Psychopharmacology Update 2023:
A Comprehensive Look at the Neuroscience of Psychotropic Medications- Psychiatric Disorders
Session II

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Basic points we'll cover today:

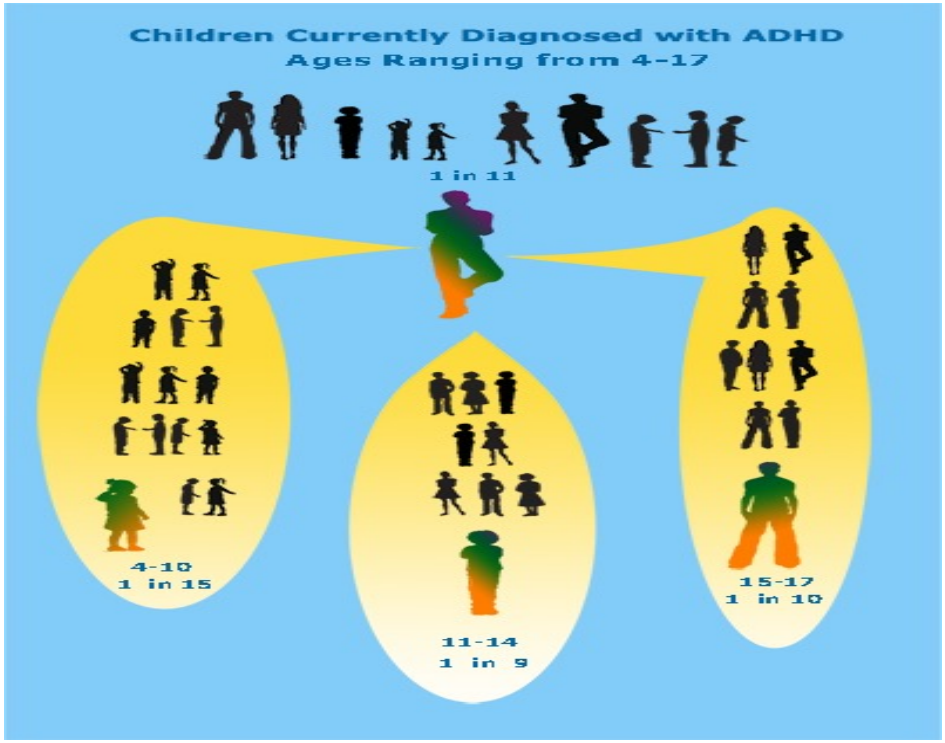
- **What's New In Psychopharmacology**
- **Updated Antidepressant Drug Drug Interactions**
- **Neurobiology of Depression**
- **Antidepressants**
- **Ketamine Psychopharmacology**
- **Antipsychotics**
- **ADHD Psychopharmacology and Medications**
- **Anxiety**
- **SUDS/Shame/Trauma Psychopharmacology**
- **CBD in the Treatment of Mental Disorders**
- **Questions**

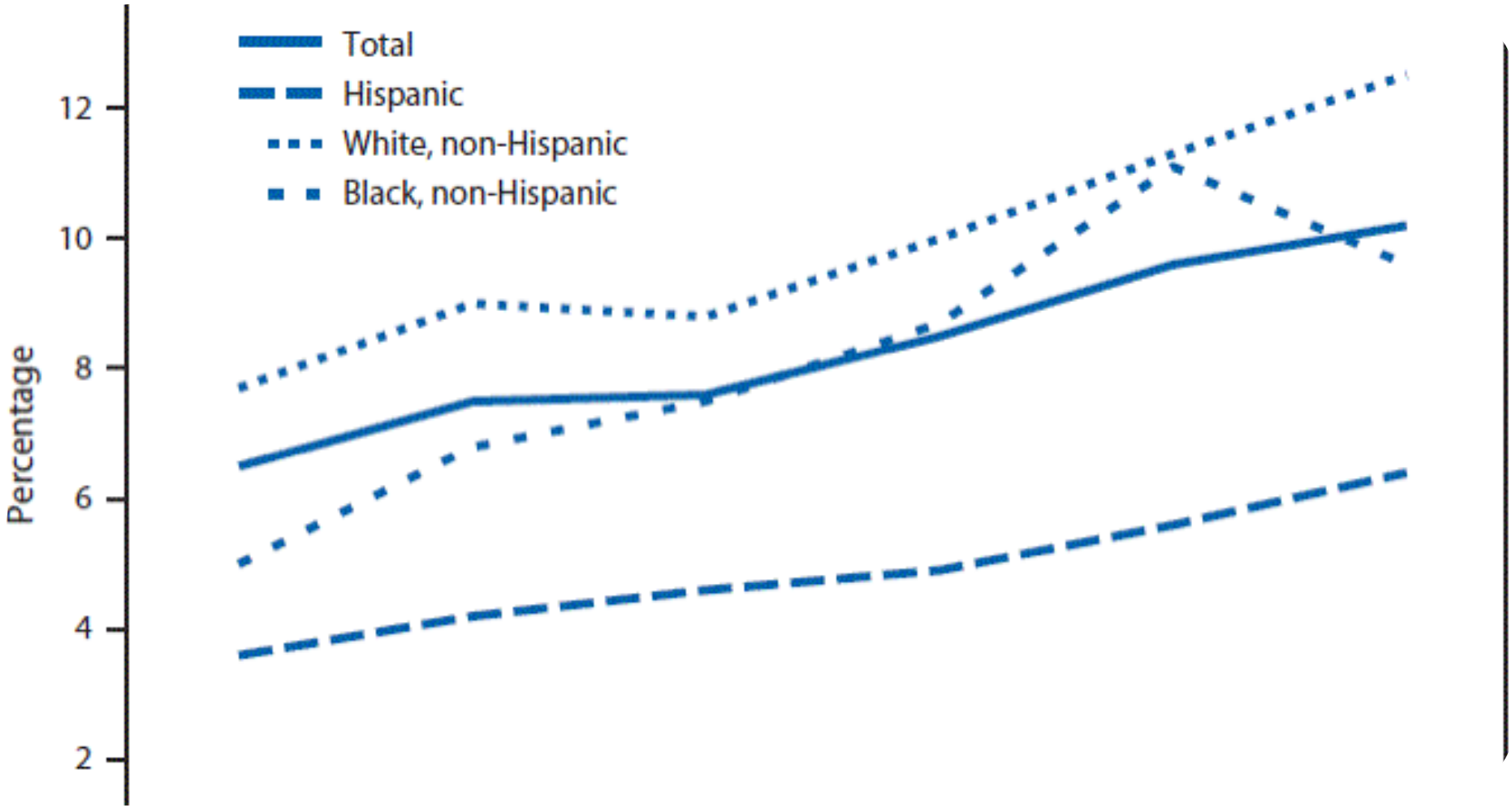
ADHD Psychopharmacology and Medications-2023

