# THE NEUROBIOLOGY OF ADHD – UNDERSTANDING THE BASICS

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# OBJECTIVES

- Understand the neurophysiology of attention
- Differentiate atypical attention from inattention
- Outline the clinical criteria required for the diagnosis of ADHD
- Identify the variety of cognitive pathways involved in ADHD symptomatology
- Utilize these pathways to target meaningful clinical techniques for management of ADHD

# WHAT IS ATTENTION?

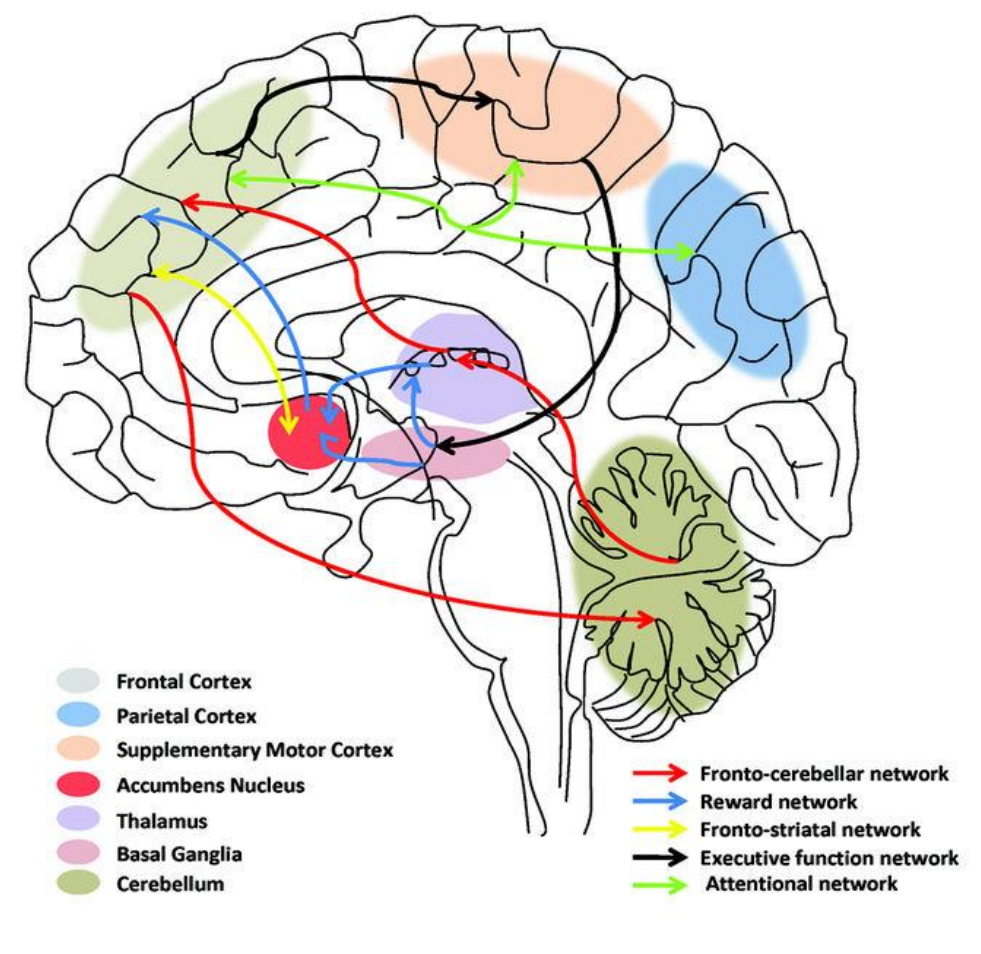
*"the taking possession by the mind, in clear and vivid form, of one out of what may seem several simultaneously possible objects or trains of thought. …It implies withdrawal from some things in order to deal effectively with others."*
*William James, The Principles of Psychology, 1890*

# THE COMPONENTS OF ATTENTION

Posner and Petersen (1990; Petersen & Posner, 2012)

- Alerting/arousal
  - Provoking consciousness
- Spatial orientation
  - Drawing attention to specific sensory inputs
- Executive function
  - Maintaining focus
  - Inhibiting distractions
  - Includes working memory, inhibitory control and cognitive flexibility

