

# PHARMACOLOGICAL STRATEGIES IN ATTENTION DEFICIT HYPERACTIVITY DISORDER

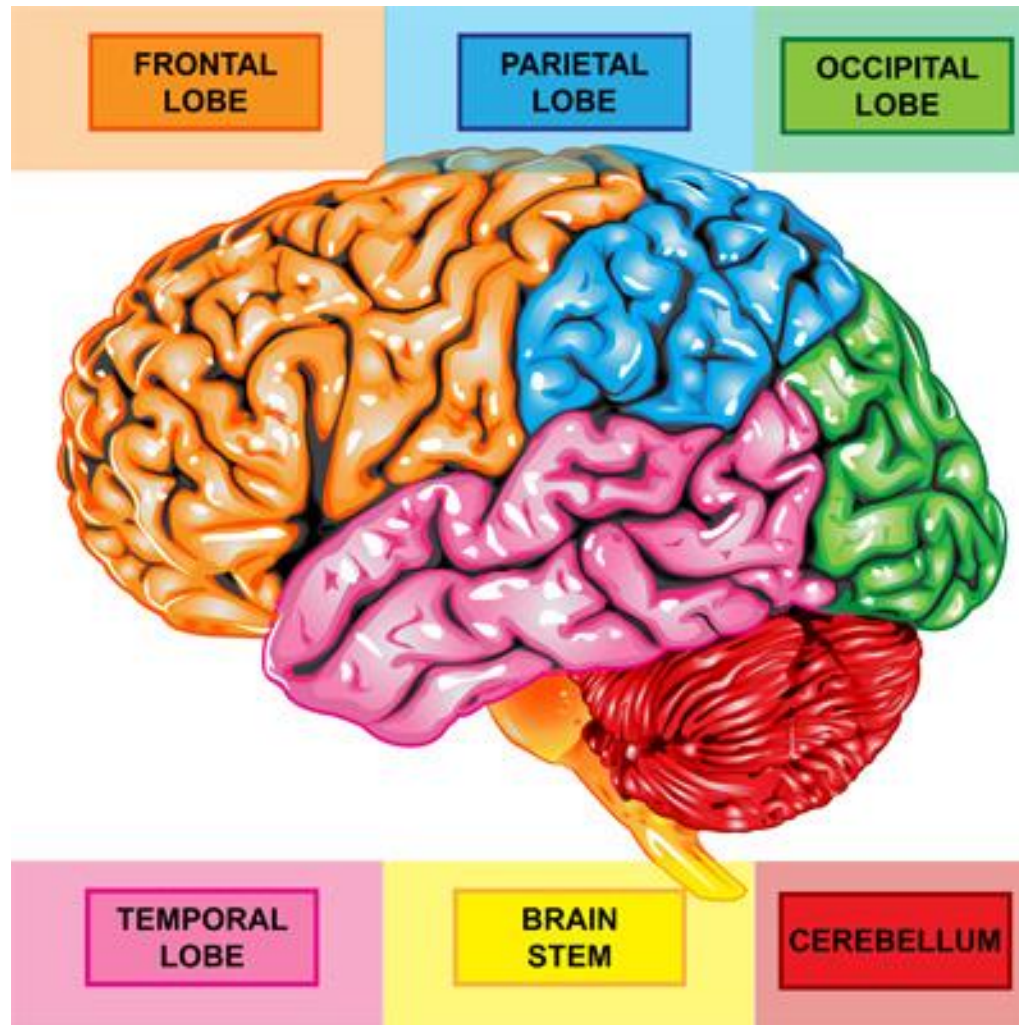
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# Goals of Lecture are to understand:

- The most common medications that are used for treatment of ADHD, how to initiate treatment, monitor and calibrate medication(s).
- Treating uncomplicated ADHD with medication.
- The complexity of ADHD and its co-morbidities and what that means re polypharmacy.
- The importance of school collaboration in calibrating medications.
- The importance of concomitant behavioral and family intervention in medication management.

# ADHD is a Brain-Based Disorder



# Defining ADHD

- “ADHD is a neurodevelopmental disorder defined by impairing levels of inattention, disorganization, and/or hyperactivity-impulsivity.” (DSM-V, p. 32)
- Attention Deficit Hyperactivity Disorder is “a complex impairment of executive functions.” (CHADD Attention! Feb. 2003).