ADHD Apps

- **Best overall:** SimpleMind Pro – Mind Mapping
- **Best for setting reminders:** Due – Reminders & Timers
- **Best for taking and organizing notes:** Evernote
- **Best for reducing overwhelm:** Remember the Milk
- **Best for collaboration:** Asana
- **Best for managing your to-do lists:** Todoist
- **Best for pomodoro:** Brain Focus
- **Best for project tracking:** Trello
- **Best for simplicity:** Clear Todos
- **Best for security:** Bear
- **Best for productivity:** Productive – Habit Tracker
- https://www.healthline.com/health/adhd/top-iphone-android-apps

Children Currently Diagnosed with ADHD Ages Ranging from 4-17




Total
Hispanic
White, non-Hispanic
Black, non-Hispanic
Percentage
12
10
8
6
4
2

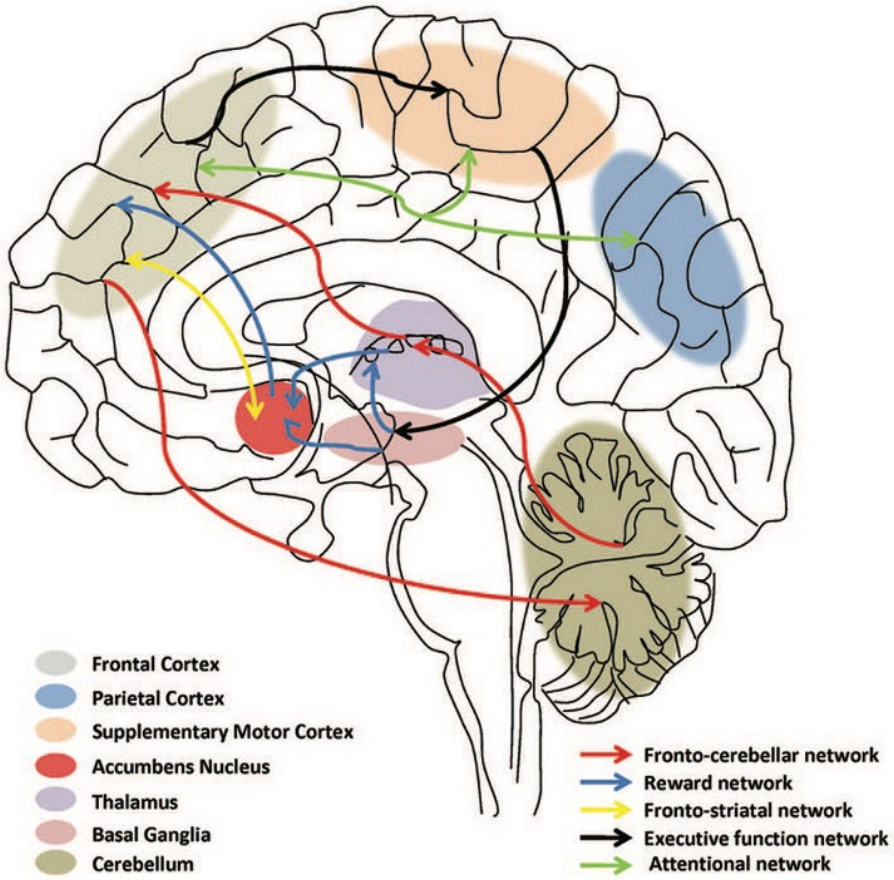
Adults with ADHD in US

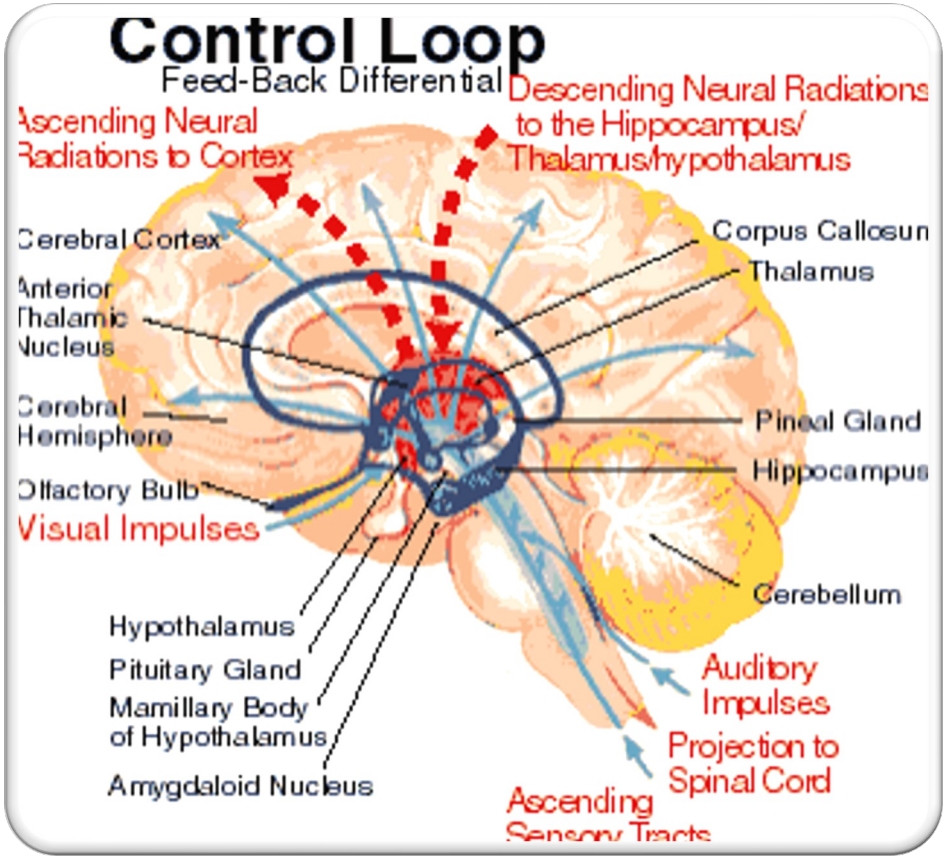
- According to a screen for ADHD in 3,199 adults aged 18–44 from the **National Comorbidity Survey Replication (NCS-R)**, 4.4% of US adults have ADHD. Of these adults with ADHD, 38% are women and 62% are men (Kessler et al. 2006).
- A systematic review and meta-analysis of 14 studies that included over 9,400 adult attendees in psychiatric outpatient clinics shows high rates of adult ADHD.
- The pooled prevalence of ADHD was about 15% in the five studies using a two-stage design and about 27% in the nine screening studies.
- The study was published in the Journal of Attention Disorders (Adamis et al. 2022).
-

Comparison of Persistence and Adherence Between Adults Diagnosed with Attention Deficit/Hyperactivity Disorder in Childhood and Adulthood

