rx, but negative Sx can persist

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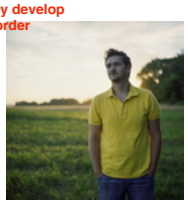
Schizophrenia

Epidemiology

- Lifetime prevalence about 1% adults globally
- Slight male predominance
- Occurs in **adolescence/young adulthood**
  - Men: 18 to 25
  - Women: 25 to 35

pts often live normal lives until they develop this disorder



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Schizophrenia

Risk Factors

- Living in **urban areas** (cities)
- Immigration
  - UK study: immigrants ten times more risk

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Schizophrenia

Risk Factors

- **Obstetric complications**
  - Hemorrhage
  - Preterm labor
  - Blood-group mismatch
  - Fetal hypoxia
  - Maternal infection

these complications can make a child more prone to developing schizophrenia

Øyvind Holmstad/Wikipedia

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Schizophrenia

Risk Factors

- **Cannabis use**
- Usually in adolescence
- Unclear if cause-effect
- Mild symptoms may lead to cannabis use

Chuck Grimmett/Wikipedia

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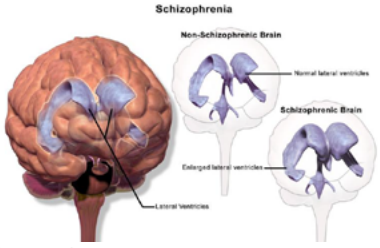
Schizophrenia

Pathology

- **Lateral ventricular enlargement** = classic pathologic finding!



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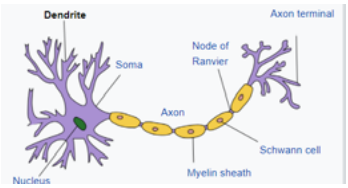
Schizophrenia
Pathology

- **Dendritic spines**
  - Small protrusions of neuron dendrites
  - Receives input from other neurons at a synapse
- Spine loss in many brain regions



Quasar Jarosz/Wikipedia

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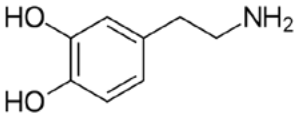
Schizophrenia
Pathology

- Excess central **dopamine** activity
- Dopamine antagonists used for therapy

"Dopamine hypothesis"



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Schizophrenia
Diagnosis

- At least **one month** of two or more:
  - Delusions
  - Hallucinations
  - Disorganized speech
  - Disorganized or catatonic behavior
  - Negative symptoms
- Continuous signs for at least **six months**

• if pt. has all of these Sx for 6 mo = scizophrenia√
• if pt. has only 2 features for just ONE month = NOT schizophrenia; UNLESS pt. has one of the other features for the next 5 months… = schizophrenia (bc that would mean at least 1 month of Sx and continuous for 6mo)

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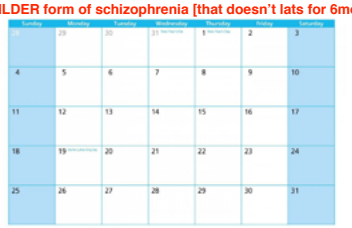
Schizophreniform Disorder

- Meets criteria for schizophrenia
- Duration **less than six months**

= a MILDER form of schizophrenia [that doesn't lats for 6mo]



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Brief Psychotic Disorder

= even milder than schizophreniform disorder

- Psychotic symptoms
- Sudden onset
- **Full remission within one month**
- More common in women than men
- Commonly follows **stressful life events**
  - Death in family
  - Loss of job

eg. woman loses job and she becomes so distressed that she becomes psychotic for a brief period (maybe ~2 weeks) but it respolves after the 2 weeks

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Schizoaffective Disorder

- Schizophrenia with mania or depression (ie. schizophrenia + mood disorder)
  - **Must have some episodes psychosis alone**
  - **Some psychosis in absence of mania/depression**
  - DSM-V: Two or more weeks with psychosis alone
- Mania or depression with psychotic features
  - All psychotic episodes occur with mania/depression

important to know schizoaffective disorder vs. pt w/ mania or depression w/ psychotic features.
• schizoaffective disorder = ≥ 2 wks w/ psychosis ALONE
• mania or depression w/ psychotic features = all psychotic episodes happen w/ the mania or depression

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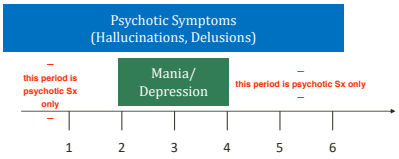
Schizoaffective Disorder

Possible Course



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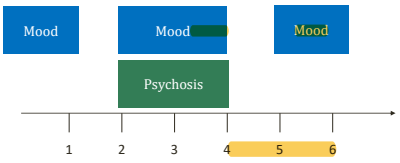
Mood Disorder with Psychosis

Possible Course



pt has recurrent episodes of mood disorder, then durine one particulary bad episode, pt has psychotic features.
**Note that psychosis doesn't occur outside of mood disorder

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Delusional Disorder

pt. ONLY has delusions

- One or more delusions
- Lasts **one month or longer**
- Otherwise, **no abnormal behavior**
  - Man believes he is being followed for past two months
  - Frequently checks for someone behind him
  - Cannot be persuaded he is safe
  - No hallucinations, disorganized thought, negative symptoms
- Folie a deux (madness of two)
  - Close friend shares delusions

bc the person having the delusions is so convincing

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Schizophrenia

Complications

- High risk of **suicide**
- 5% schizophrenics commit suicide
- 10% all suicides occur in schizophrenics

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Postpartum Psychosis

- Rare disorder (0.1 to 0.2% of births)
- Usually women with known psychiatric disorder
  - Most commonly bipolar disorder
  - Also depression with psychosis, schizophrenia, schizoaffective
  - Especially if meds stopped during pregnancy
- Occurs within 2 weeks after delivery

****

(woman stopped meds during pregnancy to avoid harming her baby)

Pixabay/Public Domain

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Postpartum Psychosis

- Delusions, hallucinations, disorganized thought
- **Delusions often involve the baby**
- Classically delusions related to patient's mood
  - Depressed: "Somethings wrong with my baby!"

Pexels/Public Domain

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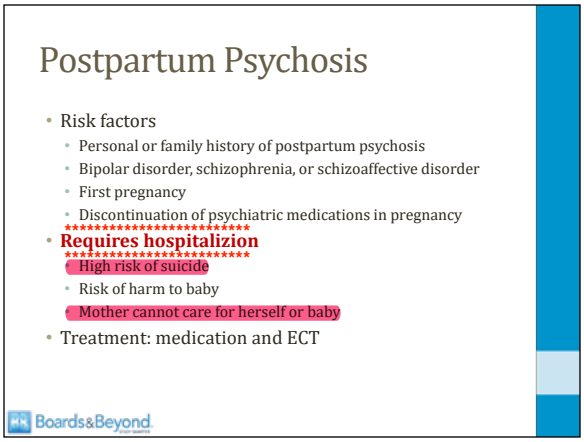
Postpartum Psychosis
Risk factors
Personal or family history of postpartum psychosis
Bipolar disorder, schizophrenia, or schizoaffective disorder
First pregnancy
Discontinuation of psychiatric medications in pregnancy
****
Requires hospitalizion
****
High risk of suicide
Risk of harm to baby
Mother cannot care for herself or baby
Treatment: medication and ECT
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Dissociative Disorders

Dissociative Disorders

Jason Ryan, MD, MPH

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Dissociation

- Detachment from reality
- Contrast with psychosis: loss of reality

"I feel like i'm outside my body"
- lost touch with reality
- ≠ psychosis pts who have lost touch with reality, in dissociation, they know the difference between reality & not reality

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Dissociative Disorders

- Feeling "like I was outside my own body"
- Extreme cases: becoming another person
  - New name, age, job, etc.
- Often associated with psychological trauma
- May allow victim to cope with trauma

(formerly called Multiple Personality Disorder)

- "Feel like objects in the room around me are unreal"

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Dissociative Identity Disorder

- Multiple personality disorder
- More common in women
- Associated with **childhood trauma/abuse**
- Especially sexual abuse, often before age 6

Woman takes on a diff personality because she can't cope with the fact of living w/ person who was abused at a young age

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Dissociative Identity Disorder

- **Two or more distinct identities**
  - "Personality states"
  - Alterations in behavior, memory, thinking
  - Observed by others or reported by patient
- Gaps in memory about events
- Symptoms cause distress or problems in functioning

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Dissociative Identity Disorder

Comorbidities

- **High rate of occurrence with other disorders**
  - **PTSD:** up to 100%
  - **Depression and substance abuse**: up to 96%
  - Personality disorders: Avoidant and borderline

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Dissociative Identity Disorder

Comorbidities

- **Somatoform conditions**
  - Physical symptoms not explained by medical condition

phee/Pixabay/Public Domain

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DDD

Depersonalization/Derealization Disorder

- **Depersonalization**
  - Feeling detached or estranged from one's self
  - "Like in a dream"
  - "Like I am watching myself"
  - Loss of control over thoughts, actions
- **Derealization**
  - Detachment from surrounding world
  - Objects seem unreal, foggy, visually distorted

Text

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DDD

Depersonalization/Derealization Disorder

- Often triggered by **trauma**
- Must cause significant distress/impairment
- **Intact reality testing**
  - Differentiates from psychosis
  - Patient aware that sensations are not real

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Dissociative Amnesia

- Inability to recall **autobiographical** memories
  - Past events
  - Job
  - Where they live
- Usually follows major trauma/stress
- Potentially reversible (memories may come back)
- Patient not bothered by lack of memory
- Amnesia not explained by another cause

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Dissociative Amnesia

Psychogenic Amneisa

- Different from simple amnesia
  - Large groups of memories: name, job, home
  - Caused by overwhelming stress
- Different from repression
  - Loss of autobiographical information: name, job, home

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Dissociative Amnesia

Psychogenic Amneisa

- Example:
  - Woman attacked in elevator
  - Does not recall her job, where she lives, etc.
  - Memories resurface later

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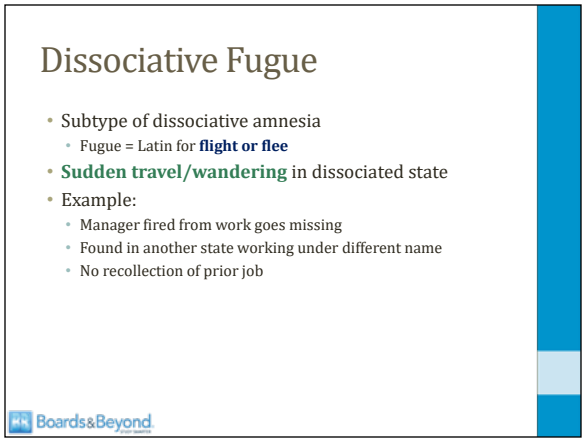
Dissociative Fugue
• Subtype of dissociative amnesia
• Fugue = Latin for flight or flee
• Sudden travel/wandering in dissociated state
• Example:
• Manager fired from work goes missing
• Found in another state working under different name
• No recollection of prior job
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Somatic Disorders

Somatic and Factitious Disorders

Jason Ryan, MD, MPH

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Somatization

- Physical symptoms not explained by medical disease
- Not consciously created for gain (factitious)
- Risk factors
  - Female gender
  - Less education
  - Minority status
  - Low socioeconomic status

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Somatization

- Pain symptoms
  - Headache, back pain, joint pain
- Gastrointestinal symptoms
  - Nausea, abdominal pain, bloating, gas
- Cardiopulmonary symptoms
  - Chest pain, dizziness, palpitations
- Neurologic symptoms
  - Fainting, muscle weakness, blurred vision
- Dyspareunia, dysmenorrhea