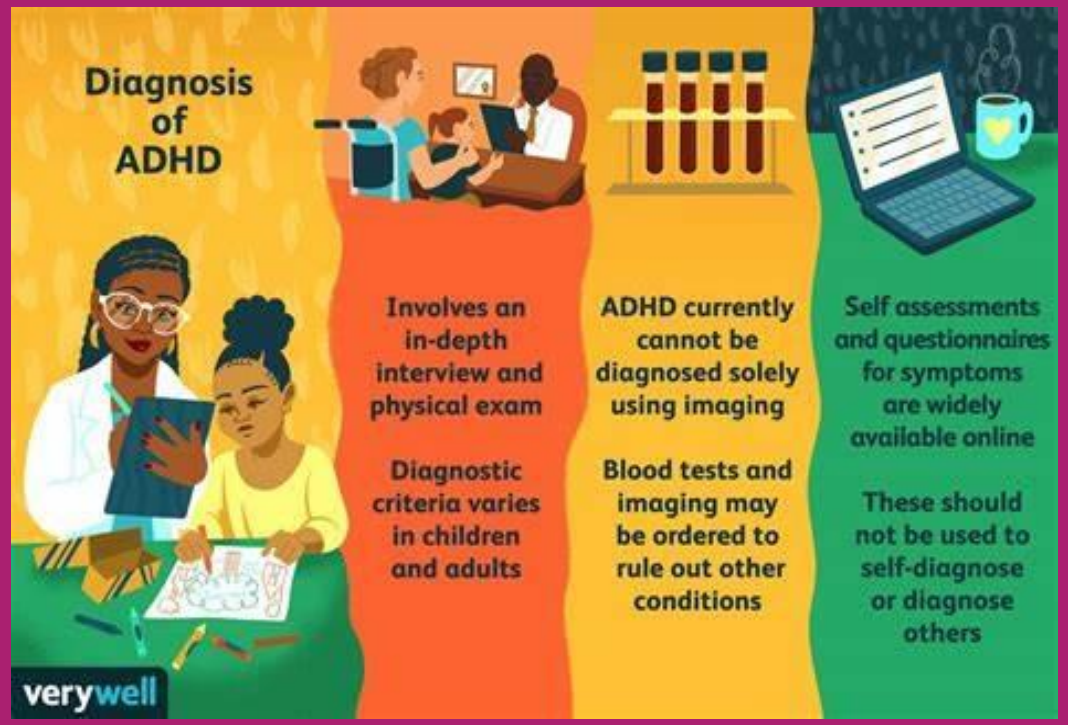
# THE NEURAL CIRCUITRY OF ATTENTION




1. Arousal
    a. Mediated by norepinephrine secretion in the locus coeruleus
2. Spatial orientation
    a. Involves connections between the parietal lobe and the frontal eye fields
3. Executive function
    a. Connections within the frontal lobe, to the anterior cingulate, and top-down influences
    b. Mediated by dopamine

Image courtesy of Purper-Ouakil et al., 2011

# DIAGNOSING ADHD



# DSM-V CRITERIA

Inattention: >= 6 symptoms of inattention for children up to age 16 or >= 5 symptoms for children over 17 and adults; present for >= 6 months and inappropriate for developmental level

- Careless mistakes
- Difficulty holding attention on tasks or activities
- Does not appear to listen when spoken to directly
- Fails to follow through on instructions and fails to finish tasks
- Difficulty with organization of tasks or activities
- Difficulty with tasks requiring prolonged mental effort
- Frequently loses things necessary for tasks or activities
- Easily distracted
- Often forgetful in daily activities

# DSM-V CRITERIA

Hyperactivity/Impulsivity: >= 6 symptoms of hyperactivity/impulsivity for children up to age 16 or >= 5 symptoms for children over 17 or adults; present for >= 6 months to an extent that is disruptive and inappropriate for developmental level

- Fidgeting
- Difficulty staying in seat
- Running or climbing in inappropriate situations
- Unable to perform leisure activities or play quietly
- Always “on the go”
- Talks excessively
- Interrupts constantly