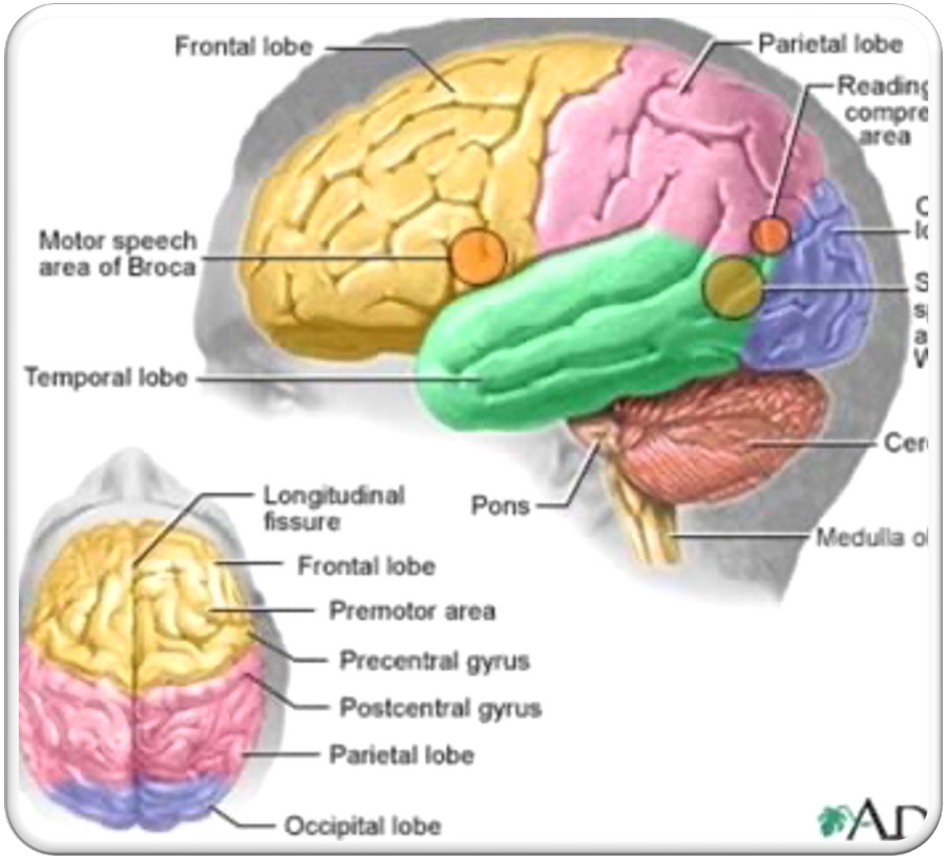
- Long-term treatment of attention deficit/hyperactivity disorder (ADHD) is important, but adherence and persistence in practice are still suboptimal.
- To better understand medication compliance for ADHD, we divided adults with ADHD into groups based on their history of childhood and adolescent ADHD, and compared their characteristics, medication adherence and persistence, and associated factors.
- The significant differences found between these groups add evidence to suggest that adult with ADHD diagnosed in adulthood may be a separate entity from those in childhood. A thorough evaluation at diagnosis and treatment in private clinics may improve medication compliance in this population.
- Lee SM, Cheong HK, Oh IH, Hong M. Comparison of Persistence and Adherence Between Adults Diagnosed with Attention Deficit/Hyperactivity Disorder in Childhood and Adulthood. Neuropsychiatr Dis Treat. 2021 Oct 15;17:3137-3146. doi: 10.2147/NDT.S337819. PMID: 34703234; PMCID: PMC8526951.

The Neurobiology of ADHD





The ADHD Brain Triangle



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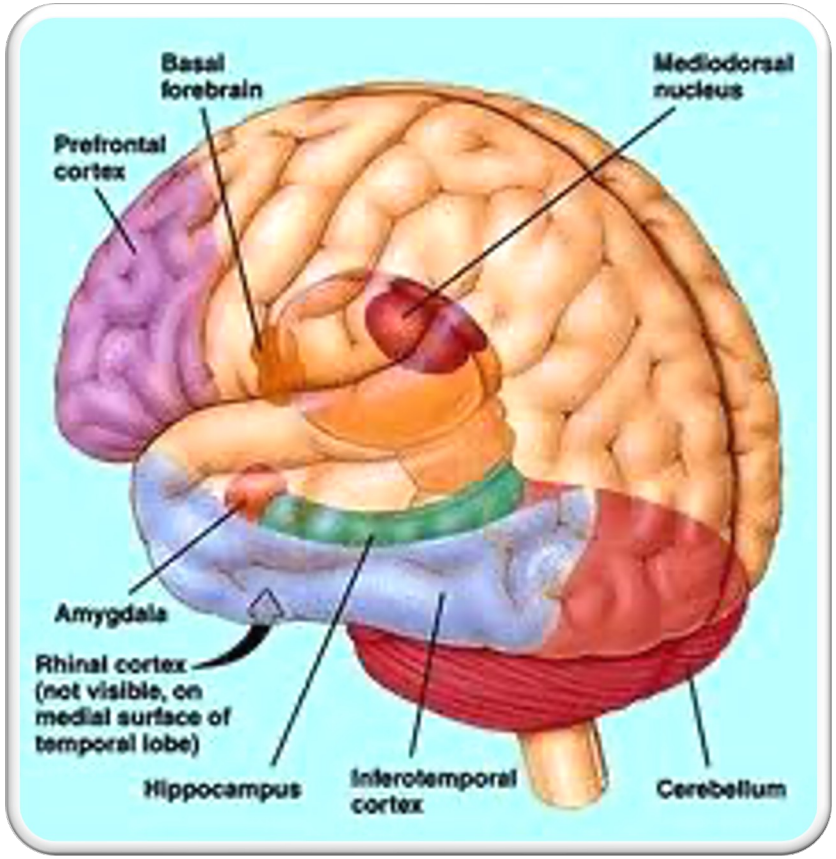


Neural Pathways of ADHD

Prenatal Nicotine Exposure (PNE)

- **PNE is linked to many psychiatric disorders**
  - **Women who smoke during pregnancy are three times as likely to have children diagnosed with ADHD**
- **1 in 5 women still smoke during pregnancy**
  - **Nicotine causes changes in the development that alters dopaminergic & noradrenergic pathways in the brain**
  - **Several studies show behavioral, neuroanatomical, & neurochemical disturbances after PNE**
    - **Benefits of methylphenidate, a common ADHD drug, point to PNE as a valuable animal model of impulsivity**

Adherence in ADHD is Dismal

- **5.4 million children (8.4 percent)** have a current diagnosis of ADHD. This includes: About 335,000 young children ages 2-5 (or 2.1 percent in this age group) 2.2 million school-age children ages 6-11 (or 8.9 percent in this age group)
- **Only 13% of patients consistently take their medication one year out;**
- **Within 2 to 3 months, a majority of patients with ADHD have stopped taking medication consistently;**
- **Patients renewed their monthly prescriptions about 2 to 3 times per year.**

Capone. Presented at CHADD Annual International Conference, Dallas, Texas; October 27, 2005.