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Somatization

- Associated with anxiety and depression
- Management
  - Avoid debating if symptoms are psychiatric or medical
  - Do not challenge belief that symptoms are medical
  - **Regular visits with same physician**
  - Limit tests and referrals
  - Reassure patient that serious medical diseases are ruled out
  - Set goals of functional improvement
  - Psychotherapy

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Somatic Symptom Disorder

DSM-V Diagnosis

- **Somatic symptoms** that cause distress
- Persistent thoughts about seriousness of symptoms
- Anxiety about symptoms
- Excessive time and energy devoted to symptoms
- Persistent (usually more than six months)

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Illness Anxiety Disorder

DSM-V Diagnosis

- Preoccupation with having **undiagnosed illness**
- **Mild or no somatic symptoms**
- Anxiety about health
- Excessive health-related behaviors
  - Repeatedly checking for signs of illness
- Present for at least six months

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Conversion Disorder

Functional neurologic symptom disorder

- Sudden onset usually following stressor
- Voluntary motor or sensory **neurologic symptoms**
  - Inability to speak or move
  - Blindness
  - Seizures
- Neurologic work-up normal
  - Positive findings incompatible with disease
  - Example: absence plantar flexion but can stand on toes
- **La belle indifference**
  - Patient shows lack of concern (indifference) about symptoms

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Factitious Disorder on Self

Munchausen syndrome

- **Falsified** medical or psychiatric symptoms
- Done **consciously** out of desire for attention
- Patient may feign illness
- May aggravate genuine illness
- Patient often willing to go for tests/surgeries

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Factitious Disorder on Self

Munchausen syndrome

- Done for primary (internal) gain from illness
  - Patient feels better in sick role
  - Sick role solves internal conflict
  - Example: patient is afraid of work or afraid to be alone
- Chronic, persistent
- Risk factors:
  - **Female gender**
  - Unmarried
  - Prior or current **healthcare worker**

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Factitious Disorder on Another

Munchausen by proxy

- Falsified medical symptoms by caregiver
- Often parent of **child** or caretaker of **elderly**

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Malingering

- Consciously falsified medical symptoms
- Done for **secondary (external) gain**
  - Allows patient to miss work but get paid
  - Obtain workman's compensation
- Self-limited
- Ends when secondary gain achieved

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Personality Disorders

Personality Disorders

Jason Ryan, MD, MPH

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Personality Trait

- Fixed pattern of behavior
- Way of interacting with environment
- No significant distress or impaired function
- Positive traits: kind, confident
- Negative traits: lazy, rude
- Person often aware of own traits

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Personality Disorder

- Fixed pattern of behavior
- Fixed way of interacting with environment
- Cause distress or impaired function
- Person often unaware
- Difficult to treat ("enduring")
- Often strains doctor-patient relationship

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Personality Disorders

- Cluster A (Weird)
  - Paranoid, schizoid, schizotypal
  - Odd and eccentric behavior
- Cluster B (Wild)
  - Antisocial, borderline, histrionic, narcissistic
  - Dramatic, erratic behavior
- Cluster C (Wacky)
  - Avoidant, Obsessive-compulsive, dependent
  - Anxious, fearful behavior

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Paranoid

Personality Disorder

- **Distrust** of others even friends/family
- Guarded
- Suspicious
- Struggles to build close relationships
- Hallmark ego defense: projection
  - Attributing unacceptable thoughts to others
  - Often accuses others of being suspicious

Aaron Tait/Flikr

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Schizoid

Personality Disorder

- **Chooses** social isolation
  - More comfortable alone
- Does not enjoys close relationships
- Little/no interest in sexual experiences
- Few/no pleasure activities (hobbies)
- Lacks close friends
- Detachment
- Flat affect

Public Domain

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Schizotypal
Personality Disorder

- Fear of social interactions and few close friends
- Odd beliefs or magical thinking
  - Superstitious
  - Believes in telepathy, sixth sense
- Ideas of reference
  - Believe events and happenings somehow related to them
- Key feature: open to challenges to beliefs
  - May reconsider superstitions, etc.
  - Contrast with delusions in schizophrenia
  - Also no hallucinations, cognitive impairment

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Antisocial
Personality Disorder


Public Domain

- More common in men
- Disregard for rights of others
- Often breaks the law
- Impulsive and lacks remorse
- Child (<18) version: conduct disorder
  - 25% girls and 40% boys with CD → ASPD
- Must be at least age 18 years old
- Must have evidence of conduct disorder before 15

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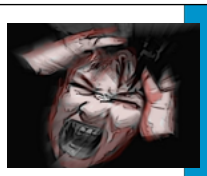
Borderline
Personality Disorder


Ingela Hjulfors Berg/Flikr

- More common in women
- Unstable personal relationships
  - **All people are very good or very bad**
  - Stormy relationships
  - "My boyfriend is the greatest guy in the world!"
  - "My boyfriend is the devil!"
- Fear of abandonment
  - May accuse others of abandoning them

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Borderline
Personality Disorder

- Impulsivity
  - Spending sprees, sex with strangers, reckless driving
- Self mutilation
  - Cutting, burning
- Suicide gestures or attempts
  - Relates to fear of abandonment
  - "You don't care about me so I'll kill myself"

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Splitting

- Major defense mechanism in borderline PD
- Black and white thinking (always-never)
- Cannot hold opposing views
- Patent's physician may be great or terrible
- All people-things-events wonderful or horrible


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Dialectical Behavior Therapy

- Form of cognitive behavioral treatment
- Designed to treat chronical suicidality
- **Gold standard** for borderline personality disorder
- Weekly therapy for 1-2 years
  - Mindfulness
  - Distress tolerance
  - Emotion regulation

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Histrionic
Personality Disorder

- Wants to be the **center of attention**
  - Talks loudly, tells wild stories, uses hand gestures
- Inappropriate sexually provocative behavior
  - Often wears provocative clothing
  - Touching others frequently
- Very concerned with physical appearance
  - Exotic outfits, shoes, hats

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Narcissistic
Personality Disorder

- **Inflated sense of self**
  - Brags, thinks everything they do is great
- Lacks empathy for others
  - Other people are competitors
- Wants to hear they are great
- Overreacts to criticism with anger/rage

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Avoidant
Personality Disorder

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- Avoids social interactions
- "Social inhibition"
- Feels inadequate
- Afraid people won't like them
- Afraid of embarrassment
- Struggles with intimate relationships
  - "Maybe he/she doesn't like me"
- Different from schizoid: wants to socialize but can't
  - Schizoid prefers to be alone (aloof)

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Obsessive-Compulsive
Personality Disorder

- Preoccupied with **order and control**
  - Loves "To Do" lists
  - Always needs a plan
- **Inflexible** at work or in relationships
- Behaviors help to achieve goals (contrast with OCD)

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Obsessive-Compulsive
Personality Disorder

- Ego
  - Mediates id (desire) and super-ego (rules, society)
- **Egosyntonic**
  - Behaviors that achieve goals of the ego
  - Obsessions/compulsions used to achieve goals
  - Seen in obsessive-compulsive personality disorder
- Egodystonic
  - Behaviors that conflict with goals of the ego
  - Obsessions/compulsions are barriers to goals
  - Seen in obsessive-compulsive disorder

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Dependent
Personality Disorder

Francisco Carbajal/Flikr

- Clingy
- Low self-confidence
- Struggle to care for themselves
- Depend on others excessively
  - Rarely alone, always in a relationship
- Hard to make decisions on their own
  - Want someone to tell them what to do
- Difficulty expressing an opinion
- May be involved in abusive relationships

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Mood Disorders

Mood Disorders

Jason Ryan, MD, MPH

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Mood Disorders

- Abnormal emotional state
- Sadness (depression)
- Extreme happiness (mania)

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Depression — **Mania**

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Major Depressive Disorder

- Depressed mood
- Loss of interest in activities (anhedonia)
- Fatigue/loss of energy
- Feeling worthless or guilty
- Suicidal ideation/attempt
- Inability to concentrate, make decisions
- **Appetite changes**
- **Weight loss/gain**
- **Sleep disturbances**
- Psychomotor agitation/retardation

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Major Depressive Disorder

Sleep Disturbances

- Difficulty getting to sleep (initial insomnia)
- Waking in the night (middle insomnia)
- Waking earlier than usual (terminal insomnia)
- Hypersomnia: excessive sleeping
- Altered **sleep rhythms**
  - REM starts quicker after sleep onset (**↓ REM latency**)
  - ↑ total REM sleep
  - ↓ slow-wave sleep
  - Sleep rhythms normalize on anti-depressant drugs

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Major Depressive Disorder

Psychomotor agitation/retardation

- **Psychomotor agitation**
  - Excessive motor activity
  - Often repetitious
  - Feeling of inner tension
  - Fidgeting, pacing
- **Psychomotor retardation**
  - Slowing of movements, thinking, or speech
  - Slow to answer questions
  - Low voice
  - Few words

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Major Depressive Disorder

Diagnosis and treatment

- At least **5 symptoms** (of 9) for **2 weeks**
  - **S**leep disturbance
  - Lack of **I**nterest
  - **G**uilt
  - **E**nergy loss and fatigue
  - **C**oncentration problems
  - **A**ppetite/weight changes
  - **P**sychomotor symptoms
  - **S**uicidal ideation
- No evidence of mania
- Treatment: antidepressants

SIG E CAPS

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Major Depressive Disorder

Subtypes

- Anxiety
- Atypical
- Catatonic
- Melancholic
- Mixed features
- Peripartum
- Psychotic
- Seasonal

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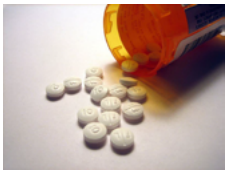
Atypical Depression

- **Mood reactivity** (core unique feature)
  - Able to react to pleasurable stimuli
  - Feels better when good things happen
- Eating and sleeping all the time
  - Increased appetite or weight gain
  - Increased sleep (hypersomnia)
- Heavy or leaden feelings in limbs
- Sensitive to rejection
  - History of interpersonal rejection sensitivity

Atypical Depression

- Most common subtype in some studies
- Older studies: increased response MAOi drugs
- SSRIs also effective
- Usually treated with SSRIs (less side effects)



Tom Varco/Wikipedia

Manic Episode

- Abnormally elevated **mood** and **energy level**
- Talking fast, pressured speech
- ↓ need for sleep
  - But not tired
  - Different from insomnia (tired but cannot sleep)
- Psychomotor agitation (pacing, fidgeting)
- Flight of ideas

Manic Episode

- **Disinhibition** and irresponsibility
  - Waste money, wearing no clothes
- **Grandiosity**
  - Increased self-esteem, confidence
  - "I can do anything!"
- Typical case:
  - Change in mood to elevated state
  - Not sleeping
  - Altered behavior
  - Disruption of social functioning

Manic Episode

Diagnosis

- Symptoms **at least one week**, most of the day
  - **D**istractibility
  - **I**rresponsibility
  - **G**randiosity
  - **F**light of ideas
  - **A**gitation
  - Less **S**leep
  - **T**alking too much, pressured speech

DIG FAST

Hypomanic Episode

- Similar to those of mania but **less severe**
- Key feature: **little/no impairment in functioning**
- Inflated self-esteem but no delusions of grandeur
- More organized thought than mania
- More energy but leads to productive activity
  - Contrast with mania: unproductive
- Milder risk taking behavior