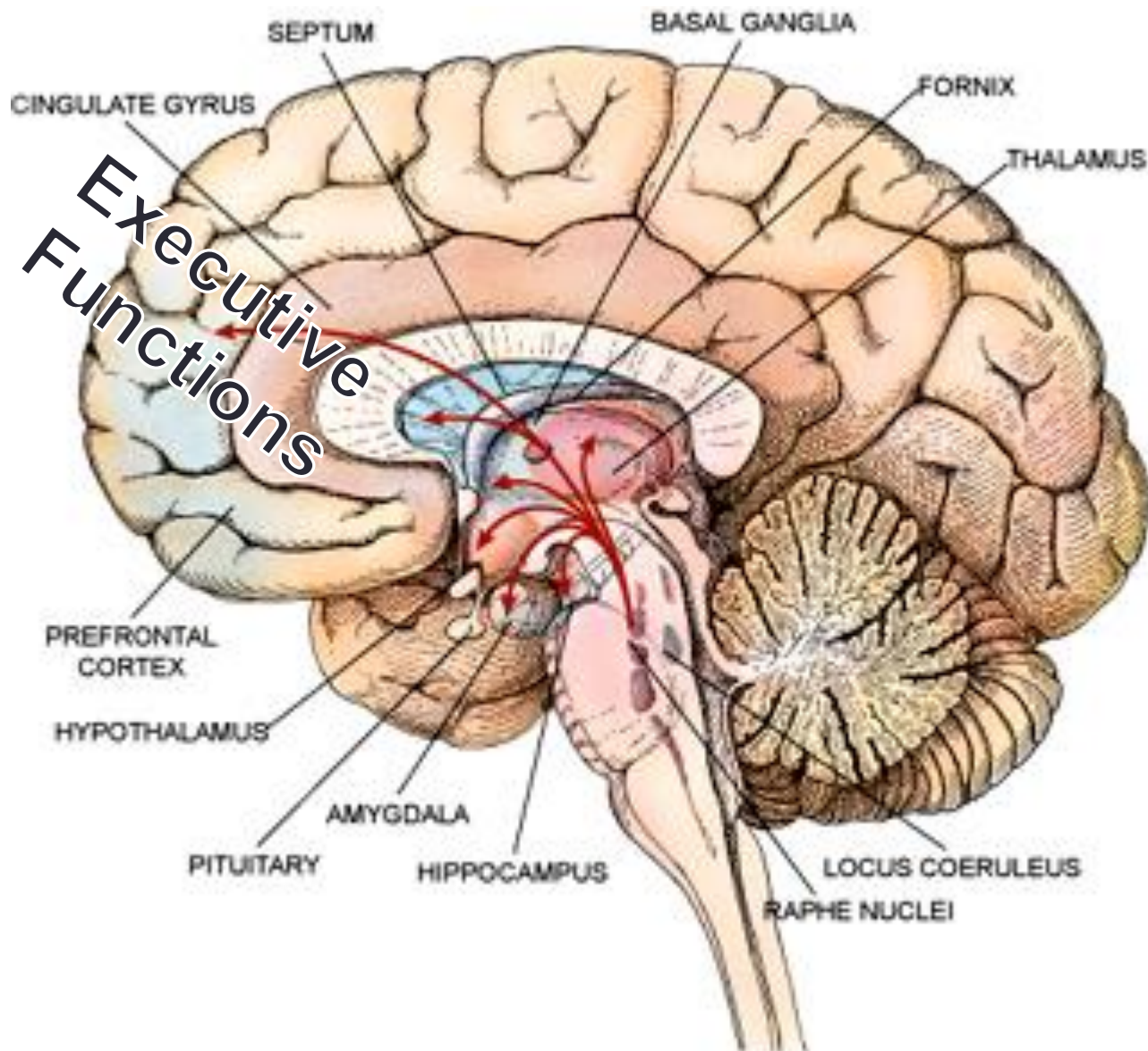
# Lifespan Presentation

- “In ***preschool***, the main manifestation is ***hyperactivity***. ***Inattention*** becomes more prominent during ***elementary school***. During adolescence, signs of hyperactivity (e.g. running and climbing) are less common and may be confined to fidgetiness or an inner feeling of jitteriness, restlessness, or impatience. In ***adulthood***, along with ***inattention*** and ***restlessness, impulsivity*** may remain problematic even when hyperactivity has diminished.” (DSM-V, p. 62)

# Executive Functions

- Organizing
- Prioritizing
- Planning
- Utilizing Working Memory
- Accessing Recall
- Focusing
- Work Initiation
- Sustaining a Task
- Shifting Attention (transitioning)
- Regulating Alertness
- Pacing Oneself (time management)
- Managing Frustration
- Modulating Emotions