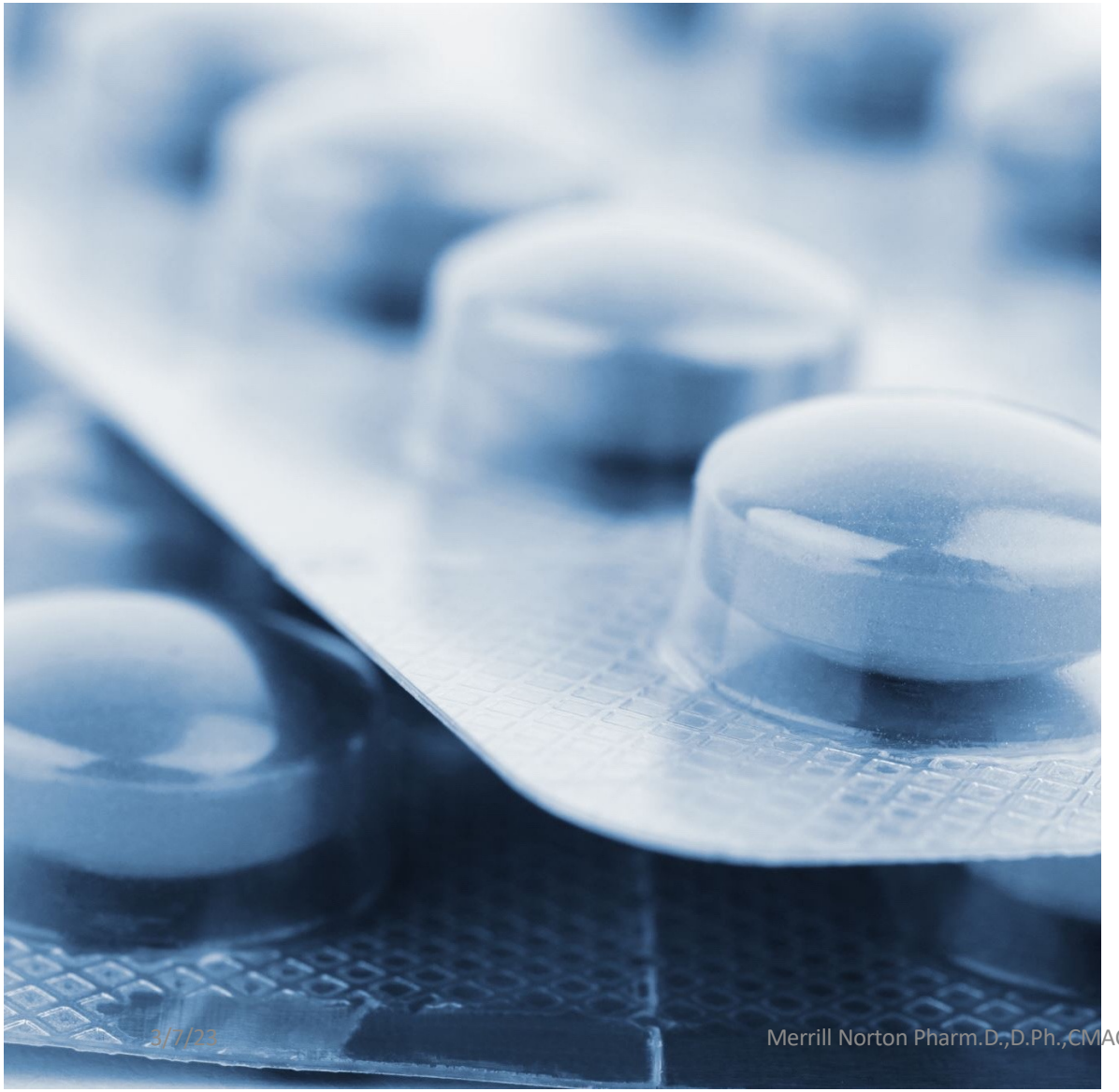
Perwien et al. *J Manag Care Pharm*. 2004;10(2):122-129.

Sanchez et al. *Pharmacotherapy.* 2005;25(7):909-917.

Inattention	Hyperactivity and impulsivity
Often fails to give close attention to details or makes careless mistakes	Often fidgets with or taps hands or feet or squirms in seat
Often has difficulty sustaining attention in tasks or play	Often leaves seat in situations when remaining in seat is expected
Often does not seem to listen when spoke to directly	Often runs about or climbs in situations where it is inappropriate
Often does not follow through on instructions and may fail to finish tasks	Often unable to play or engage in leisure activities quietly
Often has difficulty organizing tasks and activities	Is often "on the go", acting as if "driven by a motor"
Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort	Often talks excessively
Often loses things necessary for tasks or activities	Often blurts out answer before a question has been completed
Is often easily distracted	Often has difficulty waiting his or her turn
Is often forgetful in daily activities	Often interrupts or intrudes on others

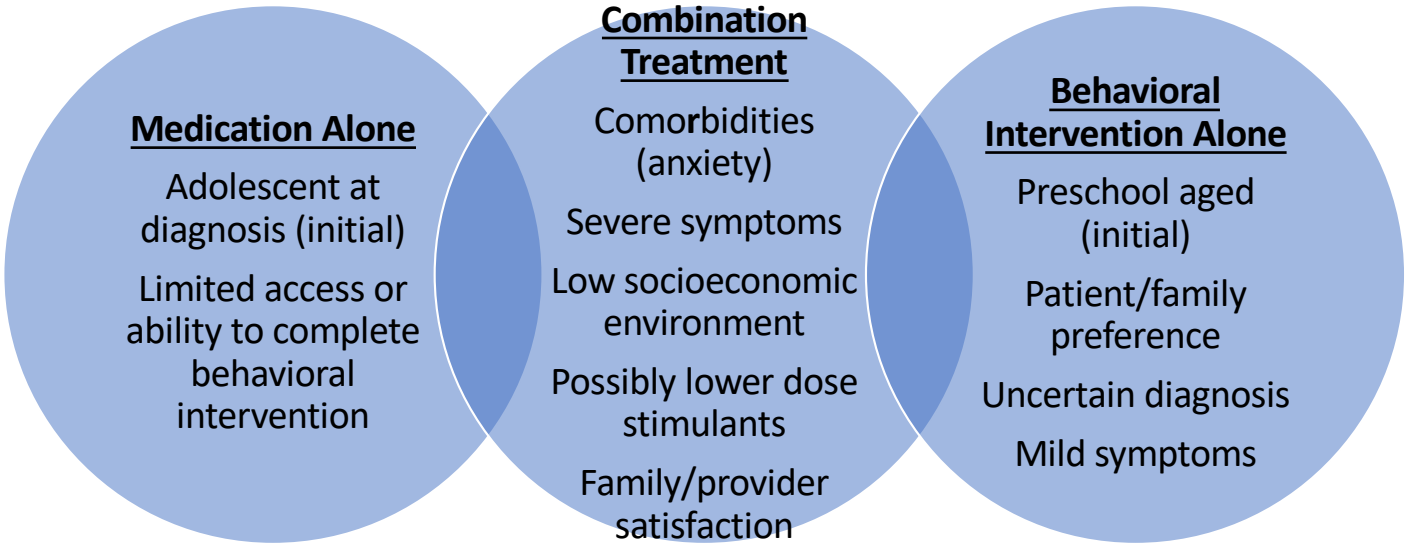
- **AT LEAST 6 SYMPTOMS IN EITHER/BOTH LIST(S) PRESENT FOR ≥ 6 MONTHS THAT IS INCONSISTENT WITH DEVELOPMENTAL LEVEL AND NEGATIVELY IMPACTING SOCIAL AND ACADEMIC/OCCUPATIONAL FUNCTION +**