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Hypomanic Episode

- Lasts **at least 4 days**
- Resolves over weeks
- **No psychotic symptoms**
  - By definition psychotic symptoms = mania
- Typical case:
  - Change in mood to elevated state
  - Continued social functioning
  - Resolves in few weeks

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Bipolar Disorder

Manic Depression

- Symptoms of mania and depression
- Can present with mania, hypomania or depression
  - Treatment with antidepressants may cause mania
- Bipolar I
  - **Manic episode** +/- depression +/- hypomania
  - Manic episodes = bipolar I
- Bipolar II
  - **Hypomania** and depression
  - No manic episodes

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Bipolar Disorder

Course

- Fluctuation: mania-hypomania-depression
- May have periods of euthymia (normal mood)

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Bipolar Disorder

Treatment

- Mood stabilizers
  - Most are also anticonvulsants
  - Valproic acid
  - Carbamazepine
  - Lamotrigine
- Lithium
- Antipsychotics
- Antidepressants may cause mania

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Psychotic Features

- Often hallucinations or delusions
- Associated with severe forms of mood disorders
- May occur in depression or bipolar disorder
- Always occur **together with mood symptoms**
- Psychosis without mood symptoms: schizoaffective

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Cyclothymic Disorder

- Mild mania symptoms
- Mild depressive symptoms
- Do not meet criteria for hypomania or MDD
- Symptoms come/go over **at least two years**
  - Come/go with ups and downs
  - Occur at least half of the time
  - Never absent for more than two consecutive months

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Persistent Depressive Disorder

Dysthymic Disorder

- Low grade form of depression
- Less severe but more chronic
- Depressed mood most of the time
- Lasts for **at least two years**
- No symptom free periods lasting >2 months

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Suicide

- Seen in depression and bipolar disorder
- 95% successful attempts have psychiatric diagnosis
  - Depression, bipolar, substance abuse, schizophrenia
- Women: more attempts, less successful
- Men: fewer attempts, more successful
- Most common method: **firearms**
- Increased risk with access to guns

Augustas Didžgalvis

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Suicide

Risk Factors

- **Sad person scale** (0-10pts)
  - **S**ex (male)
  - **A**ge (young adults or elderly)
  - **D**epression
  - **P**rior attempt (higher risk group)
  - **E**thanol or drugs
  - **R**ational thinking loss (psychosis)
  - **S**ickness (medical illness)
  - **O**rganized plan
  - **N**o spouse (or lack of social support)
  - **S**tated intent

SAD PERSONS

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Acute Grief

- Normal response to **loss of loved one**
- Five stages (Kübler-Ross model)
  - Denial ("He can't be gone there must be a mistake")
  - Anger ("This is your fault!")
  - Bargaining ("I'll do anything if she could be alive again")
  - Depression
  - Acceptance
- Visions/voices of dead person may occur
- Usually resolves within 6 months

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Persistent Grief

- Lasts longer than 6 months
- Interferes with functioning
- May lead to major depressive disorder

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Postpartum Mood Disorders

- **Postpartum blues** (up to 85% some studies)
  - Depressed mood, insomnia, fatigue, poor concentration
  - Mild symptoms that starts 2-3 days after delivery
  - Resolves within **two weeks**
  - Treatment: supportive
- **Postpartum depression** (~15%)
  - Symptoms that persist after two weeks
  - Treatment: CBT and medications (SSRIs)
- Postpartum psychosis (rare)

Øyvind Holmstad/Wikipedia

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Mood Disorders

Treatment

- Cognitive behavioral therapy (CBT)
- Antidepressants
- Mood stabilizers
  - Lithium
  - Valproic acid
- Electroconvulsive therapy

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ECT

Electroconvulsive Therapy

- Performed under general anesthesia
- Electricity administered → **seizure**
- Used in refractory depression
- May cause **amnesia**
  - Retrograde amnesia (memories before procedure)
  - Antegrade amnesia (few weeks after)
- Can be used in pregnancy

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Anxiety Disorders

Anxiety Disorders

Jason Ryan, MD, MPH

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Panic Attack

- Sudden onset of intense fear
  - Often occur with no trigger
  - Sometimes triggered by stressful event
- Brief: lasts for **minutes to an hour**

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Panic Attack

- **Physical symptoms** caused by panic
  - Palpitations, racing heart
  - Sweating
  - Trembling or shaking
  - Chest pain or discomfort

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Panic Attack

Diagnosis

- Four or more of the following:
  - Palpitations, pounding heart, or accelerated heart rate
  - Sweating
  - Trembling or shaking
  - Sensations of shortness of breath or smothering
  - Feelings of choking
  - Chest pain or discomfort
  - Nausea or abdominal distress
  - Feeling dizzy, unsteady, light-headed, or faint
  - Chills or heat sensations
  - Paresthesias (numbness or tingling sensations)
  - Fear of losing control or "going crazy"
  - Fear of dying
  - Derealization
  - Depersonalization

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Panic Attack

Diagnosis

- Derealization
  - Items in room look foggy, unreal
  - Feel like in a foreign place despite being at home
  - Often intensely scary
- Depersonalization
  - "Out of body" experience
  - Detached, looking at self from above

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Panic Disorder

Diagnosis

- Recurrent **unexpected** panic attacks
  - Not post-traumatic
  - Not in response to phobia
- Attacks followed by **1 month or more**:
  - Persistent concern or worry about panic attacks
  - Change in behavior to avoid attacks

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Panic Disorder

- Median age: 24 years
- Twice as common in women vs. men
- Risk factors
  - **Genetic component:** 1st degree relative with PD: ↑ risk
  - History of physical or sexual abuse
  - Life stress
- Treatments:
  - CBT
  - Antidepressants (SSRIs)
  - Benzodiazepines

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Generalized Anxiety Disorder

- **Chronic, persistent anxiety**
- About many different events/activities
- **Lasts ≥ 6 months**
  - More days than not for at least six months

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Generalized Anxiety Disorder

- Three or more of the following:
  - Restlessness
  - Fatigue
  - Difficulty concentrating
  - Irritability
  - Muscle tension
  - Sleep disturbance

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Specific Phobias

- Fear of a **specific object or situation**
- Leads to **avoidance behavior**
- Persists for > 6 months
- Common: flying, dental procedures, blood draw

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Specific Phobias

- Social anxiety disorder
  - Specific phobia of social settings
  - Excessive fear of **embarrassment** in social settings
  - Fear of being humiliated or judged
- Agoraphobia
  - Agora = public space (Greek)
  - Fear of leaving a safe place (home) for **public setting**
  - Fear of needing to flee with no help available
  - NOT fear of scrutiny and embarrassment
  - Example: Fear of empty bus (no people)
  - Often co-occurs with panic disorder
  - Often patients fear panic attack in public setting

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Specific Phobias

Treatments

- Medications
  - Benzodiazepines for infrequent exposure
  - Beta blockers (blunt physical symptoms)
  - SSRIs for frequent exposure

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Specific Phobias

Treatments

- Often responds to behavioral therapy
- Systematic desensitization
  - Imagining exposure to feared stimulus
  - Relaxation
- Exposure therapy
  - Confrontation of feared stimulus in safe/controlled manner
  - Fear reduced over time (extinction learning)

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OCD

Obsessive-Compulsive Disorder

- Obsessions
  - Recurrent, persistent thoughts, urges, or images
  - Intrusive and unwanted
  - Patient attempts to ignore or suppress
  - Causes distress
- Compulsions
  - Repetitive behaviors or mental acts
  - Done to relieve obsessions
  - Hand washing, checking stove
  - Praying, counting, repeating words
  - Patient feels driven to perform in response to obsessions

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OCD

Obsessive-Compulsive Disorder

- Ego
  - Mediates id (desire) and super-ego (rules, society)
- Egosyntonic
  - Behaviors that achieve goals of the ego
  - Obsessions/compulsions used to achieve goals
  - Seen in obsessive-compulsive personality disorder
- **Egodystonic**
  - Behaviors that conflict with goals of the ego
  - Obsessions/compulsions are barriers to goals
  - Seen in obsessive-compulsive disorder

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OCD

Obsessive-Compulsive Disorder

- Commonly co-occurs with:
  - Schizophrenia or schizoaffective disorder
  - Bipolar disorder
  - Eating disorders (anorexia/bulimia)
  - Tourette's disorder
- Treatment: CBT
  - "Exposure and response" therapy
  - Expose patient to obsessive thoughts/image
  - Respond with non-compulsive behavior
- Also SSRIs and clomipramine (TCA)

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Body Dysmorphic Disorder

- Occurs in physically normal patients
- Preoccupation with physical appearance
- Focus on nonexistent or minor defects
- Patient believes they look abnormal, ugly, deformed
- Leads to repetitive behavior
  - Checking mirror
  - Combing hair
- Treatment: CBT plus SSRIs

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PTSD

Post Traumatic Stress Disorder

- Follows traumatic event
  - Rape, physical assault
- Thoughts, nightmares, flashbacks
- Avoidance of reminders
- Hypervigilance (anxious, alert, scanning)
- Sleep problems (restless, can't fall or stay asleep)
- Leads to social dysfunction

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PTSD

Diagnosis

- Exposure to traumatic event
- Trauma persistently re-experienced
  - Thoughts, nightmares, flashbacks
- Avoidance of trauma-related stimuli
- Negative thoughts or feelings after trauma
- Trauma-related arousal and reactivity
- Symptoms last for **more than 1 month**

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PTSD

Treatments

- CBT
- SSRIs
- **Prazosin**
  - Alpha-1 blocker
  - Reduces nightmares and improves sleep
  - May cause orthostatic hypotension

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Acute Stress Disorder

- Exposure to threatened death, injury, sexual assault
- Recurrent, intrusive memories
- Recurrent distressing dreams
- Dissociative symptoms
  - Altered sense of reality
  - In a daze, time is slow
  - Cannot remember aspects of trauma (dissociative amnesia)
- **Lasts less than one month**
- Treatment: CBT (no drugs)

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Separation Anxiety Disorder

- Childhood anxiety disorder
- Distress when separating home/parents
  - Refusal to leave home
  - Refusal to go to school
- Worry about losing major attachment figures
- Persistent reluctance/refusal to go out

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Separation Anxiety Disorder

- Nightmares about separation
- Repeated complaints of **physical symptoms**
  - Headaches, upset stomach, nausea
  - Occurs with separation or in anticipation
- Treated with therapy
  - Goal: teach children coping skills
  - Cognitive behavioral therapy
  - Parent-child interaction therapy

D Sharon Pruitt/Wikipedia

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Eating Disorders

Eating Disorders

Jason Ryan, MD, MPH

Boards&Beyond

Eating Disorders

- Abnormal eating patterns
- Disrupt health or psychosocial functioning
- More common in women
- Usually present adolescence or young adulthood
- DSM-V Disorders
  - Anorexia nervosa
  - Bulimia nervosa
  - Binge eating disorder

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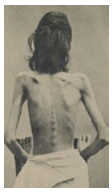
Anorexia Nervosa

- Diet and exercise that leads to **low body weight**
  - World Health Organization: BMI <18.5 kg/m^2
- Intense fear of gaining weight
- Distorted perception of body weight
- **Increased mortality** from malnutrition



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Anorexia Nervosa

- Often **co-exists** with other disorders
  - Depression
  - Anxiety
  - Obsessive-compulsive disorder
  - Posttraumatic stress disorder
  - Substance abuse
- Often secondary to eating disorder
- Improve with weight restoration
  - Especially depression

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Anorexia Nervosa

Endocrine Effects

- ↓ GnRH secretion
- ↓ LH/FSH
- **Amenorrhea**
- "Functional hypothalamic amenorrhea"