# Brain Structures



# Definition of ADHD

- Core Symptoms:

Distractibility

Impulsivity

Hyperactivity



# DSM-V Criteria (APA)

## Inattention:

- 6 required for at least 6 Months:
- Inattention to Details
- Difficulty Sustaining Attention
- Seems Not to Listen
- Fails to Finish Tasks
- Difficulty Organizing
- Avoids Tasks Requiring Sustained Attention
- Loses Things
- Easily Distracted
- Forgetful

# DSM-V Criteria (APA) - Part 2

## Impulsivity/Hyperactivity

**6 or more for at least 6 months:**

- Onset prior to age 12 vs. 7 in DSM-IV
- Difficulty awaiting turn; blurts out answers prematurely
- Unable to stay seated
- Runs about or climbs in inappropriate situations
- Interrupts or intrudes on others
- Fidgets, squirms, taps hands or feet
- Inappropriate running/climbing
- Talks excessively (poor social reciprocity)
- On the go
- Difficulty engaging in leisure activities quietly

# Subtypes of ADHD

- Primarily Hyperactive/Impulsive (more novelty seeking and risk taking; have higher oppositional defiant and conduct disorder problems)
- Primarily Inattentive
- Combined type (shows most impairment)

# Prevalence

- The literature quotes anywhere from 3% to as high as 10% depending on the studies.
- Prevalence rate differs in different countries because of cultural differences, and differences in diagnostic criteria and in case finding.
- DSM-V reports that population surveys “suggest that ADHD occurs in most cultures in about 5% of children and 2.5% of adults.”

# Gender Disparity

- Because girls are less likely to be hyperactive, they are not identified as readily as boys.
- Girls are more likely to be dismissed as “daydreamers” or “space cadets.”
- The research is now attempting to do a better job of identifying girls.

# Gender Disparity – Part 2

“Both sexes are equally prone to the disorder.” (Zametkin, NIMH)

- Ratio of males to females reported to be 2:1 in childhood and 1.6:1 in adulthood.
- Girls are underdiagnosed and show 2x prevalence of inattentive type vs. boys.  
(Newcorn, J. Mt. Sinai)

# ADHD EVALUATION

- Evaluation must also assess for :
  - Anxiety & Depression
  - Tourette's & Obsessive-Compulsive Disorder
  - Post Traumatic Stress Disorder and other psychiatric conditions
  - Specific Developmental Disorders
  - Neurologic Disorders

# Co-morbidities

## **Most Common:**

- Oppositional Defiant Disorder (*highest*)
- Depression
- Anxiety
- Learning Disabilities
- Conduct Disorder

## **Also Seen Clinically:**

- Impulsive aggression
- Tourette's Disorder
- Obsessive Compulsive Disorder
- Substance Use Disorders
- Bipolar Disorder



# ADHD & Bipolar

- Very active research ongoing to define bipolar in children and to determine the prevalence.
- NIMH study selected 1/9 referred subjects for their bipolar study.
- Research has not shown strong association.
- Attentional difficulties in both entities.
- Disruptive Mood Dysregulation D/O added to DSM V in differential diagnosis with Bipolar D/O.

# ADHD Research

- Well researched entity.
- MTA study is most comprehensive done to look at treatment efficacy and effectiveness in the community setting.
- Multisite longitudinal study followed 600 subjects to determine what might be the optimal treatment paradigm for children with ADHD.

# MTA Study

- Treatment can be effective, but found less benefit of medication on adult symptom severity.
- Poorer community outcomes were attributed to poor adherence to systematic monitoring and adjustment of medications over the study period.
- ***Community subjects were more likely to get sub-optimal doses of medication and not to receive trial of another medication as was done in the MTA if initial medication was not effective.***

# ADHD Research (MTA)

## Other Findings

Variables that influenced outcomes included:

- Parental affective illness
- Aggressivity
- Co-morbidities, especially disruptive behavior disorders (CD, ODD).

# Additional ADHD Research

- Relatives of children with ADHD have higher risk of ADHD and the corollary is true.
- Family history of higher rates of school failure, learning disabilities and impairments in intellectual functioning.
- Twin studies show increase rate of ADHD in monozygotic twins versus dizygotic twins.
- Adoptive relatives have decreased risk of ADHD compared to biological relatives.

# ADHD Research – Part 2

- No single cause
- No single gene
- Dopamine transporter gene implicated
- Thyroid receptor gene also implicated
- Genetic heterogeneity most likely
- Environment plays a role

# ADHD & Lifespan

- ADHD “frequently persists and is associated with significant psychopathology and dysfunction in later life.” (Biederman)
- Adults with ADHD have high familial occurrence and psychiatric co-morbidities.
- Early treatment in childhood can change the trajectory of a person’s life.

