Diagnosis and Management of ADD in Adults and Children

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Disclosure

- No real or potential conflict of interest to disclose.
- No experimental or investigational use of drugs or devices will be presented.

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Objectives

- At the conclusion of this session, the attendee will be able to:
  - Evaluate diagnostic criteria for ADD in adults and children
  - Analyze pharmacology of stimulant and non-stimulant options
  - Apply pharmacologic options presented in case study discussion

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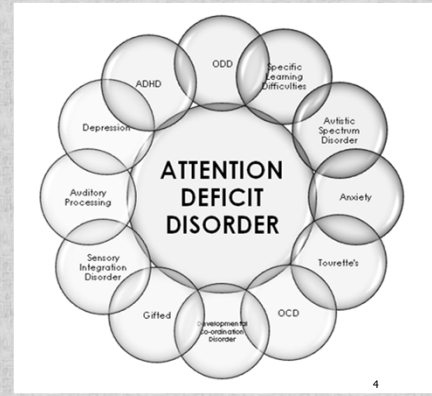
Pharmacologic Management of ADD



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Pathophysiology of ADD

- There are several postulated pathophysiologic mechanisms that involve both abnormalities of anatomy and physiology.
- Drug therapy targets abnormalities of two physiologic mechanisms.
  - Dopamine
  - Norepinephrine

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Pathophysiology of ADD (continued)

- Prefrontal cortex figures prominently
- Frontal and temporal regions theorized to develop more slowly in children.
- Critical to memory and behavior

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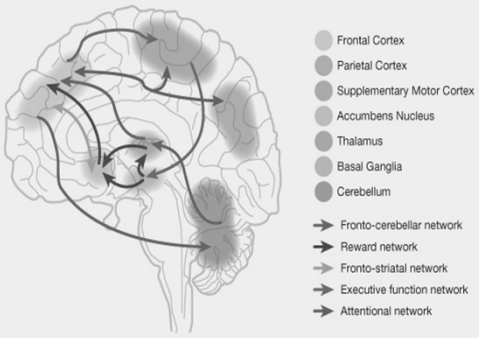
Pathophysiology of ADHD



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Pathophysiology of ADHD (continued)

- Neurochemical deficits include…
  - Dopamine dysregulation
  - Norepinephrine dysregulation
- Deduced based upon
  - Response to drug therapy
  - Molecular genetics
  - Maldistribution of neurotransmitters in the brain of affected patients

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Dopamine

- Responsible for a wide variety of neural processes
  - Maintains motivation/reward
  - Critical in the ability to attend
    - Enhances focus on a particular task
  - Facilitates joy/pleasure
    - Positive emotions
  - Features prominently in motor movement

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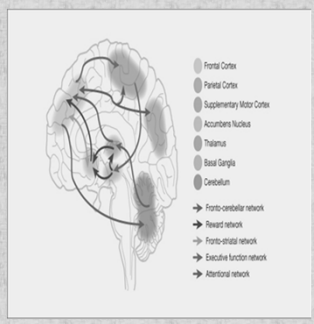
Norepinephrine

- Enhances prefrontal cortex network connections
- Frontal cortex helps dampen background noise.



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Pathophysiology of ADHD

- Core symptoms of ADD
  - Inattention
  - Impulsivity
- Core symptom of ADHD
  - Hyperactivity
- Directly linked to imbalances of dopamine and/or norepinephrine in relevant neurological pathways

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Pathophysiology of ADHD (continued)

- Under normal or healthy circumstances
  - Pyramidal neurons in the prefrontal cortex maintain a baseline "tonic" or slow synaptic firing of these neurotransmitters.
  - Additionally, these neurons can produce "phasic" or bursts of synaptic activity.

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Pathophysiology of ADHD (continued)

- In a healthy patient with well-developed anatomy…
  - Neurotransmitters maintain appropriate balance of communication.
- With respect to memory, attention, and concentration these neurotransmitters have specific roles.

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Pathophysiology of ADHD (continued)

- Dopamine and norepinephrine work together to tune the pyramidal neurons in the prefrontal cortex.
- When these neurotransmitters are out of balance, a collection of symptoms can occur that produces the clinical syndrome ADD.

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Pathophysiology of ADHD (continued)

- Norepinephrine stimulates alpha$_{2a}$ receptors.
  - Result is increased connectivity in the relevant pathways
    - This results in increased strength of the incoming signal as background noise is minimized.
      - Sustained attention
      - Alertness
      - Response to stimuli

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Pathophysiology of ADHD (continued)

- Dopamine activates D_1 receptors.
  - This results in enhanced focus
  - Prevents inappropriate connections from occurring
    - Working memory
    - Behavior
    - Motivation

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Pathophysiology of ADHD (continued)

- A steady state balance of both dopamine and norepinephrine is the desired state.
- Extremes on either end can result in a collection of ADD symptoms.