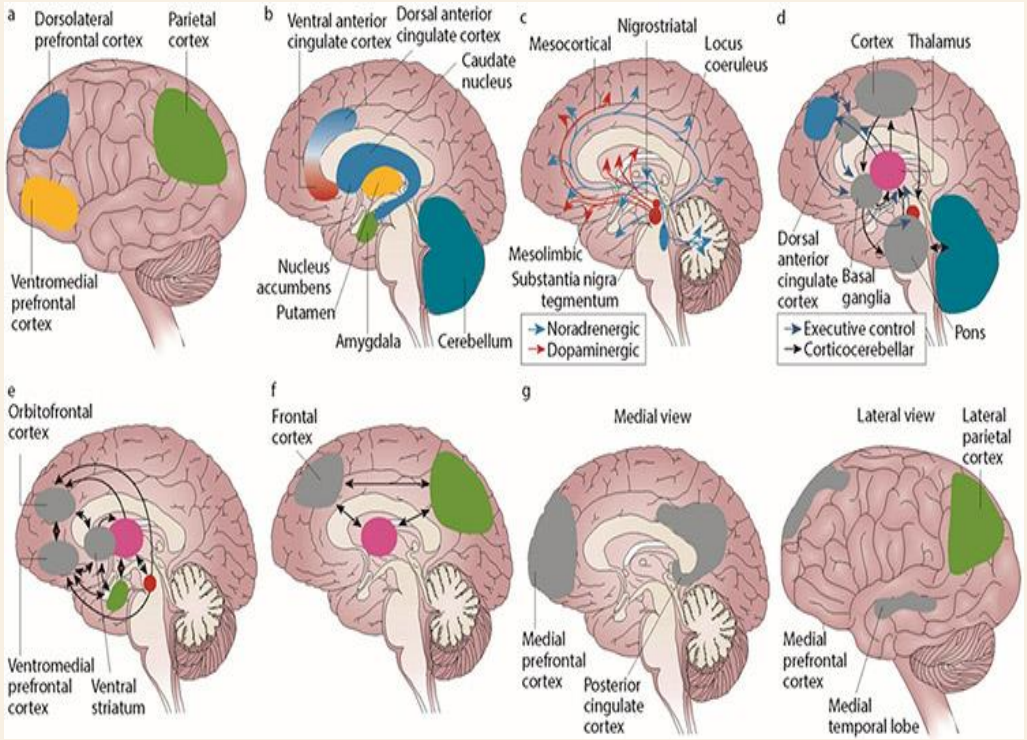
# DYSFUNCTIONAL ATTENTION (NOT ABSENCE OF ATTENTION)

- He seems to have strong academic potential but interrupts in class frequently and cannot sit still
- Distraction to other students and teacher ("class clown")
- At home, he loves to climb the backyard trees, and jump on the trampoline, which has resulted in many skinned knees and a few trips to the ER for stitches.
- He drives his parents crazy watching a few minutes of one show and then changing the channel, over and over again
- But he could play Minecraft for hours!!!