# The Child with ADHD

“Parenting a child with ADHD can be stressful, demanding and exhausting.”

Hester, N (CHADD Attention! Feb. 2003)



# When Is Medication Considered?

- After evaluation by a mental health specialist e.g. child psychiatrist, specialist nurse practitioner, child psychologist or child trained psychiatric social worker.
- After an evaluation by qualified physician: child psychiatrist, pediatrician, developmental pediatrician or pediatric neurologist.
- For adults, would recommend referral for psychological or neuropsychological testing. Insurance companies tend to require it now to approve stimulant medication in newly diagnosed adults.

# What Does Medication Do?

- Helps individual to focus attention.
- Decreases hyperactivity.
- Decreases impulsivity.
- Because individual is more attentive, s/he can listen, follow directions and comply better with programmatic demands.
- Adults report significant improvement in focusing and completing tasks. Medication dosing has to be highly individualized to lifestyle/work demands e.g college students.

# TREATMENT OF ADHD

- Stimulant medications remain the first choice after >50 years!: Dextroamphetamine and derivatives; methylphenidate and derivatives.
- OROS delivery method has gained popularity as it makes several daytime doses un-necessary and decreases need for in school administration.
- SR/ER dosing delivery systems also preferred for same reason.
- Most young patients reject the patch!

# TREATMENT OF ADHD

- ***Uncomplicated ADHD:*** This is truly a wonderful thing when it happens, and it does! This means that there are no complex psychosocial issues, no learning disabilities, no other medical issues, and you simply have to prescribe medication to mitigate the distractibility, hyperactivity (if present), impulsivity and the patient functions optimally and successfully!

# ADHD: Medication cont'd

- Clonidine & guanfacine, FDA approved, are blood pressure medications, also effective for more highly impulsive sub-types. Extended -release preparations preferred to be used at bedtime since have secondary effect of promoting improved sleep, often an issue for individuals with ADHD.
- Side effects must be considered before starting usage, e.g. clonidine and guanfacine are highly sedating and can impair child's ability to stay awake in the classroom. Adults experience similar side effect which compromises work. (Describe students asleep for entire morning).

# TREATMENT OF ADHD: CONT'D

- Non-stimulant **atomoxetine** takes longer (4 to 6 weeks) to calibrate and to have desired effect but useful when adverse side effects of stimulants are intolerable.
- Anti-depressants: **imipramine & bupropion**: not often used but in patients with comorbid depression can be useful. ***Imipramine & cardiac issues.***
- **Viloxazine**: new non-stimulant with promising results. Has sedating side effect so can be given at bedtime.

# Initiating Medication

- Educate patient and family, get informed consent to proceed with medicating.
- “Start low, go slow!” Use immediate release preparation to start. I start on weekends when parents available to observe side effects.
- Advise patient/family re your expectations, i.e. no major immediate change, but monitoring for side effects.
- Calibrate medication upwards; monitor and increase until stable.
- Shift to long lasting preparation i.e. OROS, SR or ER for once/daily dosage.

# ADHD: Medication cont'd: Treating co-morbidities

- With high comorbid impulsivity and aggression, combining a stimulant medication with an alpha agonist such as clonidine or guanfacine may improve outcomes.
- When depression and/or anxiety are co-morbid, using an SSRI such as sertraline or fluoxetine after ADHD stabilization may be useful.
- When OCD, bipolar d/o, substance use d/o, or Tourettes is co-morbid, pharmacological management becomes challenging and is best referred to a specialist.



# Treatment of ADHD cont'd

- Psycho-education is important so that identified patient and family understand ADHD, its impact on all areas of functioning and on family.
- Look for residual ADHD in adult family members and, if present, refer for evaluation & treatment.
- Environmental manipulation (decrease overstimulation) and behavioral management (to decrease negative behaviors and increase positive behaviors) often necessary. ***Address sleep issues prior to medicating.***
- Need for accommodations (IDEA); FMLA for parents.
- Refer to helpful organizations e.g CHADD or local self-help groups.

# Monitoring for Side Effects

- Headache and stomach-ache may be likely complaints. Having breakfast and having fluids should be encouraged.
- Decreased appetite, especially at lunchtime is common. I encourage eating a fruit, yogurt, crackers etc.
- Rebound appetite in the evening often occurs. Encourage parents to provide adequate healthy meal.
- Mood changes have been reported. May improve with time.
- Concerns of growth have remained with some research showing a decrease. This should be monitored. Over 40 years I have not seen this to be a problem in my patients, many now adults.
- If there are cardiac concerns *apriori*, consult with patient's cardiologist to help decide on medication management.