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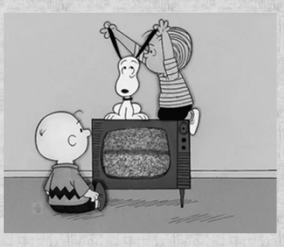
Dysregulation

Dopamine



Norepinephrine

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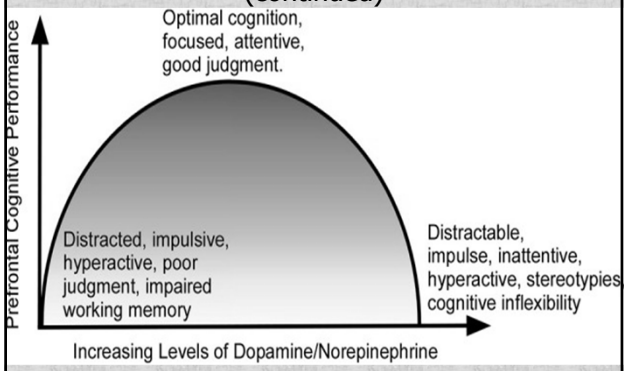
Pathophysiology of ADHD (continued)



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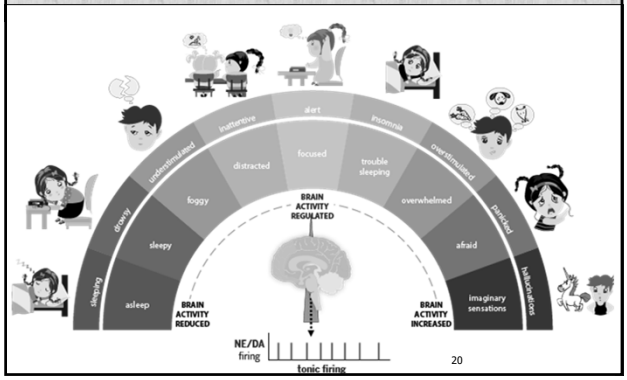
Pathophysiology of ADHD (continued)



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Pharmacotherapy

- First consider and treat any comorbidities.
  - Substance abuse
  - Mood disorders
    - Bipolar
    - Depression
    - Anxiety
- Remember nonpharmacologic therapy

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Psychostimulants

- Mainstay of ADD therapy
  - Achieves on average 70% symptom reduction
- These medications *modulate* amount of DA and NE.
  - Effectiveness determined by symptom control vs. functional outcomes

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Psychostimulants (continued)

- Exist in two broad categories
  - Methylphenidates
  - Amphetamine salts
- Very similar in most ways
  - Symptom control
  - Dose formulations
  - Adverse effect profile
  - Abuse potential

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Psychostimulants (continued)

- Adverse effects rare when used properly
- Appetite suppression occurs early in therapy.
  - Weight should be monitored.

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Psychostimulants (continued)

- Growth restriction can occur.
  - Final adult height may be shortened by 1" (2.54 cm).
- No documented relationship to cardiovascular events *when used properly*

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Stimulants

- Dosing
  - Numerous long-acting and short-acting forms exist.
  - Long-acting forms provide better "tonic phase" control leading to…
    - More consistent symptom control
    - More convenient dosing
    - Minimization of postdose euphoria

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Stimulants (continued)

- Methylphenidates
  - Blocks dopamine and norepinephrine reuptake
  - Formulations include Ritalin® and Concerta®
  - Have the most rapid onset and shortest duration
    - Several long-acting forms available, including Daytrana® patch

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Stimulants (continued)

- Methylphenidates (cont.)
  - Cotempla XR ODT® for once-daily dosing
  - Dexmethylphenidate (Focalin®) twice as potent as others in class

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Stimulants (continued)

- Amphetamine salts
  - Adderall®, Dexedrine®, Vyvanse®
  - Mechanism of action very similar to methylphenidates
  - Modulation of tonic NE and DA is goal.
  - Speculation abuse potential is higher than methylphenidate.