# DYSFUNCTIONAL ATTENTION (NOT ABSENCE OF ATTENTION)

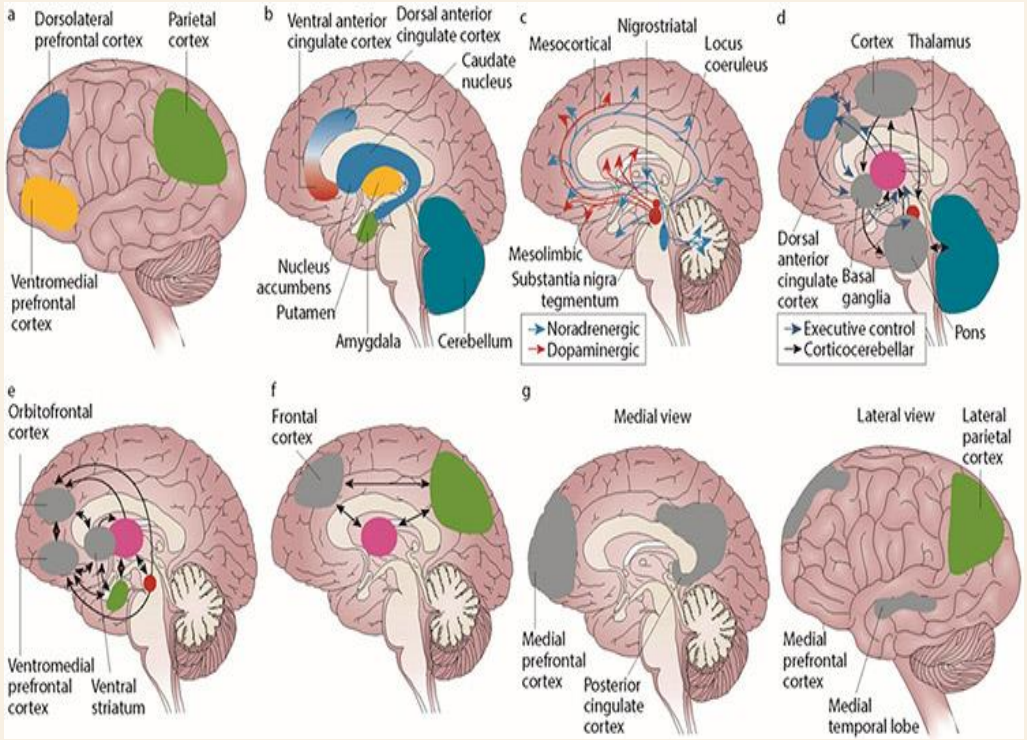
- She has model behavior in class. She is never disruptive to others.
- She can appear disengaged in school, seeming to daydream frequently. But when called on, she always knows the answer.
- Has difficulty turning in assignments on time, usually because she finished but left it at home.
- At home, she cannot seem to complete a series of tasks, and often has to ask for reminders of what she was doing.
- Loves to read. She has started several chapter books (but only completed one or two).