# Shortage of supply of stimulant medications

- This has remained a significant problem since COVID and has caused providers to make medication changes to whatever drug may be available. This results in disruption in treatment and instability in patients.

## Cases from my files:

- Cases of teacher, lawyer and physician: difficulty completing tasks, passing certifying exams.
- Children & father with ADHD.
- Multiple issues may be in play here: task initiation, time management, learning disabilities, other co-morbidities.
- ***Toll on self-esteem!!***

# Cultural Barriers to Treatment

*When medications are offered as first line intervention:*

- African Americans are reluctant to use “drugs” prescribed for “behavior.” Students at therapeutic school.
- Hispanic population is less inclined than whites to take medications.
- Caribbean and African families tend to think of the behaviors as being willful and the children in need of harsher discipline.

# ADHD: Family Issues

- How are parents and other family members affected by identified child with ADHD?
- Family adaptation is disrupted with treatment and change may be resisted.
- What if the family refuses medication trial?
- Are there “natural” treatments?
- Be patient : educate and model.

# Summary

- **ADHD is REAL!** And so is **STIGMA!**
- It is not a simple issue. *Morbidity is high, and affects many across the lifespan.*
- There is excellent research on the issue.
- Diagnosis and treatment are available.
- Medications are effective!
- Case finding is not as good as it should be.
- Education of families, physicians, teachers, and employers should be a major effort.
- Education of legislators is necessary so that they facilitate, not hinder access to treatment.

# Suggested Readings

1. ADHD: A Complex Disorder of the Brain's Self-Management System. (*Psychiatric News*, October 2021; pp17-20 by Thomas E. Brown, Ph.D.).
2. Boland H; DiSalvo M. et al. (2020) A literature review and meta-analysis on the effects of ADHD medications on functional outcomes. *J Psychiatr Res Apr: 123:21-30. doi:10.101/j.psychires.2020.01.006*
3. Cherkasova, MV et al. (2022) Review: Adult Outcome as Seen Through Controlled Prospective Follow-up Studies of Children With Attention-Deficit/Hyperactivity Disorder Followed Into Adulthood. *J Am Acad Child Adolesc Psychiatry 61(3):378-391.*
4. Drechsler R, Brem S. et al (2020) ADHD: Current Concepts and Treatments in Children and Adolescents. *Neuropediatrics 2020;51:315-335*
5. Park J, Amaladoss N.: Dietary Interventions for ADHD: Emerging Research and Considerations. (*Psychiatric Times*, July 18, 2022).



# Suggested Readings – Part 2

6. Groenman AP et al. (2022). An Individual Participant Data Meta-analysis: Behavioral Treatments for Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. *J Am Acad Child Adolesc Psychiatry* 2022;61(2): 144-158.

7. Larsen LB et al. (2021). Effect of Parent Training on Health-Related Quality of Life in Preschool Children With Attention-Deficit/Hyperactivity Disorder: A Secondary Analysis of Data From a Randomized Controlled Trial.

*J AM Acad Child Adolesc Psychiatry* 2021;60(6):734-744.

8. Blader JC, Pliska SR et al (2021). Stepped Treatment for Attention-Deficit/Hyperactivity Disorder and Aggressive Behavior: A Randomized, Controlled Trial of Adjunctive Risperidone, Divalproex Sodium, or Placebo After Stimulant Optimization. *J AM Acad Child Adolesc Psychiatry* 2021;60(2): 236-251.

# Suggested Readings – Part 3

9. Sibley MH, Coxe SJ *et al.* (2022) Predictors of Treatment Engagement and Outcome Among Adolescents With Attention-Deficit/Hyperactivity Disorder: An Integrative Data Analysis. *J Am Acad Adolesc Psychiatry* 2022:61(1) 66-79.
10. Sibley MH, Kuriyan AB *et al.* (2014) Pharmacological and psychosocial treatments for adolescents with ADHD: An updated systematic review of the literature. *Clin Psychol Rev* 2014:34:218-232.
11. Swanson JM, Arnold LE, Molina BSG *et al.* (2017) Young adult outcomes in the follow up of the multimodal treatment study of attention-deficit/hyperactivity disorder: Symptom persistence, source discrepancy, and height suppression. *J Child Psychol Psychiatry*. 2017:58:663-678. <https://doi.org/10.1111/jcpp.12684>