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Anorexia Nervosa

Electrolytes

- Inability to concentrate urine
  - Free water loss
  - **Hyponatremia**
  - Volume depletion
  - ↓ GFR
- **Creatinine low** (↓ muscle mass)
- If purging: hypokalemia

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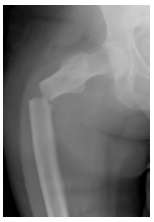
Anorexia Nervosa

Bones

- **↓ bone density**
  - Low estrogen
  - High cortisol
- Loss of cortical and trabecular bone
- Osteopenia
- Osteoporosis



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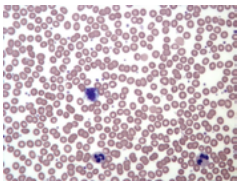
Anorexia Nervosa

Hematology

- Bone marrow suppression
- Anemia
- Leukopenia
- Thrombocytopenia



Keith Chambers/Wikipedia

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Anorexia Nervosa

Physical Exam

- Low body mass index (<18.5 kg/m^2)
  - Mild: 17 to 18.5
  - Moderate: 16 to 16.99
  - Severe: 15 to 15.99
  - Extreme: <15

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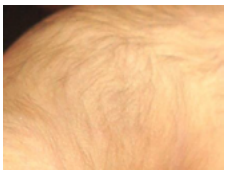
Anorexia Nervosa

Physical Exam

- Bradycardia
- Hypotension
- ↓ bowel sounds
- Dry, scaly skin (xerosis)
- Hair loss
- Lanugo hair growth
  - Soft, fine hair



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Anorexia Nervosa

Treatment

- **Nutritional rehabilitation**
  - Structured meals with observation
  - Calorie goals
- **Psychotherapy**
- Olanzapine (antipsychotic)

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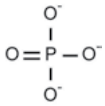
Refeeding Syndrome



Phosphate

- Hallmark: **hypophosphatemia**
  - Low PO4 from poor nutrition
  - Glucose → ↑ insulin → ↑ metabolism
  - Further ↓ PO4 from cellular uptake
  - Loss of ATP → cardiac and respiratory failure
- Most fatalities: **cardiac**
  - Poor contractility, low stroke volume
  - Heart failure, arrhythmias
- Prevention: slow refeeding (gentle ↑ calorie intake)

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Bulimia Nervosa

- Binge eating
- Inappropriate compensation to avoid weight gain
  - Vomiting (purging)
  - Laxatives, diuretics, enemas
  - Excessive exercise
  - Fasting
  - Severely restrictive diets

Bulimia Nervosa

- Occurs at least once a week for **three months**
- Weight usually normal (contrast with anorexia)
- Commonly coexists with other disorders
  - Anxiety
  - Depression
  - Posttraumatic stress disorder
  - Substance abuse

Bulimia Nervosa

Purging Complications

- Contraction alkalosis
- Loss of K^+
- Urinary chloride is low (<20)

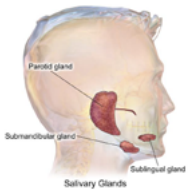
Urinary Chloride

- Useful in metabolic alkalosis unknown cause
- Low (<10-20) in vomiting
  - Loss of Cl in gastric secretions
- High (>20) in many other causes alkalosis
- Classic scenario:
  - Young woman with unexplained metabolic alkalosis
  - Urinary chloride low

Bulimia Nervosa

Purging Complications

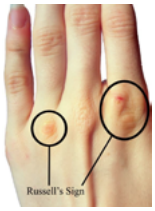
- Parotid swelling
  - "Parotid gland hypertrophy"
  - Sialadenosis
- Erosion of dental enamel



BruceBlaus/Wikipedia

Russell's Sign

- Scars on knuckles from induced-vomiting



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Bulimia Nervosa

Treatment

- Nutritional rehabilitation
- Psychotherapy
- SSRIs

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Binge Eating Disorder

- Binge eating
  - Compulsive overeating
  - Excessively large amounts of food
  - Often eaten quickly
  - Patient feels they lack control
  - Patient feels shame/embarrassment
- No inappropriate compensation
- Weight gain
- Occurs at least once a week for **three months**

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Binge Eating Disorder

- Often occurs with other disorders
  - Anxiety, depression
- Studies show high risk of type II diabetes
- First line treatment: **Psychotherapy (CBT)**
  - Large clinical effect in trials
  - Greater than medication effect
- SSRIs used but less effective

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Binge Eating Disorder

- **Lisdexamfetamine**
  - ADHD stimulant
- **Topiramate**
  - Seizure medication
- Clinical trials: ↑ abstinence from binge episodes
- Both lead to reduced weight

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Sleep Disorders

Sleep Disorders

Jason Ryan, MD, MPH

Boards&Beyond

Sleep Physiology

- Several stages
- Non-REM sleep (N1, N2, N3)
- REM
- Unique EEG findings to each phase

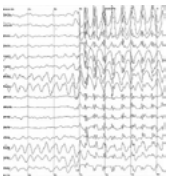

Image courtesy of Der Lange

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Sleep Physiology

- Awake, eyes open
  - **Beta waves**
  - "Low amplitude, high frequency"
- Awake, eyes closed
  - Alpha waves
  - Increased amplitude, more synchronous

Beta

Alpha

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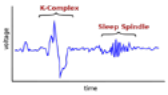
Sleep Physiology

Theta

- N1
  - **Theta waves**
  - Lightest sleep (easy to wake)
  - Smallest percentage (5-10%) sleep time
- N2
  - Theta waves
  - **K complexes**: Sudden ↑ amplitude
  - **Sleep spindles**: Sudden ↑ frequency
  - Largest percentage (50%) sleep time
  - Teeth grinding (bruxism)



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Sleep Physiology

- N3
  - Last phase before REM sleep
  - **Delta waves**
  - "Slow waves"
  - Lowest frequency, highest amplitude
  - Deepest sleep (hardest to wake sleeper)
  - Sleep walking, sleep talking, bed wetting

Delta

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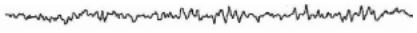
REM Sleep

- **Rapid eye movements**
  - **PPRF** (paramedian pontine reticular formation)
- Low voltage pattern
- Often appears "saw-toothed"



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REM Sleep

- **Loss of motor tone** (muscle paralysis)
- Dreaming, nightmares
- Penile tumescence

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Sleep Physiology

- Sleep goes through "cycles" during the night
- NREM → REM → NREM → REM
- Repeated during the night
- One cycle from NREM to REM about **90 minutes**
- Length of REM *increases* during cycles
- Length of N3 *decreases* during cycles

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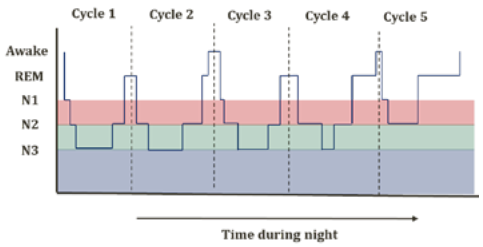
Hypnogram



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Drugs

- Many drugs alter "sleep architecture"
- N3 and REM sleep % decreased by sedative drugs
  - Alcohol
  - **Benzodiazepines**
  - Barbiturates
- Nonbenzodiazepine hypnotics
  - Zolpidem, zaleplon, eszopiclone
  - Activate benzodiazepine (GABA) receptor
  - High affinity for BZ_1 receptor
  - Decrease time to fall asleep (sleep latency)
  - Less effect on sleep cycle than benzodiazepines

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Depression

- REM starts quicker after sleep onset
  - **↓ REM latency**
- ↑ total REM sleep
- ↓ slow-wave (N3) sleep
- Sleep rhythms normalize on anti-depressant drugs

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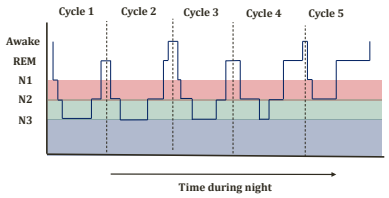
Hypnogram



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Parasomnias

- Occur during sleep
- Undesirable physical events (movements, behaviors)
- Unwanted experiences (emotions, dreams)
- Non-rapid eye movement (NREM)-related
- Rapid eye movement (REM)-related
  - Sleep paralysis (wake but cannot move)
  - Nightmare disorders

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NREM Disorders

- Disorders of arousal during sleep
- Occur during non-REM sleep
  - Usually occur in **N3** (deepest sleep)
  - Usually occur earlier in night (more N3 sleep)
- Patient does not recall arousal activities
- Sleepwalking
- Sleep terrors (sitting up, screaming)
- Sleep-related eating disorder
- Treatment: benzodiazepines (↓ N3 sleep)

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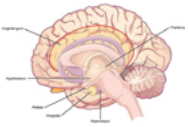
Narcolepsy

- Neurologic disorder of sleep-wake cycles
  - Sleep during wakefulness
  - Wakefulness during sleep
- Causes excessive **daytime sleepiness**
- Caused by ↓ neuropeptides in **lateral hypothalamus**
  - Orexin-A (also called hypocretin-1)
  - Orexin-B (also hypocretin-2)
- Rarely CSF tested for diagnosis
  - Orexin-A/hypocretin-1 levels



OpenStax College/Wikipedia

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Narcolepsy

- Daytime sleepiness
- Fall asleep during day often at inappropriate times
- "Sleep attacks": sudden dozing
- **Not tired when waking in morning**

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Cataplexy

- Sudden **loss of muscle tone**
  - Usually affecting face, neck, or knees
- Muscle weakness
- May lead to collapse
- No loss of consciousness (contrast with syncope)
- Triggered by **strong emotions**
- Classically laughter or excitement
- Sometimes anger or grief

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Hallucinations

- Visual, tactile, or auditory
- Usually **hypnagogic**: occur when falling asleep
- Rarely hypnopompic: occur when awakening

Nevit Dilmen/Wikipedia

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Sleep Paralysis

- Inability to move after awakening for 1-2 minutes
- Caused by **REM sleep** while awake
  - Limited movement during REM sleep activity
- May also occur just before falling asleep
- May occur with hallucinations (scary for patient!)