# THE NEUROBIOLOGY OF CLINICAL SYMPTOMS



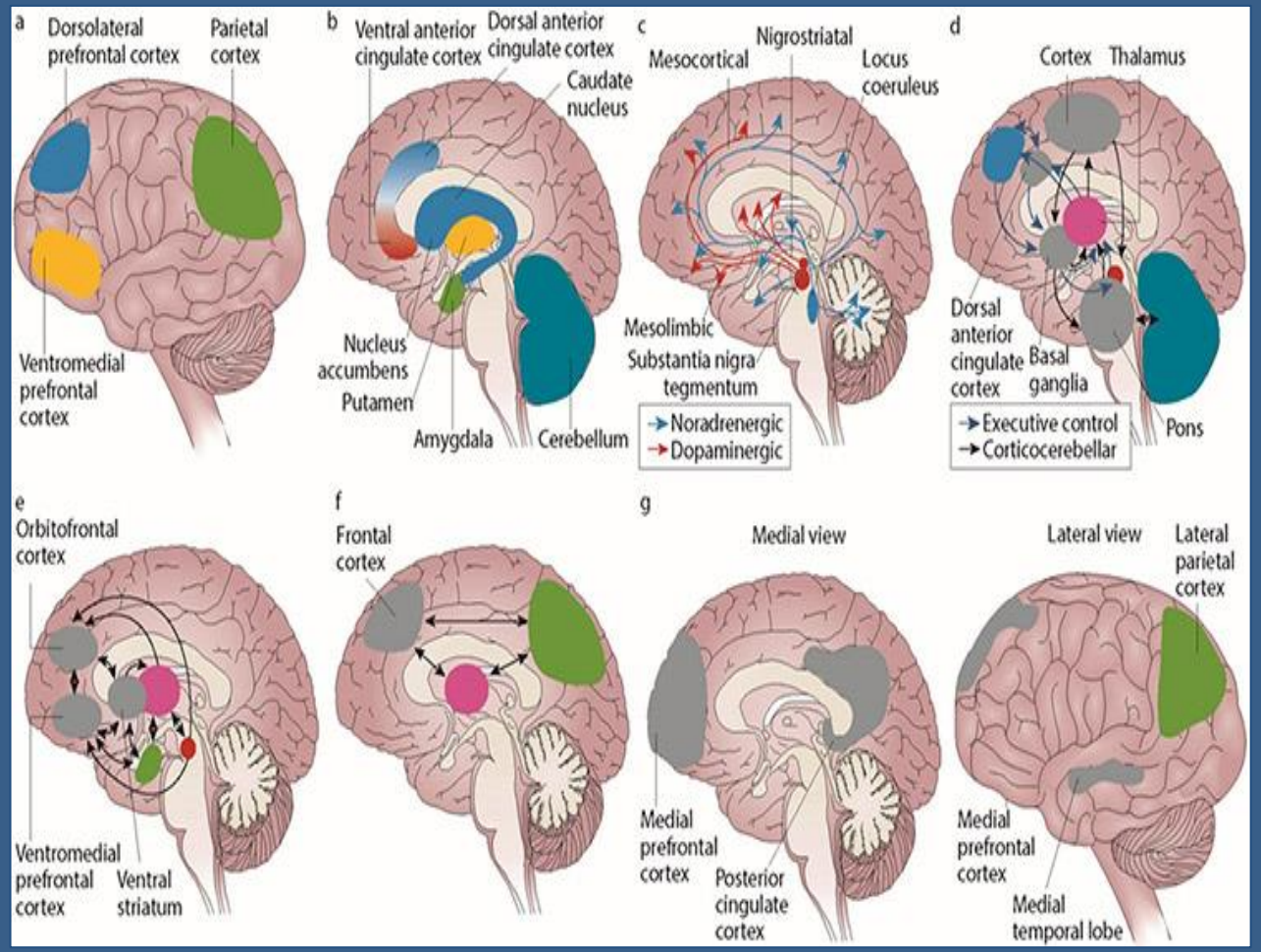

- Cortex
  - Dorsolateral prefrontal cortex is involved in **working memory**
  - Ventromedial prefrontal cortex is involved in **complex decision making**
  - Parietal cortex is involved in orientation of **attention**
  - Neuroimaging studies show structural and functional differences in these areas of the brain in ADHD
- Cortico-Cerebellar Circuitry
  - Assist **in planning, goal-directed behavior, inhibition, working memory, and adaptation to context**
  - These connections are underactivated and have lower functional connectivity in individuals with ADHD

# THE NEUROBIOLOGY OF CLINICAL SYMPTOMS




- Reward Network
  - Ventromedial prefrontal cortex
  - Orbitofrontal cortex
  - Circuitry involving thalamus, amygdala and dopaminergic neurons
  - Involved in **motivation and response to reward.**
  - Behavioral and neural responses to reward are atypical in individuals with ADHD
- Alerting Network
  - Frontal and parietal cortex
  - Circuitry involving the thalamus
  - Involved in **initiation of attention** and functional connectivity is weaker in individuals with ADHD