American Psychiatric Association, 2013



ADHD Treatment Recommendations

Treatment Options



ADHD Medications

Can help greatly with quality of life by affecting the ability to focus, decrease physical hyperactivity

Combination of medications and behavioral interventions have been shown as a superior treatment to either alone [7]

The goal of medication is *symptom reduction*, which requires careful assessment and ongoing monitoring of mental status/psychosocial functioning

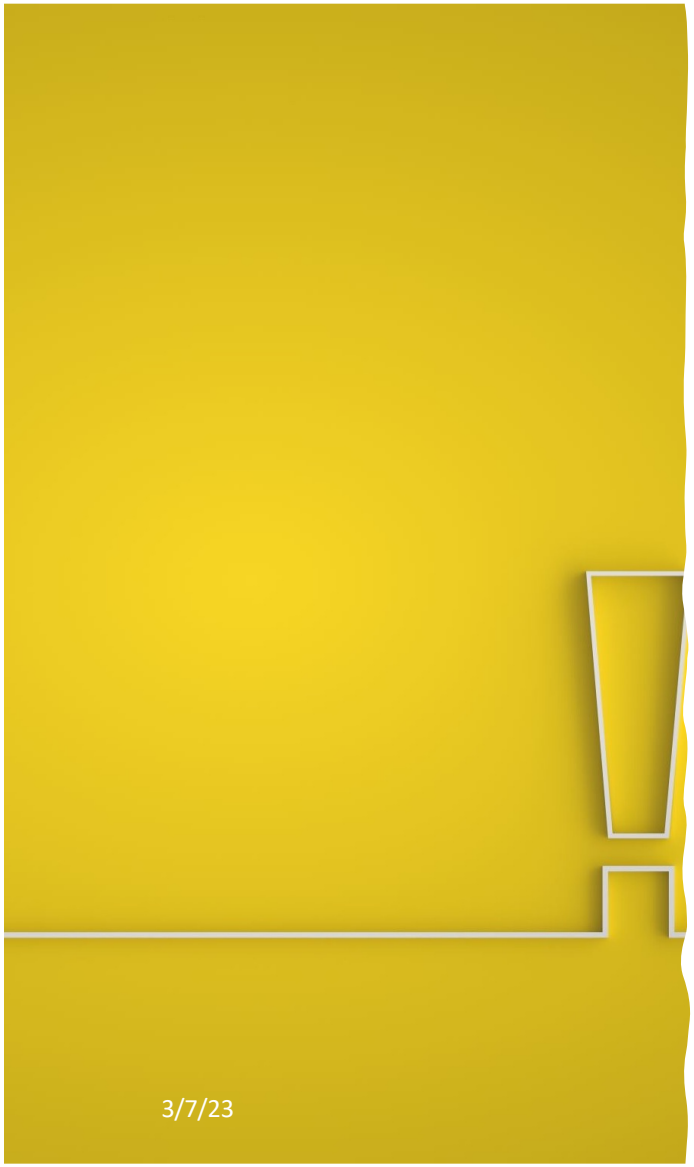
Use of Subscales can be helpful (Vanderbilt, Connors,etc) but not diagnostic – clinical judgment remains most important

Stimulants

- Most widely used
- 65-75% efficacy in treating ADHD symptoms vs 4-30% placebo response
- Only 55% of patients with ADHD get medication treatment

Non-stimulants

- May have fewer (or different) side effects
- Typically considered second line treatment
- Adrenergic Uptake Inhibitors(Strattera, Qelbree)
- Omega 3-6(Equazen Pro)



Practical Steps in Stimulant Treatment

- **Refer to package inserts for dosing information**
- **Can titrate with short acting as needed on top of long acting**
- **Base your clinical decisions on the *best interests of the child***
- **Adverse effects:**
  - **Common (10-50%): nausea, stomach upset, decreased appetite, insomnia, headache**
  - **Uncommon: motor tics (9%), dysphoria, irritability, hallucinations, "zombie"**
  - **Cardiac: 25 cases of sudden death; risk is 0.7-1.5/100K children <16**
  - **Growth: MTA – 1cm/year decrease in height over 1-3 yrs. of continuous treatment, but other studies show no difference**

Mechanism/Generic Name	Brand Name	Duration (hours)	Formulation
Immediate release- Methylphenidate-based stimulants	**Focalin®+**	4-6	Tablet
	Methylin®+	3-4	Liquid
	Ritalin®+	3-4	Tablet
Sustained release-Methylphenidate-based stimulants	**Ritalin-SR®+**	4-8	Tablet
	Desoxyn®+	4-8	Tablet
Extended release-Methylphenidate-based stimulants	**Aptensio XR™**	12	Capsule
	Concerta®+	10-12	Tablet
	Contempla™ XR-ODT	12	Tablet
	Daytrana®	10-12 (9 applied and 3 after)	Transdermal patch
	Focalin XR®+	6-10	Capsule
	Metadate CD®+	8-10	Capsule
	Ritalin LA®+	8-10	Capsule
	QuilliChew ER™	8	Chewable tablet
	Quillivant XR®	8, 10, 12	Liquid
Immediate release- Amphetamine-based Stimulants	**Adderall®+**	4-6	Tablet
	Evekeo®	4-6	Capsule
	ProCentra®	4-6	Liquid
	Zenzedi®	4-5	Tablet
Extended release- Amphetamine-based Stimulants	**Adderall XR®+**	8-12	Capsule
	Adzenys XR-ODT™	9-10 children; 11 adults	Tablet
	Dexedrine®+	8-10	Capsule
	Dyanavel® XR	13	Liquid
	Mydavis™	16	Capsule
	Vyvanse®	10-12	Capsule
Selective norepinephrine inhibitor- Atomoxetine	**Strattera®+**	24	Capsule
Alpha 2 agonists- Clonidine	**Kapvay®+**	12-24	Tablet
Alpha 2 agonists- Guanfacine	**Intuniv®+**	12-24	Tablet

Adverse Effects

Appetite Decrease	**Weight Loss/ Growth Suppression**	**Insomnia**
Headache	**Tics***	**Emotional Lability/Irritability***

*= less common

JAACAP, 2007
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Managing Adverse Effects