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Narcolepsy

Epidemiology and etiology

- Begins in teens and early twenties
- Men = women
- Usually occurs sporadically (rarely in families)
- **Autoimmune hypothesis**
  - Orexin neurons killed by autoimmune process
  - Narcolepsy strongly associated **HLA DQB1**

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Narcolepsy

Treatment

- **Modafinil**
  - Controlled substance
  - Promotes wakefulness
  - Poorly understood mechanism
  - Effects on dopamine, NE, GABA

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Narcolepsy

Treatment

- Methylphenidate and amphetamines
  - Indirect sympathomimetics
  - ↑ dopamine and norepinephrine CNS levels in synapses
  - Also used in ADHD

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Narcolepsy

Treatment

- **Sodium oxybate**
  - Salt form of **gamma-hydroxybutyrate (GHB)**
  - GABA metabolite
  - Mechanism of action not known
  - CNS depressant (similar to anesthetic)
- Main benefit: reduces **cataplexy**
  - Also improves nocturnal sleep, reduces daytime sleepiness
- Illegal version GHB: "date rape drug"
- One dose at bedtime
- Repeat dose 2.5 to 4 hours later (set alarm)
- Many patients learn to wake on their own

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Alcohol and CNS Depressants

Alcohol & CNS Depressants

Jason Ryan, MD, MPH

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Substance Use Disorder

- DSM-V: Two or more during 12 month period
  - Tolerance
  - Withdrawal
  - Taken in larger amounts or over a longer period
  - Unsuccessful efforts to cut down or control use
  - Lots of time spent to obtain, use, or recover from
  - Craving or a strong desire or urge to use
  - Failure to fulfill obligations at work, school, home
  - Continued use despite social or interpersonal problems
  - Social/occupational activities given up or reduced
  - Use in situations in which it is physically hazardous
  - Use despite knowledge of having a problem

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Stages of Change

Toddatkins

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Stages of Change

- Precontemplation
  - No intention of behavior change
  - May not recognize/acknowledge problem
- Contemplation
  - Aware problem exists
  - Not yet willing to change
- Preparation
  - Intending to take action
- Action
- Maintenance
- Relapse

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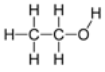
Alcohol



Ethanol

- "Alcohol" = ethyl alcohol = **ethanol**
- Found in alcoholic beverages
- Commonly abused substance
- Metabolize by liver
- Numerous biochemical effects

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Alcohol Intoxication

- CNS depressant
- Slurred speech
- Incoordination
- Unsteady gait
- Stupor
- Coma

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Alcohol Intoxication

- Serum blood alcohol concentration (BAC)
- Most US states: legal limit **80 mg/dL**
  - "0.08 g/dL" or "0.08" or "8%"
- Number of drinks to reach limit varies with size

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Alcohol Biomarkers

- Markers of liver damage
- Used to screen for heavy, chronic use

Biomarker	Abstinence Time for Return to Normal
Gamma-glutamyltransferase (GGT)	2-6 weeks
Aspartate aminotransferase (AST)	7 days

Also seen in chronic use: ↑ **MCV** and **hypertension**

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Alcohol Poisoning

- Very high BAC → respiratory depression
- Can be fatal
- Treatment is supportive
- May require ICU care

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Alcohol Withdrawal

- Heavy drinkers after abrupt cessation
- 6 to 24 hours after last drink
  - **Tremors**
  - Anxiety
  - GI upset
  - Headache
  - Sweating
  - Palpitations
  - Mental status intact

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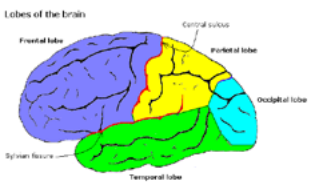
Alcohol Seizures

- 6 to 48 hours after last drink
- Generalized tonic-clonic seizures
- Single or in clusters of two to three



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Alcohol Hallucinosis

- 12 to 48 hours after last drink
- Often **visual** hallucinations
- Seeing insects or animals
- Hearing voices
- Tactile sensations

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Delirium Tremens

- 72 and 96 hours after last drink
- Most severe withdrawal manifestation
- **20% mortality** in some studies

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Delirium Tremens

- Delirium
- Markedly altered mental status
- Agitation
- Fever
- Drenching sweats
- **Autonomic hyperactivity**
  - Tachycardia, hypertension
- Death from:
  - Hyperthermia
  - Arrhythmias
  - Fluid/electrolyte abnormalities

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Alcohol Withdrawal

Treatment

- **Benzodiazepines**
- Improve agitation
- Prevent progression
- Symptom-triggered therapy
  - CIWA scale
  - Clinical Institute Withdrawal Assessment for Alcohol
  - Point system for assessing withdrawal symptoms
  - Regular assessment of patent
  - Benzodiazepine given if score is high

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Alcoholism Therapy

- Support groups (Alcoholics Anonymous)
- **Three FDA approved drugs**
  - Reduce risk of relapse
- Disulfiram (Antabuse)
- Naltrexone
- Acamprosate

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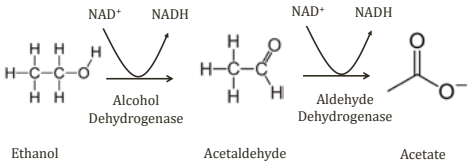
Disulfiram

Anatabuse

- Inhibits aldehyde dehydrogenase
- Acetaldehyde accumulates
- Triggers catecholamine release
- **Sweating, flushing**, palpitations, nausea, vomiting



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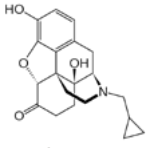
Naltrexone

- Long acting **opioid antagonist**
- Endogenous opioids reinforce alcohol effects
- Given orally to prevent relapse
- Also used in opioid abuse



Naltrexone

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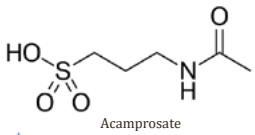
Acamprosate

- Mechanism incompletely understood
- Modulates NMDA receptors
  - Alcohol disrupts CNS equilibrium
  - Excitatory glutamate activity (NMDA receptor)
  - Inhibitory GABA activity
- Common side effect (~15%): **diarrhea**



Acamprosate

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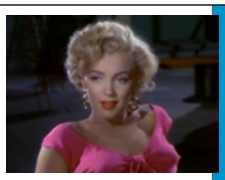
Barbiturates

Phenobarbital, pentobarbital



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- Anti-seizure drugs
- GABA activators
- Used as sedatives in past
- Now largely replaced benzodiazepines
- Similar effects to alcohol (CNS depressants)
- Narrow therapeutic index
- Dangerous used **together with alcohol**

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Barbiturates

Phenobarbital, pentobarbital

- Overdose: **respiratory depression**
  - No antidote
  - Supportive care
- Heavy users must be weaned
- Abrupt withdrawal:
  - Delirium
  - Hallucinations
  - Seizures
  - Cardiovascular collapse → death

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Benzodiazepines

Diazepam, oxazepam, lorazepam

- Many medical uses (anxiety, alcohol withdrawal)
- Classic overdose presentation:
  - **CNS depression with normal vitals**
  - Altered mental status
  - Slurred speech
  - Ataxia
- Rarely cause respiratory depression (safer drugs)

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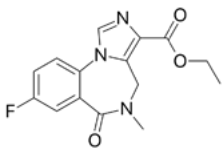
Flumazenil

- **Antagonist** of benzodiazepine receptor
- Use to treat overdose controversial
- Overdose has low mortality rate
- Flumazenil may cause withdrawal seizures



Flumazenil

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Benzodiazepine Withdrawal

- Occurs with abrupt cessation in chronic user
  - Timing depends on drug
  - Long acting BZD → longer washout
- Tremors
- Anxiety
- Depressed mood ("dysphoria")
- Hypersensitivity to sensations (noise, touch)
- Psychosis
- **Seizures**
- Can be life-threatening
- Treatment: benzodiazepines

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Opioids

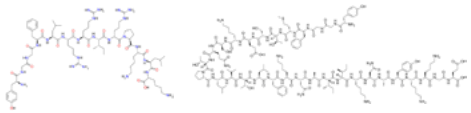
Opioids

Jason Ryan, MD, MPH

Boards&Beyond

Endorphins

- Peptides activators of **opioid receptors**
- Three families: endorphins, enkephalins, dynorphins



Dynorphin A

Beta-endorphin

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Opioid Receptors

- Central and peripheral **nervous system** (neurons)
- Activated by endorphins
- Three key subtypes
- **Mu (μ) receptor**: highest affinity endorphins
- **Delta (δ) receptor**: enkephalins
- **Kappa (κ) receptor**: dynorphins

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Opioid Receptors

Nerve Effects

- Coupled to G-proteins
- **Closes Ca^{2+} channels** on presynaptic nerves
  - Reduce neurotransmitter release
- **Open K+ channels** postsynaptic neurons
  - Leads to hyperpolarization
  - Less signal transmission
- Decreased activity of neurotransmitters
  - Glutamate (excitatory)
  - Acetylcholine, norepinephrine, serotonin, substance P

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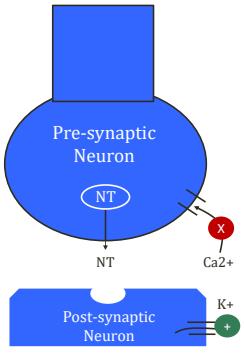

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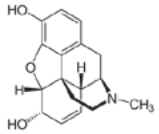
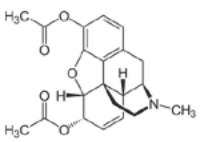
Opioid Drugs

- Activate opioid receptors
- Prototype: **morphine**
  - Also hydromorphone, meperidine, fentanyl, codeine
- Drug of abuse: **heroin** (diamorphine)



Morphine



Heroin

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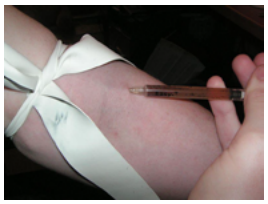
Heroin

- Usually **injected** into vein
- Dirty needle or contaminated drugs:
  - Bacteremia → tricuspid endocarditis
  - Hepatitis B & C
  - HIV



Psychonaught/Wikipedia

Opioids

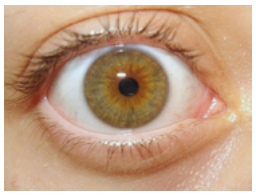
Central nervous system effects

- Mostly mediated through **mu receptor**
- Pain relief (analgesia)
- Euphoria
- Sedation

Opioids

Central nervous system effects

- Respiratory depression
- Cough suppression
- Miosis (small pupils)
  - Exception: meperidine



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Opioids

Peripheral nervous system effects

- Constipation
- Skin warmth and flushing

John Johnson/Pexels

Opioids

Clinical Uses

- Pain control
- Acute pulmonary edema (IV morphine)
- Cough suppression (codeine)
- Diarrhea (loperamide)
- Shivering: (meperidine/Demerol)

Addiction & Tolerance

- Highly addictive
- **Tolerance** develops
  - Less effect of drugs over time
  - Higher dosages required to achieve effects
  - **No tolerance to miosis and constipation**

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John Johnson/Pexels

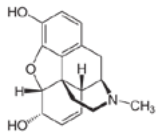
Acute Intoxication

- Opioids: most common cause drug overdose death
- Euphoria to depressed mental status
- **Decreased respiratory rate**
- **Decreased bowel sounds**
- **Miotic (constricted) pupils**
- Seizures
  - Commonly with tramadol or meperidine

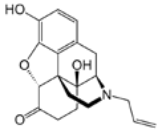
Acute Intoxication

Treatment

- **Naloxone**
- Short-acting opioid antagonist
- May cause withdrawal if dose too high ("overshoot")



Morphine



Naloxone

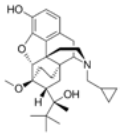
Withdrawal

- Occurs in opioid-dependent individuals
- Usually starts 6-12 hours after last dose
- Reversal of CNS, eye, skin, GI effects
- Restlessness
- **Yawning**
- **Rhinorrhea and lacrimation**
- **Piloerection**
- Nausea, vomiting, abdominal cramps
- Diarrhea

Withdrawal/Addiction

Treatment

- **Buprenorphine**
  - Partial agonist (agonist and antagonist effects)
  - Long duration of action
  - Sublingual tablet
  - Not regulated/controlled like methadone
  - May cause withdrawal (like naloxone)
- Combined with naloxone
  - Prevents abuse
  - Naloxone not absorbed sublingually
  - Crushed pill → IV injection → no effect

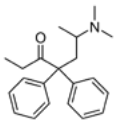


Buprenorphine

Withdrawal/Addiction

Treatment

- **Methadone**
  - Long-acting oral opiate
  - Reduces cravings
  - Maintenance
  - Strictly regulated/controlled

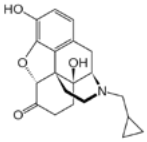


Methadone

Withdrawal/Addiction

Treatment

- **Naltrexone**
  - Long acting opioid antagonist
  - Blocks effects of opioids if taken
  - Administered to detoxified patients to prevent relapse
  - Some data show prevention of relapse
  - Also used in alcohol abuse