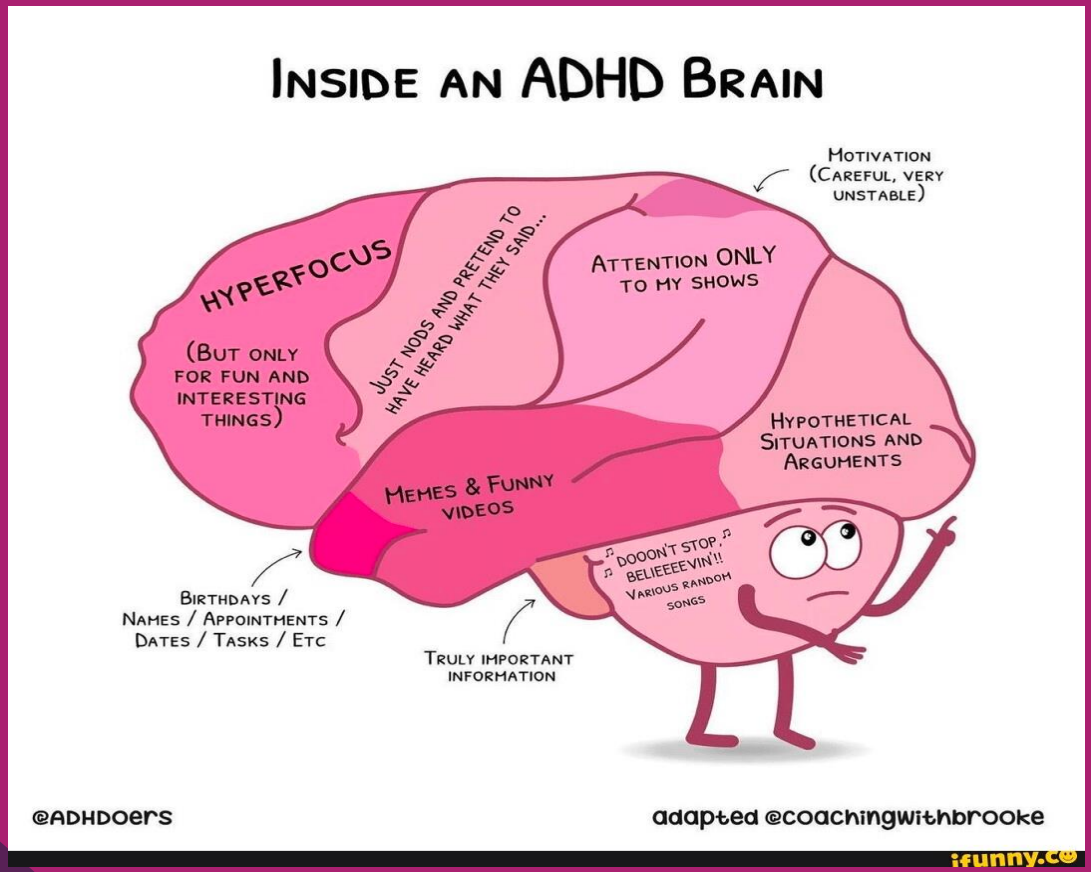
# THE ROLE OF NEUROTRANSMITTERS IN ATTENTION



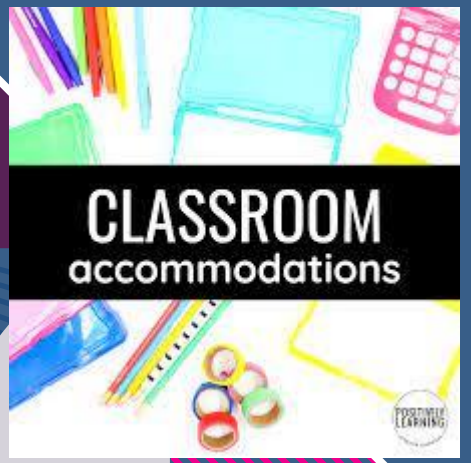

1. The Dopamine System
   a. Planning and initiating of motor systems
   b. Activation
   c. Switching Tasks
   d. Reacting to Novelty
   e. Processing of Reward

2. The Norepinephrine System
   a. Arousal modulation
   b. Signal to noise ratio
   c. State dependent cognitive activation
   d. Activation of cognitive processes during urgency

# WHY DOES THE NEUROSCIENCE MATTER?



# MANAGING ADHD




# MANAGEMENT IS INDIVIDUALIZED AND MULTI-DISCIPLINARY

# MULTI-MODAL TREATMENT APPROACH

- Educational Strategies
- Psychotherapeutic interventions
- Family based therapies (Parent Management Training)
- Medication Management

# EDUCATIONAL STRATEGIES

Campeno-Martinez et al. (2017) studied the effect of an educational intervention on Spanish children ages 7-10 diagnosed with ADHD

Intervention: Educational Intervention Program to Increase Attention and Reflexivity (Gargallo, 2000)

- 25 sessions, 2 sessions per week, 20-30 minutes each
- Contains "questions with uncertain responses and problems with alternative solutions in which the response in not immediately obvious. The intervention techniques used include enhancement of time delay, attention and discrimination; and increase in problem-solving capacity, analysis of detail, response delay, verbal self-monitoring, analysis of detail, and use of cognitive strategies." (Campeno-Martinez et al., 2017, p. 68).