Adverse Effect	Possible Response
Appetite Decrease/Weight Loss	**-Time meals when effect worn off** **-Calorie dense foods** **-Cyproheptadine**
Growth Suppression	**-Increase monitoring of height** **-Consider drug holiday** **-Change medication or dose** **-Weight risk/benefit**
Insomnia	**-Change formulation** **-Add alpha 2 agonist** **-Add melatonin** **-Add antihistamine**
Headache	**-Monitor** **-Adjust dose** **-Alternate therapy (stimulant or non-stimulant)**
Tics*	**-Alternate treatment** **-Monitor** **-Adjust dose**
Emotional Lability/Irritability*	**-Adjust dose** **-Correlate behavior change with time when stimulant active ("rebound")** **-Discontinue stimulant and trial alpha 2 agonist**

*= less common

JAACAP, 2007

http://www.chadd.org/portals/0/Content/CHADD/NRC/Parents&Caregivers/Medication-Chart-October-2017.pdf

Melatonin

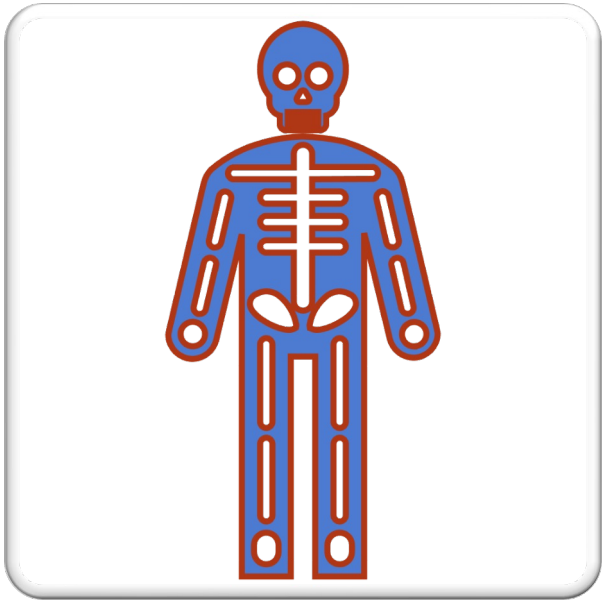
Melatonin for treatment of sleeping disorders in children with attention deficit/hyperactivity disorder: a preliminary open label study	
Patients	**24 children with insomnia on methylphenidate for ADHD**
Intervention	**Melatonin 3mg at bedtime nightly for 3 months**

Results	• **Reduced time to fall asleep:**
	  • **Prior to melatonin ranged 15-240 minutes**
	  • **After melatonin 15-64 minutes**
	• **Persisted for 3 months trial**
	• **Only reported adverse effect as restless sleep**
	• **3 patients excluded once enrolled:**
	  • **1 reported nightmares**
	  • **1 aggressiveness**
	  • **1 incorrect data recording**

Eur J Pediatr. 162: 554-55

Non-Stimulant Treatment of ADHD

- **Atomoxetine:**
  - **Selective NE reuptake inhibitor**
  - **Advantages: low abuse potential, less insomnia/growth problems**
  - **Disadvantages: delayed onset of effect (2-4 wks), lower efficacy than stimulants**
  - **Dose based on weight: 0.5mg/kg/day, up to 1.2mg/kg/day as tolerated**
  - **Adverse effects: nausea, stomach pain, moodiness, increased heart rate, Black Box – suicidality**



Atomoxetine Overview

	ATOMOXETINE
Mechanism	**Selective norepinephrine inhibitor**
Initial Dose	**≥6 years and ≤70 kg: 0.5mg/kg/day may divide into 2 doses ; ≥6 years and ≥70 kg 40mg per day**
Maintenance Dose	**Increase after at least 3 days to 1.2mg/kg/day; ≥6 years and ≥70 kg : may increase to 80 mg after 3 days Max daily dose: 1.4mg/kg/day or 100 mg**
Metabolism	**Hepatic via CYP2D6 and CYP2C19 -Genetic variability may affect bioavailability**
Excretion	**Urine (80%); feces (17%)**
Interactions	**CYP2D6 inhibitors *dose adjustment required***
Comments	**May have 24 hour duration of action Wait up to 4 weeks to determine efficacy**

- *JAACAP,* 2007
- *Pediatrics* 2011
- Lexicomp Online® , Pediatric & Neonatal Lexi-Drugs® , Hudson, Ohio: Lexi-Comp, Inc.; March 2, 2018

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Atomoxetine Adverse Effects

- Sleep Disturbance
- Headache
- Gastrointestinal Symptoms
- Hyperhidrosis
- Sexual Dysfunction
- Suicidal Ideation (0.4%)

JAACAP, 2007

Pediatrics 2011

Elevated LFTs

December 17, 2004 FDA required warning be added due to reports of 1 adult and 1 child who developed severe liver disease

Clinical trials of 6,000 patients no hepatotoxicity seen

No recommendation to routinely monitor hepatic function

Discontinue medication in patients who develop jaundice, dark urine, or any symptoms of hepatic disease

JAACAP, 2007

Pediatrics 2011

Other Non-stimulant Meds for ADHD

Buproprion:

- **NE reuptake and DA reuptake inhibitor**
- **Dosing is somewhat unclear in children; adults = mean 393mg/day of Wellbutrin XR**

a_2 Adrenergic Agonists:

- **May strengthen working memory by improving functional connectivity in prefrontal cortex**
  - **Clonidine: less effective than stimulants, used as adjunct to manage tics, sleep problems and aggression**
    - **Adverse Effects include bradycardia and sedation**
  - **Guanfacine: more selective for a_{2a} receptor**
    - **less sedation/dizziness than clonidine**
    - **2-4 mg with effect between 2-4 weeks**

Alpha 2 Agonist Overview

	Clonidine	Guanfacine
Mechanism	**Alpha 2A adrenoreceptor agonist**	
Initial Dose	**Extended release (Kapvay®) for children ≥6 years: 0.1 mg at bedtime**	**Extended release for children ≥6 years and adolescents ≤17 years: 1 mg once daily**
Maintenance Dose	• **Increase in 0.1 mg/day increments every 7 days until desired response** • **Doses should be administered twice daily in the morning and at bedtime** • **Maximum daily dose: 0.4 mg/day**	• **Adjust by increments of no more than 1 mg/week** • **Recommended target dose: 0.05 to 0.12 mg/kg/dose (1 to 7 mg) once daily, depending on clinical response and tolerability** • **Maximum Monotherapy: children 6 to 12 years: 4 mg/day; Adolescents: 13 to 17 years: 7 mg/day** • **Maximum Adjunct therapy (with psychostimulants): 4 mg/day**
Metabolism	**Hepatic to inactive metabolites** ***Half life prolonged in renal impairment**	**Hepatic via CYP3A4. Approximately 50% of clearance is hepatic**
Excretion	**Urine**	**Urine**
Interactions	**CNS depressants, antihypertensives**	

JAACAP, 2007
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Clonidine Adverse Effects

- Drowsiness/Fatigue
- Dry mouth
- Abdominal Pain
- Dizziness
- Bradycardia
- Headache