Naltrexone

Stimulants

Stimulants

Jason Ryan, MD, MPH

Boards&Beyond

Stimulants

- Cocaine
- Amphetamines
- Caffeine
- Nicotine

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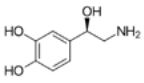
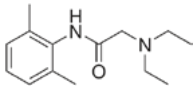
Cocaine

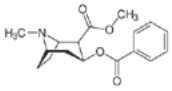


Norepinephrine

- Two key physiologic effects
  - #1: Local **anesthetic** (Na channel blocker)
  - #2: Inhibits **monoamine reuptake**
  - Monoamines: Dopamine, serotonin (5HT), NE
- Sympathetic activation



Lidocaine



Cocaine

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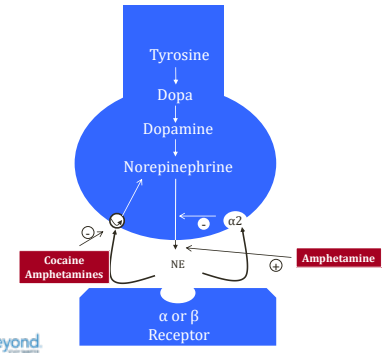
Adrenergic Synapses



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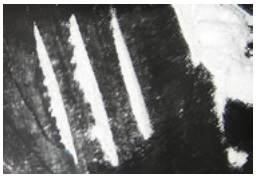
Cocaine Intoxication

- Increased energy
- Decreased need for sleep
- Alertness
- Euphoria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Cocaine Intoxication

- Hallucinations
  - Classically tactile
  - **"Bugs crawling on my skin"**
- **Fever**
  - Increased muscle activity
  - Central dopamine release
- Anxiety
- Paranoia
- May mimic psychosis
- Treatment: **benzodiazepines**

Michael "BuZZeR" Kadykov

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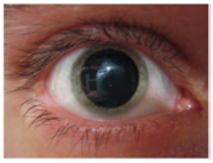
Cocaine Intoxication

Signs

- Sympathetic nervous system activation
- Stimulation of alpha and beta receptors
- **Dilated pupils**
- Tachycardia and increased blood pressure



OpenStax College/Wikipedia

Cocaine Chest Pain

- Common among cocaine users
- ↑ O2 demand (tachycardia, elevated BP)
- ↓ O2 supply (coronary vasoconstriction)
- O2 mismatch → angina
- May lead to thrombosis → myocardial infarction

Freestocks.org

Cocaine Chest Pain

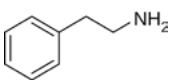
- Treatment: **benzodiazepines**
  - Sedating/calming
  - Diminish cocaine-related stimulating effects
- Aspirin
- **Avoid beta blockers**
  - Increased alpha effects
  - Worsening of hypertension and chest pain

Cocaine Withdrawal

- Occurs with stopping after chronic, heavy use
- **Usually not life-threatening**
- Depression
- Fatigue
- Difficulty concentrating
- Increased sleep

Amphetamines

- Contain modified phenethylamines
- **Stimulants**
- Indirect sympathomimetics
- Increase synaptic **dopamine/NE** levels



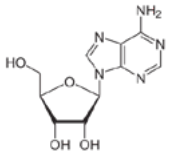
Phenethylamine

Amphetamine Intoxication

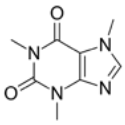
- Hyper-alert state
- Decreased need for sleep
- Sympathetic stimulation
  - Tachycardia, hypertension
  - Pupillary dilation
- Fever
- Agitation
- May cause chest pain
- Rarely causes **seizures**
- Treatment: **benzodiazepines**

Caffeine

- Methylxanthine
- Antagonist of **adenosine receptors**
- Leads to release of dopamine/NE
- Renal adenosine blockade → diuresis



Adenosine



Caffeine

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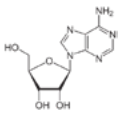
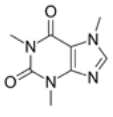
Chemical Stress Tests

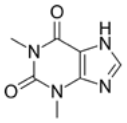
- Intravenous adenosine used as a **vasodilator**
- Induces coronary steal for chemical stress testing
- Effects blocked by caffeine
- Also blocked by theophylline (COPD drug)



Adenosine



Caffeine



Theophylline

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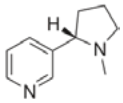
Nicotine

- Addictive substance found in tobacco
- Acts on nicotinic acetylcholine receptors
- **CNS stimulant**
- Activates **sympathetic nervous system**



Nicotine

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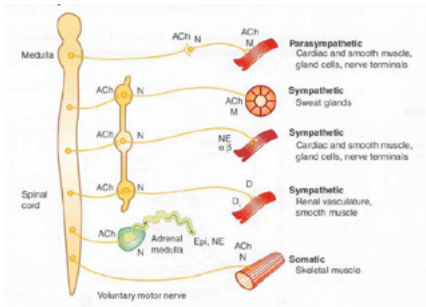
Autonomic Nervous System



Use with permission, Katzung BG, Basic and Clinical Pharmacology, 10th ed. New York, McGraw Hill, 2007

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Nicotine Withdrawal

- Increased appetite
- Weight gain
- Depression
- Insomnia
- Irritability
- Anxiety
- Difficulty concentrating
- Restlessness
- Peak in **first three days** after cessation
- Subside in 3-4 weeks


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Smoking Cessation

- Primary barrier is nicotine addiction
- Assess barriers to quitting
  - Discuss benefits of quitting
  - Address patient concerns
- Set a quit date
  - Often a few weeks in the future
  - Stop smoking completely on this date
  - Begin supportive therapies

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Smoking Cessation

- Nicotine replacement therapy
  - Nicotine patches
  - Nicotine gum
- **Bupropion**
  - Antidepressant
  - Blocks reuptake of NE and dopamine

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Smoking Cessation

- **Varenicline**
  - Partial nicotinic receptor agonist
  - Agonist effects: limit withdrawal symptoms
  - Antagonist effects: block nicotine
- Adverse effects:
  - Nausea
  - Sleep disturbance (insomnia, abnormal dreams)

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Other Drugs

Other Drugs

Jason Ryan, MD, MPH

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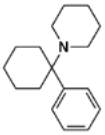
PCP

Phencyclidine



- "Angel dust"
- Antagonist of **NMDA** receptor in CNS
  - N-methyl-D-aspartate
  - Glutamate receptor
  - Blockade: hallucinations and psychosis
- Inhibits **reuptake** of dopamine, NE, 5HT
  - Increases sympathetic activity

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PCP

Phencyclidine

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- Stimulant
- Altered mental status
- Psychosis (with hallucinations)
- "Psychomotor agitation"
- Classically agitated, **violent** behavior
- Tachycardia, hypertension
- Nystagmus (repetitive involuntary eye movements)
- Rarely coma and seizures

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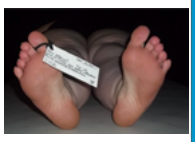
PCP

Phencyclidine

- Fatalities most commonly from **trauma**
  - Psychosis plus **loss of pain/sensation**
  - Patients may dissociate
  - Walk into traffic
  - Jump from buildings
- Treatment:
  - Benzodiazepines
  - Haloperidol (rapid-acting anti-psychotic)



Alisha Vargas/Flikr

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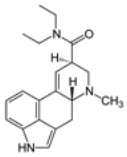
LSD

Lysergic acid diethylamide

- Hallucinogen
- Exact mechanism unknown
  - Binds **serotonin 5-HT2A receptors**
- Not a stimulant (contrast with PCP)



LSD

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LSD

Lysergic acid diethylamide

- Causes LSD "trip"
  - Feeling of expanded consciousness
  - Can sense things beyond usual reality
- Synesthesia (a blending of the senses)
  - "Hearing" colors or "seeing" sounds
- Depersonalization
  - Feeling disconnected or detached from body
- "Bad trip"
  - Paranoia, anxiety

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LSD

Lysergic acid diethylamide

- May causes "**flashbacks**"
  - Return of hallucinogen effects after stopping drug
  - May occur days, weeks, even months later
- Intoxication management: supportive

Pariroxy/Wikipedia

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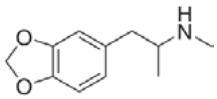
Ecstasy

Methylenedioxy-methamphetamine (MDMA)

- Amphetamine
- Structurally similar to serotonin
- Major effects on **serotonin**
  - Increased release of serotonin
  - Inhibition of serotonin reuptake

Serotonin



MDMA

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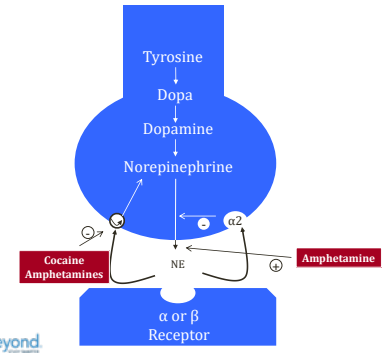
Adrenergic Synapses



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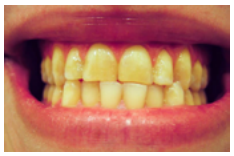
Ecstasy

Methylenedioxy-methamphetamine (MDMA)

- Euphoria
- Alertness
- **Bruxism** (grinding teeth)



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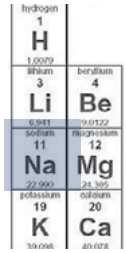
Ecstasy

Methylenedioxy-methamphetamine (MDMA)

- Tachycardia and hypertension
- Hyperthermia
- **Hyponatremia**
  - Increased fluid intake
  - Secretion of antidiuretic hormone
  - Reports of **seizures and death**
- **Hepatotoxicity**
  - RUQ pain
  - Increased AST/ALT



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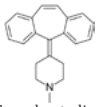
Serotonin Syndrome



Cyproheptadine

- Classic triad: Three As
- #1: Mental status changes
  - **A**gitation, restlessness, and disorientation
- #2: **A**utonomic hyperactivity
  - Diaphoresis, tachycardia, **hyperthermia**
- #3: Neuromuscular hyper**a**ctivity
  - Tremor, clonus, hyperreflexia, bilateral Babinski sign
- Treatment: **cyproheptadine**
  - 5 –HT antagonist

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Ecstasy Withdrawal

- "Crash" after being high on MDMA
- **Depression** and anxiety
- Fatigue and lethargy
- Difficulty concentrating
- Loss of appetite
- Jaw soreness (from grinding teeth while high)

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Marijuana

- Derives from cannabis (plant)
- Psych activity from tetrahydrocannabinol (THC)
  - Also called Dronabinol
- Stimulates cannabinoid receptors in CNS
- Euphoria
- Increased appetite
- Ataxia
- Slurred speech
- Impaired judgement, cognition
- Rarely anxiety or panic attacks

Wikipedia/Public Domain

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Synthetic Cannabinoids

- Pharmaceutical forms of **dronabinol**
- Available in capsule form
- Two FDA-approved uses
- #1: Chemotherapy-induced nausea and vomiting
- #2: Appetite stimulation in wasting illnesses
  - Often end stage HIV/AIDS patients

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Antidepressants

Antidepressants

Jason Ryan, MD, MPH

Boards&Beyond

Antidepressants

- Tricyclics
- MAO inhibitors
- SSRIs
- SNRIs
- Others

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Depression

- Associated with:
  - ↓ **serotonin**
  - ↓ **norepinephrine**
  - ↓ **dopamine**
- Improved symptoms with increased CNS levels
- Most antidepressants → increase levels
- Ways to increase levels
  - Block re-uptake → higher levels in synapses
  - Inhibit breakdown