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Stimulants (continued)

- Short-acting forms have highest potential for abuse.
  - Crushing, snorting, chewing – More consistent with abuse delivery

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Stimulants (continued)

- Dextroamphetamine-amphetamine (Mydayis®)
  - Extended-release only
  - Taken once daily upon awakening
    - Clinical efficacy up to 16 hours
- Amphetamine extended-release orally disintegrating tablets (Adzenys XR-ODT®) also once daily

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Non-stimulant Options

- A variety exist
  - Abuse potential- Limited
  - Efficacy approximately 40%
  - Typically used when stimulants not indicated
    - Abuse potential
    - Intolerable adverse effects
    - Patient preference

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Atomoxetine (Strattera®)

- Norepinephrine reuptake inhibitor
  - Purely norepinephrine reuptake inhibitor
  - No impact on dopamine
  - Typically well tolerated
  - No abuse potential
  - Response rate – less
  - Primarily improves filter of background noise

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Alpha$_{2a}$ Receptor Agonists

- Subgroup includes guanfacine and clonidine
  - Guanfacine (Tenex®, Intuniv®)
  - Clonidine (Catapres®, Kapvay®) (Off-label)
- Both of these drugs directly activate anti-adrenergic responses.

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Alpha$_{2a}$ Receptor Agonists (continued)

- Mechanism of action
  - Very different than other ADHD drugs
- Primary symptom utility for
  - Hyperactivity
  - Impulsivity
- Does not increase attention as well as other options

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Bupropion

- Not indicated for ADHD
  - Primary actions related to dopamine and norepinephrine reuptake.
- Consider as an option for someone with depression and mild ADHD symptoms.

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Modafinil and Armodafinil

- Wakefulness agents
  - MOA is unclear.
  - Not approved at this time for ADHD, but are used off-label for this purpose
- These drugs produce prolonged wakefulness and attention.
  - Adverse effect profile is minimal.

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Case Study

42-year-old Male

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Case Study

- A 42-year-old male presents for evaluation.
  - He has been seeing a therapist for bipolar disorder and anxiety for several months.
- He really thinks he has ADD.
  - He was reading about it online.

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Case Study
(continued)

- He reports trouble staying focused at work and at home.
- Shares custody of his daughter
  - He knows he does not pay attention.
  - He tries to be engaged but cannot focus.

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Case Study
(continued)

- The patient has been on bipolar meds for years.
- He can't get much done at work.
  - Produces anxiety
  - Becomes an insomniac
- He is not following through on things at work.
  - Decreases productivity

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Case Study
(continued)

- He acknowledges not paying attention to his daughter.
  - She says, "You never listen."
- The patient has never been diagnosed with ADD.
  - He googled ADD and thinks that is the problem.

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Case Study (continued)

- So what do you do with a new patient?
  - Complete medical history
    - Bipolar
    - Anxiety
  - Complete surgical history
  - Complete medication history
    - Lamotrigine (Lamictal®) 100 mg BID

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Case Study (continued)

- Complete ROS
  - Chronic anxiety about work
  - Sleep is generally not good.
    - Difficulty falling asleep (DFA)
    - Nocturnal awakenings
  - Occasional palpitations
  - Remainder of ROS- Negative

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Case Study (continued)

- HPI
  - Persistent sense of difficulty attending to important things
  - Often misses important details at work
    - Loses focus
    - Not productive at work

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Case Study (continued)

- HPI (cont.)
  - Inattentive to daughter and fiancée
  - Worries about…
    - Personal relationships
    - Work
    - Things he cannot define
  - Denies panic attacks but gets agitated

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Case Study (continued)

- HPI (cont.)
  - Diagnosed with BPD as an adolescent
  - Has been on numerous medications including lithium
  - Currently controlled with lamotrigine 100 mg BID
  - Denies mood swings
  - Admits to being "a little obsessive"

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Diagnostic Criteria for Anxiety

- Excessive anxiety and worry occurring more days than not for at least 6 months about several activities or events such as work or school performance.
  - The worry is difficult to control.

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Diagnostic Criteria for Anxiety (continued)

- Anxiety and worry are associated with at least one of the following…
  - Restlessness or feeling "keyed up" or "on edge"
  - Being easily fatigued
  - Difficulty concentrating or mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance

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Analysis of HPI

- Anxiety
  - Excessive worry/anxiety which is difficult to control
  - Irritability
  - Concentrating difficulty
  - Sleep problems

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Case Study (continued)

- Physical exam
  - Normal
  - Well groomed
  - Attends to hygiene
  - Good eye contact
  - Voice well modulated
  - Conversation- Mildly distracted

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Case Study
(continued)

- What's your diagnostic impression?
  - He thinks it is ADD.
  - We know he has a history of anxiety.
- Typically adults with ADD have a childhood history of ADD although it's not required.
- So is this uncontrolled anxiety or a symptom of ADD?