Outcome measure: scores on rating scales (EMA-DDA) as measured by teachers and parents

- Subscales of ADHD-hyperactivity, ADHD-inattention, Aggressivity, Social Isolation, and Anxiety

Results

- Decreased aggressivity reported by teachers
- Decreased social isolation reported by parents
- Trend towards decreased ADHD symptoms

# PSYCHOTHERAPEUTIC INTERVENTIONS

Veenstra, van Geert, & van der Meulen (2012) studied improvement on a computer task looking at behavior with a computer mouse in a groups of ADHD, ASD and typically learning Dutch children ages 3-6

Intervention: computer game of "Hide and Seek" where children are instructed to click on objects to find a specific person

Outcome: assessment of 6 behaviors

1. Incorrect object clicks (errors)
2. Number of clicks during instruction moments (response inhibition)
3. No clicks during clicking moments (response inhibition)
4. Response times (reaction times)
5. Number of clicks during clicking moments (response inhibition)
6. Repeated clicks on the same object (perseveration)

Results

- Children with ADHD experienced improvements in reaction time, errors, response inhibition and perseveration over repeated trials

Conclusion: Computer programs designed to improve executive function can lead to behavior change in ADHD children

# PARENT MANAGEMENT TRAINING

- Meta-analysis published in 2019 found parent training for preschool children with ADHD was associated with
  - Moderate reduction in parent reported ADHD
  - Moderate reduction in conduct problems
  - Small reduction in negative parenting
  - No significant  difference for independently assessed ADHD symptoms

Rimestad ML, Lambek R, Zacher Christiansen H, Hougaard E, 2019. Short- and Long-Term Effects of Parent Training for Preschool Children With or at Risk of ADHD: A Systematic Review and Meta-Analysis. *J Atten Disord* 23, 423–