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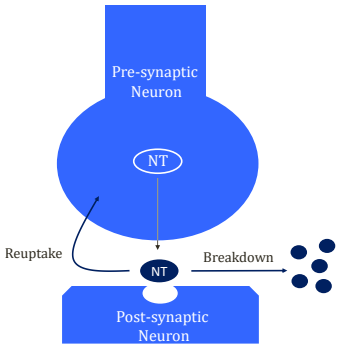

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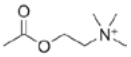
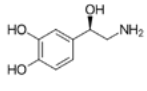
Depression

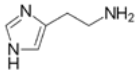


Acetylcholine

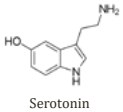
- **Monoamines**
  - Serotonin, norepinephrine, histamine, dopamine
- Most drugs affect more than one monoamine
- Anti-histamine effects
  - Common: sedation, dry mouth
- NE blockade: hypotension (alpha-1)
- Muscarinic blockade: tachycardia, urinary retention



Norepinephrine



Histamine



Serotonin
5-HT

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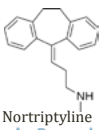
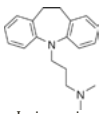
Tricyclic Antidepressants

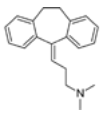
- Old antidepressants (1970s)
- Block re-uptake of **5-HT** and **norepinephrine**
- "Broad spectrum"
  - Anti-histamine
  - Anti-muscarinic
  - Block alpha-1 receptors
  - Many side effects



Nortriptyline



Imipramine



Amitriptyline

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Tricyclic Antidepressants

- Anti-histamine
  - Sedation, weight gain, confusion (especially elderly)
- Anti-cholinergic (muscarinic)
  - Blurry vision, constipation, dry mouth, urinary retention
- Alpha-1 block
  - Orthostatic hypotension

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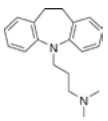
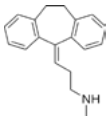
Tricyclic Antidepressants

- **Tertiary amines** (3 nitrogen attachments)
  - Amitriptyline, clomipramine, doxepin, imipramine, trimipramine
  - More sedating (anti-histamine effects)
- **Secondary amines** (2 nitrogen attachments)
  - Desipramine, nortriptyline, protriptyline
  - More activating (norepinephrine effects)



Imipramine



Nortriptyline

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Tricyclic Antidepressants

Overdose

- Potentially fatal
- **Seizures** and coma
  - TCAs antagonize GABA receptors
- Anticholinergic toxicity
  - **Hyperthermia** (loss of sweating)
  - Skin flushing, dilated pupils
  - Ileus, urinary retention
- **Hypotension** (alpha blockade)
  - Major cause of death
- Prolongation of QT interval → arrhythmias

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Tricyclic Antidepressants

Overdose

- Monitor ECG for **increased QRS interval**
  - Most prominent manifestation of toxicity
  - TCAs block cardiac sodium channels
- Treatment: **Sodium bicarbonate**
  - Extra sodium overcomes TCA Na-channel blockade
  - Also ↑ pH favors inactive form of drug

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Tricyclic Antidepressants

Non-depression uses

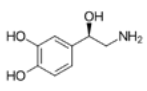
- Obsessive-compulsive disorder (clomipramine)
- Diabetic peripheral neuropathy
  - Amitriptyline, desipramine
- Chronic pain
  - Amitriptyline, doxepin, imipramine, nortriptyline, desipramine
- Prevention of migraine headaches
  - Amitriptyline
- Bed wetting (enuresis)
  - Not first line therapy (desmopressin)
  - Imipramine, amitriptyline, and desipramine
- Insomnia (doxepin)

Boards&Beyond

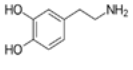
MAO Inhibitors

Monoamine Oxidase Inhibitors

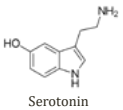
- Inhibits monoamine oxidase
- **↓ breakdown of monoamines**
  - Serotonin, norepinephrine, dopamine
- MAO-A
  - Dopamine, serotonin, norepinephrine
- MAO-B
  - Dopamine



Norepinephrine



Dopamine



Serotonin
5-HT

Boards&Beyond

MAO Inhibitors

Monoamine Oxidase Inhibitors

- Non-selective MAO inhibitors
  - Tranylcypromine, phenelzine, isocarboxazid
- MAO-b selective: selegiline
- Rarely used in modern era
  - Refractory depression
  - Anxiety
  - Selegiline (selective MAO-B inhibitor) used in Parkinson's

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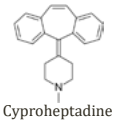
Serotonin Syndrome



Cyproheptadine

- Classic triad: Three As
- #1: Mental status changes
  - **A**gitation, restlessness, and disorientation
- #2: **A**utonomic hyperactivity
  - Diaphoresis, tachycardia, **hyperthermia**
- #3: Neuromuscular hyper**a**ctivity
  - Tremor, clonus, hyperreflexia, bilateral Babinski sign
- Treatment: **cyproheptadine**
  - 5 –HT antagonist

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Serotonin Syndrome

- Often caused by MAOi **plus another serotonin drug**
- Any drug that that ↑ serotonin activity
  - SSRIs, MAO inhibitors, SNRis, TCAs
  - MDMA (ecstasy)
  - Ondansetron (nausea; 5-HT3 antagonist)
  - Tramadol (weak opioid; inhibits 5-HT reuptake)
  - Meperidine (opioid; inhibits 5-HT reuptake)
  - Triptans (migraines; 5-HT agonists)
  - Linezolid (antibiotic; weak MAO inhibitor)
  - Dextromethorphan (cough suppressant; weak SSRI)
  - St. John's wort (herbal supplement; increase 5-HT activity)
- Two week washout (stopping/starting)

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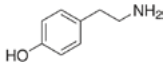
Tyramine



Tyramine

- Naturally occurring monoamine
- Sympathomimetic
- Causes sympathetic activation
- Normally metabolized GI tract
- Patients on MAOi → tyramine in blood
- Hypertensive crisis
- **"Cheese effect"**
  - Cheese, red wine, some meats

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SSRIs

Selective serotonin reuptake inhibitors

- Inhibits **5-HT reuptake** by neurons
- Leads to ↑ 5-HT levels in synaptic cleft
- Take 4-8 weeks to have effects
- Used in many psychiatric disorders
  - Depression
  - Generalized anxiety disorder
  - Panic disorder
  - Obsessive-compulsive disorder
  - Bulimia
  - Social anxiety disorder
  - PTSD

Fluoxetine
Fluvoxamine
Paroxetine
Sertraline
Escitalopram
Citalopram

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SSRIs

Selective serotonin reuptake inhibitors

- Common side effect: **sexual dysfunction**
  - Increased serotonin effects in spinal cord
  - Decreased libido (54 percent)
  - **Anorgasmia**: difficulty achieving orgasm (36 percent)
  - Erectile dysfunction in males (37 percent)

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SSRIs

Selective serotonin reuptake inhibitors

- GI upset
  - GI serotonin effects
  - Nausea, abdominal pain, constipation and diarrhea
- Drowsiness
- Weight gain
- SIADH and hyponatremia (rare)
- QT prolongation (rare)

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SNRIs

Serotonin-norepinephrine reuptake inhibitors

- Inhibits **5-HT and NE reuptake** by neurons
- Take 4-8 weeks to have effects
- Used in many psychiatric disorders
  - Depression
  - Generalized anxiety disorder
  - Social anxiety disorder
  - Panic disorder
  - PTSD
  - Obsessive-compulsive disorder
- Fibromyalgia (duloxetine)
- Diabetic neuropathy (venlafaxine)

Venlafaxine
Desvenlafaxine
Duloxetine
Levomilnacipran
Milnacipran

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SNRIs

Serotonin-norepinephrine reuptake inhibitors

- May **increase blood pressure**
  - Norepinephrine effects
- Nausea (diminishes with time)
- Sexual dysfunction
  - Highest rate: venlafaxine

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Bupropion

- Blocks reuptake of NE and dopamine
- Increases presynaptic release of catecholamines
- No effects on serotonin
- Used in **depression** and **smoking cessation**
- May *improve* sexual dysfunction of SSRIs
- Toxicity related to stimulant effects
  - Anxiety
  - Insomnia
  - **Seizures**

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Mirtazapine

- Blocks presynaptic **alpha-2 receptors**
  - More norepinephrine and serotonin release
- Blocks postsynaptic serotonin **5-HT2 and 5-HT3**
  - More 5-HT1 activity
- Also anti-histamine → side effects
  - **Sedation**
  - Dry mouth
  - Increased appetite
  - Weight gain

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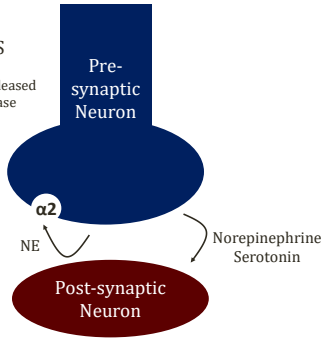
Alpha 2 Receptors

α2 receptors in CNS
Presynaptic receptor
Feedback to nerve when NE released
Activation leads to ↓NE release



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Serotonin Modulators

- Inhibit reuptake of serotonin
- Antagonists and agonists of serotonin receptors
- Minimal effects on norepinephrine or dopamine
- Trazadone
- Vilazodone
- Vortioxetine

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Trazadone

- Weak serotonin reuptake inhibitor
- Affects serotonin 5-HT2A and 5-HT2C receptors
  - Low doses: serotonin antagonist
  - High doses: serotonin agonist
- No longer used as antidepressant
- Main clinic use is **insomnia** (sedating)

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Vilazodone

- Blocks reuptake of serotonin
- Partial agonist at postsynaptic 5-HT1A receptors
- Diarrhea (28%)
- Sexual dysfunction
- Case reports of **serotonin syndrome**

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Vortioxetine

- Blocks reuptake of serotonin
- Various properties on **serotonin receptors**:
  - Antagonist 5-HT3
  - Weak antagonist 5-HT7/5-HT1D
  - Partial agonist 5-HT1B
  - Full agonist 5-HT1A
- Main side effect: nausea

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Lithium

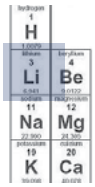
Lithium

Jason Ryan, MD, MPH

Boards&Beyond

Lithium

- Chemical element/cation
- First medical therapy of **bipolar disorder** (1949)
- Many toxicities
- Narrow therapeutic index
- Serum level monitored to titrate dose
  - Low level = subtherapeutic
  - High level = risk of toxicity



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Lithium

Mechanism

- Incompletely understood
- Inhibits **inositol** monophosphatase (IMPase)
  - Used to regenerate inositol
  - **Depletes inositol** → ↓ intracellular **2nd messenger** levels
  - Phosphatidylinositol-4,5-bisphosphate (PIP2)
  - Inositol trisphosphate (IP3)
  - Diacylglycerol (DAG)

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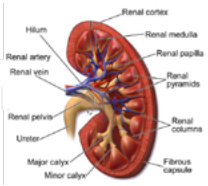
Lithium

Elimination

- Primarily **renal** excretion
- Mostly reabsorbed in proximal tubule (like Na)
- Contraindicated with significant renal impairment



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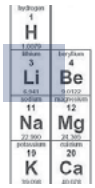

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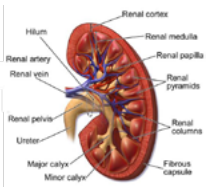
Lithium Toxicity

Risk Factors

- Renal insufficiency
- Volume depletion
- Elderly patients (low glomerular filtration rate)



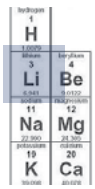


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Image courtesy of BruceBlaus