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Diagnosis and Management

- He was diagnosed with anxiety and started on escitalopram.
  - His lamotrigine was continued.
- Advised to continue working with a therapist
  - Follow-up in 4 weeks

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4-Week Follow-up

- He reports no response to escitalopram.
  - Escitalopram is discontinued.
- Amphetamine salts (short-acting) 10 mg each morning is ordered.
- Follow-up in 4 weeks

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Next Follow-Up
4 Weeks Later

- The patient reports marked improvement in symptoms
  - Much more productive at work
- His fiancée tells him he is less distracted.
  - Requests additional dose at noon

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Case Study

14-year-old Male

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Case Study
(continued)

- A 14-year-old male is encouraged to care by his mother.
  - Mom reports that during all his childhood he has been more difficult than siblings.
- He is in junior high school.
  - His inattentiveness is producing failing grades.

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Case Study
(continued)

- During the office visit the adolescent sits quietly while his mother talks.
- Mother appears very frustrated.
  - Patient just does not remember to do school assignments or home chores.
  - He just wants to play videogames all day.

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Case Study
(continued)

- So what do you do with a new patient?
  - Complete medical history
    - None to report
    - Mom reports normal developmental progression.
    - No childhood diseases
    - Vaccines UTD

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Case Study
(continued)

- So what do you do with a new patient? (cont.)
  - No surgical history
  - No medications
  - Social history
    - Denies cigarettes, EtOH, substances of abuse
    - Has friends at school and a best friend
    - No concerns about bullying

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Case Study
(continued)

- So what do you do with a new patient? (cont.)
  - Social history (cont.)
    - No interest in girls
    - Per Mom, teachers deny behavioral problems at school.

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Case Study
(continued)

- Complete ROS
  - Denies any physical complaints
  - Describes good appetite
  - No anxiety, depression, SI
  - Denies visual or hearing problems

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Case Study
(continued)

- HPI
  - Mom describes a clear pattern of inability to focus on multiple-step instructions.
  - If given tasks individually, he will complete them.
  - Punishment is not helping.
    - Patient loses video game privileges when homework or chores are not done.

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Case Study
(continued)

- HPI (cont.)
  - The patient concentrates in school and is studying Mandarin.
    - He maintains an "A" in this class.
  - He appears to do better in classes that do not have a large self-study component.

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Case Study
(continued)

- HPI (cont.)
  - The patient admits that he forgets things when he must be self-directed.
    - He can pay attention in school when there is consistent direct video and audio reinforcement.
    - He remains focused on video games for the same reason.

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Case Study
(continued)

- HPI (cont.)
  - Both Mom and patient describe persistent episodes of losing things.
    - Cell phone
    - Video games
    - School assignments

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Case Study (continued)

- HPI (cont.)
  - Mom states that the patient is urinating on the bedroom rug.
    - Patient admits this. He says he gets so focused on video games that he forgets to go to the bathroom.
    - There is no bedwetting, incontinence at school.

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Case Study (continued)

- HPI (cont.)
  - The patient specifically denies anxiety; maintains he just forgets.
  - Otherwise both Mom and patient deny extremes of anger, moodiness, hallucinations, delusions, learning disability or defiance.

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Case Study (continued)

- Physical exam
  - Obese 14-year-old male
    - Estimate Tanner stage 2
  - Grooming/hygiene appropriate
  - Fair eye contact
  - Voice well modulated; speech appropriate
  - Good insight and judgment
  - Persistent left leg tapping during exam

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Diagnostic Criteria for ADD

- Six or more of the following…
  - Fails to give close attention to details or makes careless mistakes in work or other activities
  - Difficulty sustaining attention in tasks
  - Does not seem to listen when spoken to directly

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Diagnostic Criteria for ADD (continued)

- Six or more of the following… (cont.)
  - Does not follow through on instructions and fails to finish schoolwork, chores or duties in the workplace
  - Difficulty organizing tasks and activities
  - Avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort

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Diagnostic Criteria for ADD (continued)

- Six or more of the following… (cont.)
  - Loses things necessary for tasks or activities
  - Easily distracted by extraneous stimuli
  - Forgetful in daily activities

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Diagnosis and Management

- The patient was started on amphetamine salts 10 mg at noon.
- Two-week follow-up
  - Mom and patient reported significant improvement.
- Patient continued regimen.
  - Mom and patient were encouraged to therapy.

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