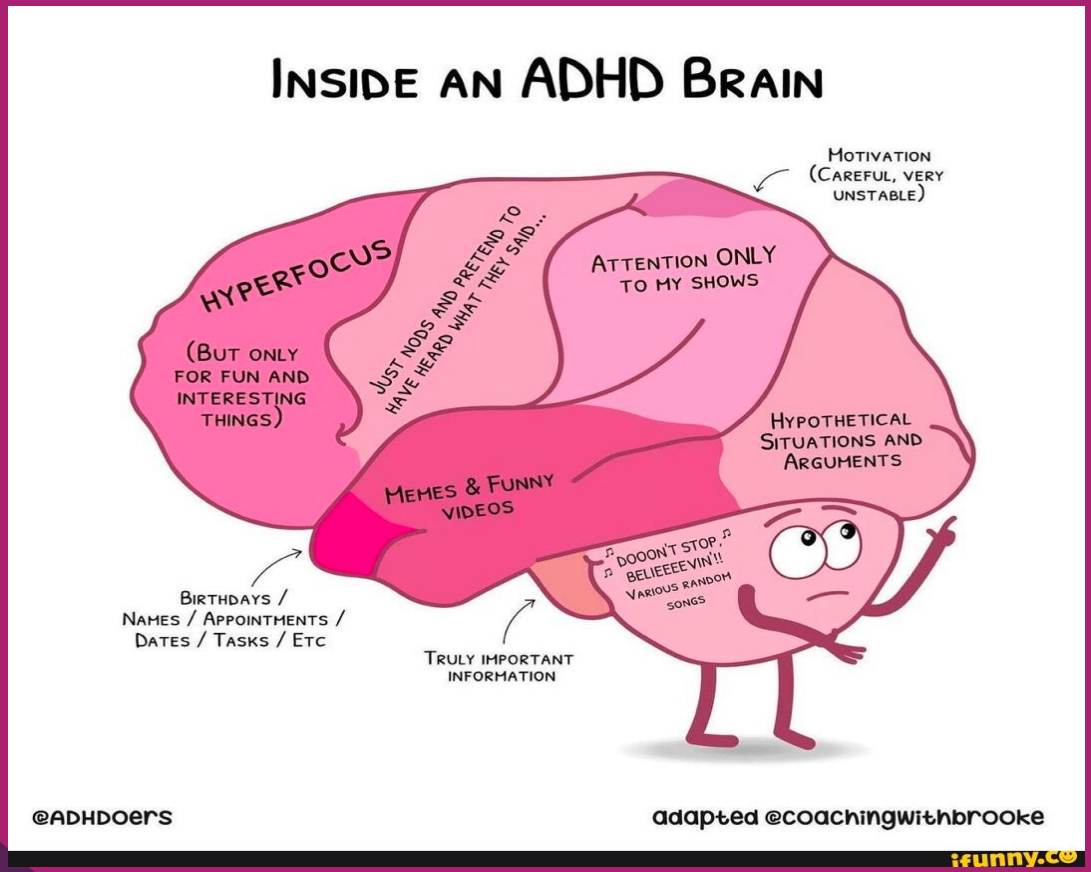
# PHARMACOLOGIC INTERVENTIONS



**Table 1**
Overview of available medications for treatment of ADHD.

| | Substance | (Likely) mode of action | Major adverse effects | Parameters to be monitored under therapy | Potential advantages | Potential disadvantages |
|---|---|---|---|---|---|---|
| Stimulants | Methlyphenidate, lisdexamfetamine | Reuptake inhibition (plus release in amphetamines) of dopamine and norepinephrine | Decreased appetite<br>Sleep disturbances<br>Increased blood pressure and pulse<br>Headaches<br>Irritability<br>Stomach pain | Height<br>Weight<br>Pulse<br>Blood pressure | Large effect sizes for reducing ADHD core symptoms<br>Rapid onset of treatment effects<br>Available in short-acting and various long-acting formulations<br>Chewable tablets, liquid formulations and transdermal patches available<br>Positive effects on conduct disorder and oppositional defiant disorder | Limited daily duration of effects<br>Partial potential for rebound of symptoms when effect wears off in the afternoon/evening<br>Controlled substance |
| Non-stimulants | Atomoxetine | Norepinephrine reuptake inhibition | Decreased appetite<br>Headache<br>Stomach pain<br>Nausea<br>Vomiting<br>Sleep disturbances<br>Increased blood pressure and pulse | Suicidality<br>Clinical worsening<br>Unusual changes of behavior<br>Especially during the first few months of treatment or at times of dose change<br>Pulse<br>Blood pressure | "Around-the-clock" effects<br>Uncontrolled substance<br>Possible first-line option in comorbid substance use disorders, disruptive behavior disorders, tic/Tourette's disorder<br>Augmentation of stimulant treatment possible | Smaller effect size in comparison to stimulants<br>6–12 weeks until effects are observed |
| | Clonidine, guanfacine | Agonism at alpha-2 adrenergic receptors (leading to enhanced noradrenergic neurotransmission) | Somnolence/sedation<br>Fatigue<br>Hypotension<br>Bradycardia<br>Irritability<br>Insomnia | Pulse<br>Blood pressure | "Around-the-clock" effects<br>Uncontrolled substance<br>Possible first-line option in comorbid sleep disorder, substance use disorder, disruptive behavior disorders, tic/ Tourette's disorder<br>Augmentation of treatment with stimulants possible<br>Clonidine: transdermal patch available | Smaller effect size in comparison to stimulants<br>2–4 weeks until effects are observed<br>Somnolence/sedation frequent adverse effect (administration in the evening preferable)<br>Clonidine: twice daily dosing necessary |

# WHY DOES THE NEUROSCIENCE MATTER?



# THE NEUROBIOLOGY OF ADHD

- Clarifying the neurobiological underpinnings of attention
- Understanding atypical cognitive and executive function
- Tailoring the interventions needed for the individual

# FUTURE RESEARCH

- Clarifying subtypes of clinical ADHD
- Gender and age based evaluations and normative data
- Integrating advanced technologies such as functional MRI into the diagnostic process
- Using pharmacogenetics to individualize medication management

# QUESTIONS?

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