Lithium

Drug Interactions

- Increased lithium level
  - **Thiazide diuretics**
  - NSAIDS
  - ACE inhibitors
- Decreased lithium level
  - **Potassium-sparing diuretics**
- Varying effects: loop diuretics

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Lithium

Adverse Effects

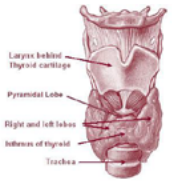
- Acute effects
  - Tremor
- Long term effects
  - Hypothyroidism
  - Nephrogenic diabetes insipidus
  - Cardiac
- Fetal effects
  - Ebstein's anomaly

Tremor

- Occurs when drug started or dose increased
- Symmetric
- Usually limited to hands or arms
- Often resolves over time
- **Most common symptom** of lithium toxicity

Thyroid Effects

- Lithium: goitrogen
- Inhibits hormone release
- Commonly causes **goiter** (enlarged thyroid)
  - 40-50% of patients on lithium
- May cause **hypothyroidism**



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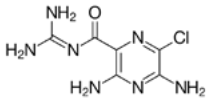
Diabetes insipidus

- "Chronic tubulointerstitial nephropathy"
  - Loss of tubule urine concentrating ability
- Tubules do not respond to ADH
- Dilute urine (low Uosm)
- **Polyuria and polydipsia**
- Serum sodium normal or increased

Diabetes insipidus

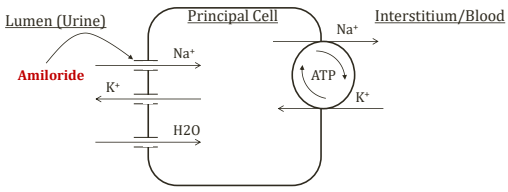
Treatment

- Vasopressin: no response (no change Uosm)
  - Nephrogenic DI
- Discontinue lithium (if possible)
- **Amiloride**
  - Potassium-sparing diuretic
  - Inhibits **Na channels (ENaC)** of principal cells
  - Blocks lithium entry into renal cells



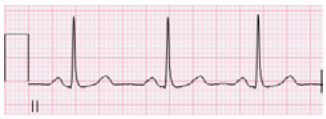
Amiloride

Amiloride



Cardiac Effects

- Suppression of **sinus node**
- Make cause sinus node dysfunction
- Bradycardia
- Pauses
- Syncope



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Maternal Lithium

- Teratogen
- Completely equilibrates across the placenta
- Teratogenic effects primarily involve heart
- **Ebstein's anomaly** most common

Ebstein

Øyvind Holmstad/Wikipedia

Boards&Beyond

Antipsychotics

Antipsychotics

Jason Ryan, MD, MPH

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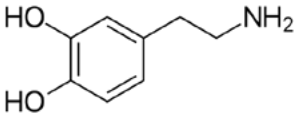
Dopamine

- 1950s: **chlorpromazine** found to improve psychosis
- Also found to block CNS **dopamine** receptors
- Dopamine hypothesis



Dopamine

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Antipsychotics

First Generation or Typical

- Haloperidol
- Chlorpromazine
- Trifluoperazine
- Fluphenazine
- Thioridazine
- Pimozide

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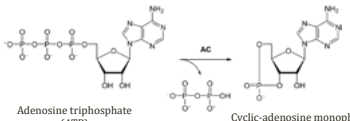
Antipsychotics

First Generation or Typical

- Primary antipsychotic effect: **D2 receptor blockade**
  - Found on post-synaptic CNS neurons
  - Limbic system, basal ganglia, prefrontal cortex
  - G-protein coupled
  - D1: activates adenylyl cyclase → ↑ cAMP
  - D2: inhibits adenylyl cyclase → ↓ cAMP
  - **D2 blockade → ↑ cAMP**



Adenosine triphosphate (ATP)

Cyclic-adenosine monophosphate (cAMP)

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Antipsychotics

First Generation or Typical

- "Neuroleptics": depresses nervous system activity
- Schizophrenia (positive symptoms)
- Psychosis
- Mania
- Bipolar disorder
- Obsessive-compulsive disorder
- Delirium (haloperidol)
- Tourette syndrome
- Huntington disease

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Parkinson's Disease

- Motor dysfunction
- Tremors, rigidity
- Associated with **↓ CNS dopamine activity**

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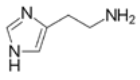
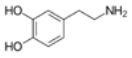
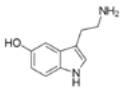
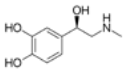
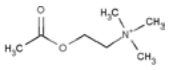
Neurotransmitters


Histamine


Dopamine


Serotonin
5-HT


Epinephrine


Acetylcholine
(Muscarinic)

Antipsychotics

First Generation or Typical

- Dopamine blockade
- Serotonin blockade
- Histamine blockade
- Acetylcholine (muscarinic) blockade
- Epinephrine (alpha-1) blockade

Chlorpromazine: α1=5HT> D2
Haloperidol: D2 > α1 > 5HT > H1

Antipsychotics

First Generation or Typical

- Dopamine blockade
  - Parkinsonian effects (extrapyramidal)
  - Hyperprolactinemia
  - Amenorrhea
  - Galactorrhea
  - Gynecomastia
  - **Anti-emetic** (Prochlorperazine/Chlorpromazine)
- ACh muscarinic receptor blockade
  - Dry mouth
  - Constipation

Antipsychotics

First Generation or Typical

- α1 receptor blockade
  - Hypotension
- Histamine receptor blockade
  - Sedation
  - Constipation

Pyramidal vs. Extrapyramidal

- Pyramidal system
  - Corticospinal tract
  - Run in pyramids of medulla
  - Damage → weakness
- Extrapyramidal system
  - Basal ganglia nuclei and associated tracts
  - Modulation of movement
  - Damage → movement disorders

EPS

Extrapyramidal Symptoms

- Response to dopamine receptor blockade
- **Movement** side effects
- Dystonia
- Akathisia
- Bradykinesia
- Tardive dyskinesia

Dystonia

Extrapyramidal Symptoms

- Acute side effect
- Occurs within hours/days
- Involuntary contraction of muscles
- Spasms, stiffness
- Treatment: **benztropine**
  - Anticholinergic
  - Blocks M1 receptors
  - Improves dystonia

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Akathisia

Extrapyramidal Symptoms

- Occurs within days
- Most common EPS adverse effect
- Restlessness, urge to move
- Sometimes misdiagnosed as worsening agitation
- Treatment: Lower dose, benzos, propranolol

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Bradykinesia

Extrapyramidal Symptoms

- Occurs weeks after starting drug
- "Drug-induced Parkinsonism"
- Slow movements (Parkinson-like)
- Treatment: **benztropine**

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Tardive dyskinesia

Extrapyramidal Symptoms

- Occurs months or years after starting drug
- **Choreoathetosis**
  - Chorea: irregular migrating contractions
  - Athetosis: twisting and writhing
  - Mouth, tongue, face, limbs
- Smacking lips
- Grimacing
- **Often irreversible**
  - Stopping drug doesn't help

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Antipsychotics

First Generation or Typical

- **High potency** agents
  - Haloperidol, trifluoperazine, fluphenazine
- Lower dose required to achieve effect
- Example: Haldol 1mg
- Little effect on histamine and muscarinic receptors
  - Less dry mouth (muscarinic), sedation (histamine)
- **Extrapyramidal side effects**

Chlorpromazine: α1=5HT> D2
Haloperidol: D2 > α1 > 5HT > H1

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Antipsychotics

First Generation or Typical

- **Low potency** agents
  - Thioridazine, chlorpromazine
  - Example: Thioridazine 50-100mg
- Less extrapyramidal side effects
- More **non-neurologic side effects**
  - Sedating ("sedatives")
  - Dry mouth

Chlorpromazine: α1=5HT> D2
Haloperidol: D2 > α1 > 5HT > H1

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Antipsychotics

First Generation or Typical

Low Potency
Thioridazine
Chlorpromazine

High Potency
Haloperidol
Trifluoperazine
Fluphenazine

Non-EPS Effects
Sedation
Dry mouth

EPS Effects
Movement symptoms

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NMS

Neuroleptic Malignant Syndrome

- Rare, dangerous reaction to neuroleptics
- Usually 7-10 days after treatment started

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NMS

Neuroleptic Malignant Syndrome

- **Fever** and **rigid muscles**
- Mental status changes (encephalopathy)
- Elevated creatine kinase (muscle damage)
- Myoglobinuria → acute renal failure (rhabdomyolysis)
- Treatment:
  - Dantrolene (muscle relaxant)
  - Bromocriptine (dopamine agonist)
- Similar to malignant hyperthermia
  - Reaction to halothane, succinylcholine
  - Same treatment: dantrolene (muscle relaxant)

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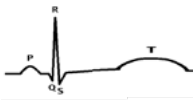
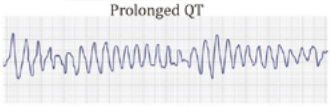
QT interval

- May block cardiac potassium channels
- Prolongs QT interval
- Strongest association with IV haloperidol



Prolonged QT



Torsade de Pointes

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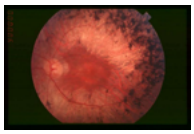
Ocular Effects



Christian Hamel

- **C**hlorpromazine
  - May cause **corneal** deposits
  - May accelerate aging of lens
- Thio**r**idazine
  - **Retinal** deposits
  - Advanced cases resemble retinitis pigmentosa
  - May cause "browning" of vision
  - Uses lower doses to avoid this complication

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Antipsychotics

Second Generation or Atypical

- Clozapine
- Olanzapine
- Quetiapine
- Asenapine
- Iloperidone
- Paliperidone
- Risperidone
- Lurasidone
- Ziprasidone
- Aripiprazole
- **Defining feature: Less EPS adverse effects**

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Serotonin

5-hydroxytryptamine (5 HT)

- LSD (lysergic acid diethylamide)
  - 5-HT agonist
  - Produces hallucinations via **5-HT$_{2A}$ activity**
- **↓ 5-HT$_{2A}$** activity seen with many atypicals
  - As or more effective 5-HT blockade versus dopamine

Clozapine: α1 > 5HT > D2
Olanzapine: 5HT > H1 > D2 > α1

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Antipsychotics

Second Generation or Atypical

- Schizophrenia
  - Improve positive and negative symptoms
- Bipolar disorder
- Obsessive-compulsive disorder
- Anxiety disorder
- Depression
- Tourette syndrome
- **Fewer EPS and anti-cholinergic effects**
- May prolong QT interval

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Metabolic Syndrome

- May occur with any antipsychotic
- Common with **clozapine** and **olanzapine**
- Weight gain
- Hyperglycemia
- Hyperlipidemia

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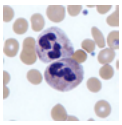
Clozapine

- Toxic to bone marrow
- May cause **agranulocytosis** (1-2% of patients)
- Must monitor WBCs during therapy
  - Weekly at start
  - Every few weeks to monthly thereafter
- Reversible when drug stopped
- May also cause **seizures** (2-5% of patients)
  - Dose related



Dr Graham Beards

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Hyperprolactinemia

- Antipsychotics: **most common** drug-induced cause
- Dopamine blockade → ↑ prolactin
  - Amenorrhea in women
  - Gynecomastia in men
  - Galactorrhea
- Highest rates:
  - Haloperidol
  - Fluphenazine
  - **Risperidone**
  - **Paliperidone**

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Aripiprazole

- D2 **partial agonist**
  - Some blockade, some agonist effects
- Less dopamine blockade adverse effects
- Most common side effect: akathisia

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