JAACAP, 2007

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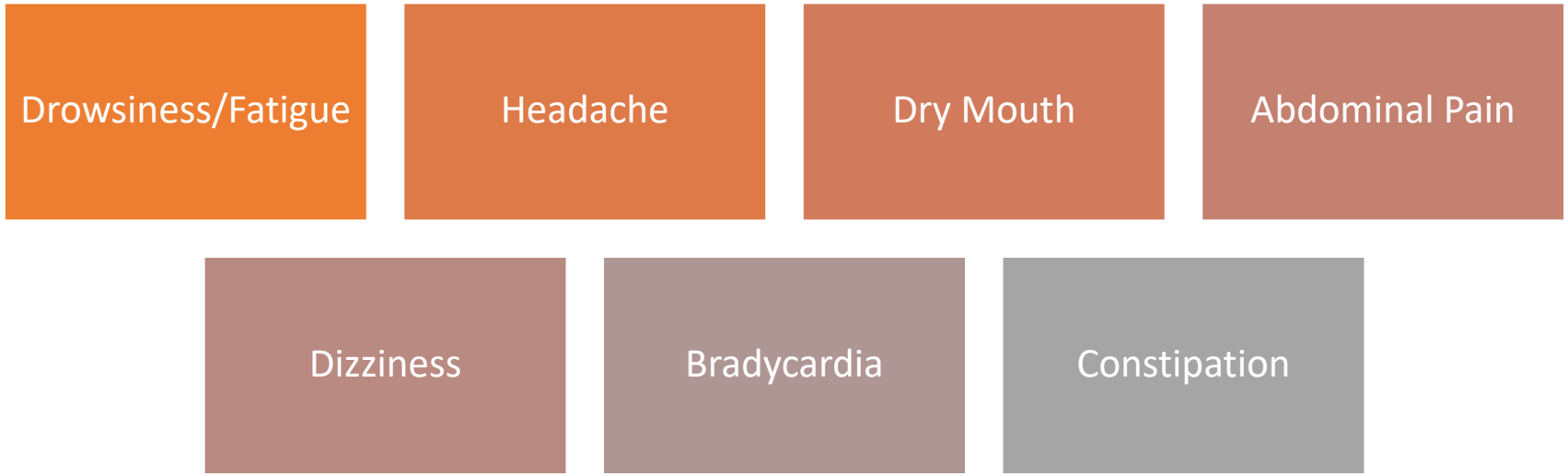
Guanfacine Adverse Effects



JAACAP, 2007

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What to Ask Your Child's Doctor About New ADHD Medications

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- **The US Food and Drug Administration approved two new medications for ADHD in the spring of 2021: Azstarys, a stimulant medication, and Qelbree, a nonstimulant. Both can be prescribed for children age six and older.**
- **Stimulant versus nonstimulant medications**
- Stimulants are typically the front-line treatment for ADHD symptoms, but nonstimulants can be used alone and along with stimulants in managing symptoms. Some parents are hesitant to have a stimulant medication prescribed for their child and some children do not react well to stimulants. In cases like these, nonstimulant medications can be tried to reduce a child's symptoms.
- ADHD Weekly June 17,2021

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Possible Side Effects of Azstrays and Qelbree

- The most common side effects of Qelbree are sleepiness, tiredness, vomiting, irritability, decreased appetite, nausea, and trouble sleeping. For a few people there was an increase in suicidal thoughts and actions, especially within the first few months of treatment or when the dose was changed.
- Side effects noted for Azstarys include decreased appetite, nausea, indigestion, weight loss, dizziness, mood swings, increased blood pressure, trouble sleeping, vomiting, stomach pain, anxiety, irritability, and increased heart rate.
- Most often side effects go away after a little while on the medication. Sometimes the prescriber will need to adjust the dosage. If side effects continue or are difficult to tolerate, medications can be switched to a better tolerated medication.

The Neuroscience of Mood Disorders, Shame, Trauma, and Substance Use Disorders Series:

I. Anxiety

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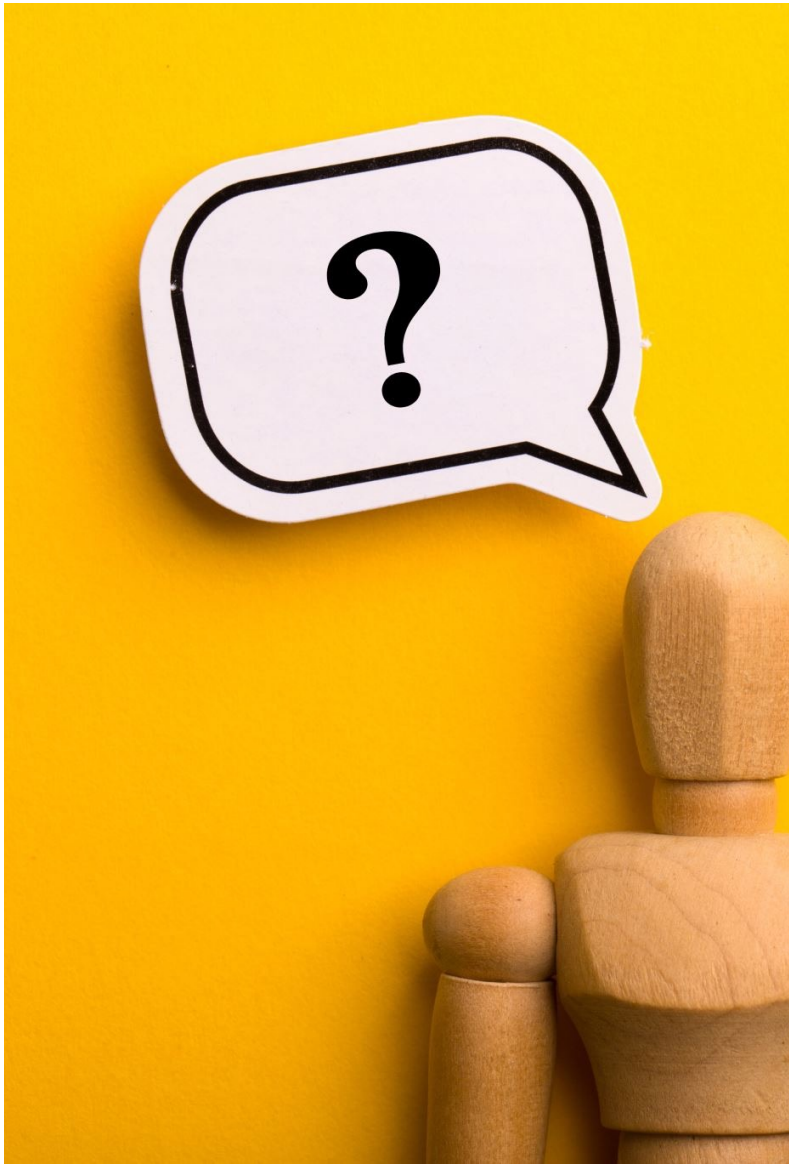
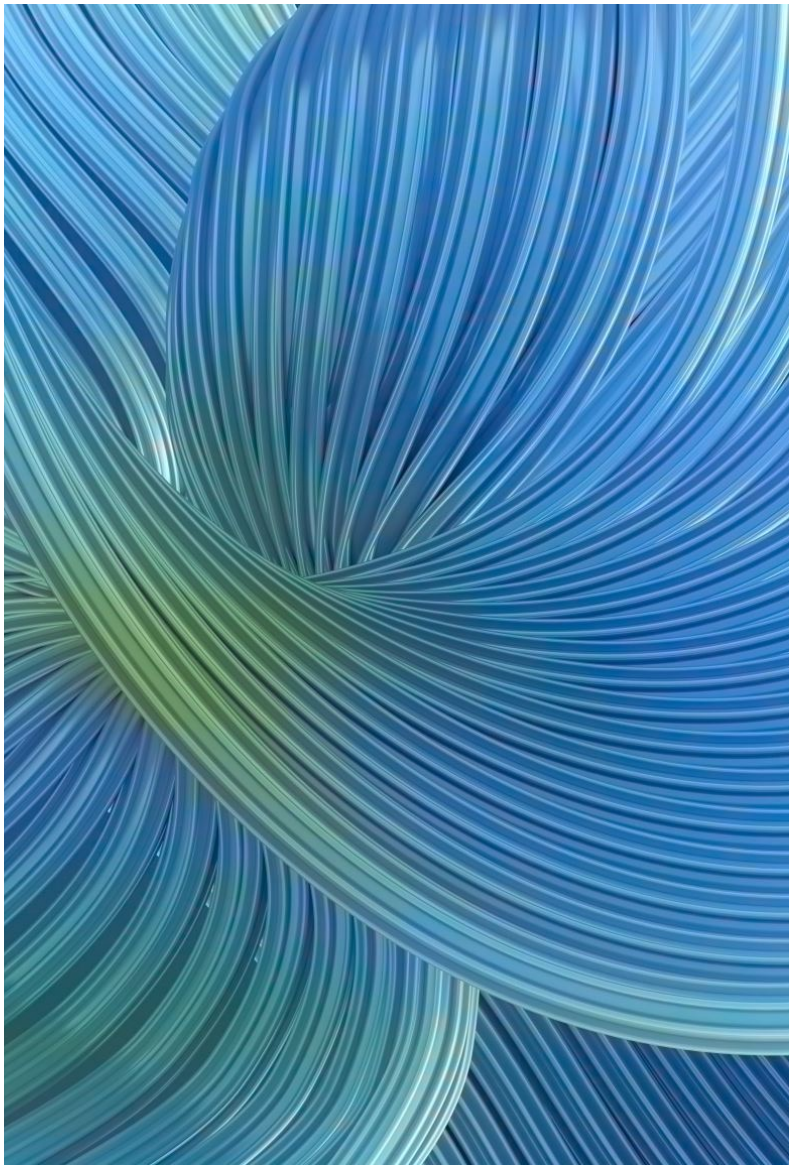
"Nothing diminishes anxiety faster than action."

-Walter Anderson



Anxiety as a Normal and an Abnormal Response

- Some amount of anxiety is “normal” and is associated with optimal levels of functioning.
- Only when anxiety begins to interfere with social or occupational functioning is it considered “abnormal.”



Anxiety vs. Fear

Anxiety

- Apprehension about a future threat

Fear

- Response to an immediate threat

Both involve physiological arousal

- Sympathetic nervous system

Both can be adaptive

- Fear triggers "fight or flight"
  - May save life
- Anxiety increases preparedness
  - "U-shaped" curve (Yerkes & Dodson, 1908)
    - Absence of anxiety interferes with performance
    - Moderate levels of anxiety improve performance
    - High levels of anxiety are detrimental to performance

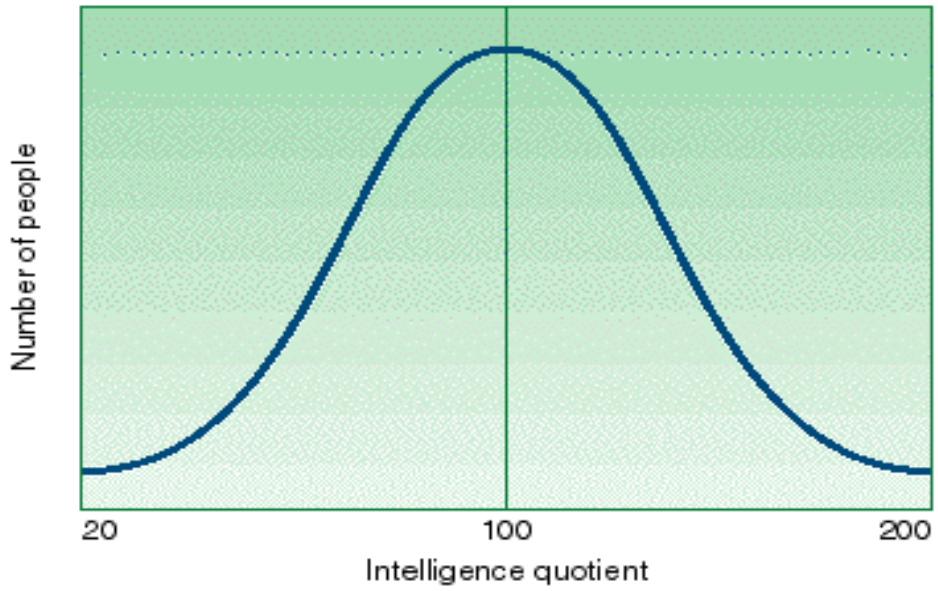
Anxiety Disorders

- DSM-5 Anxiety Disorders
  - **Specific phobias**
  - **Social anxiety disorder**
  - **Panic disorder**
  - **Agoraphobia**
  - **Generalized anxiety disorder**
- Most common psychiatric disorders
- 28% report anxiety symptoms
- **Most common are phobias**

The Fear and Anxiety Response Patterns

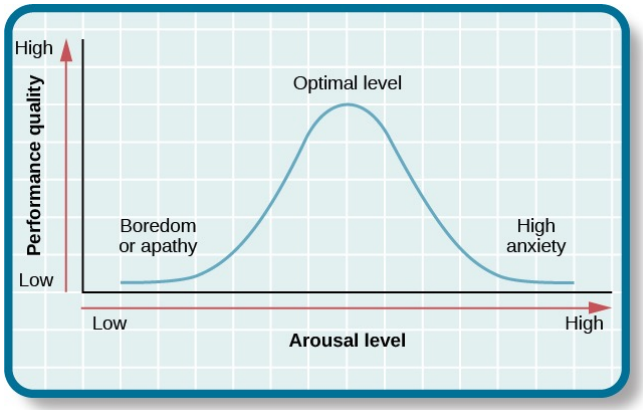
- Fear
- Panic
- Anxiety
- Anxiety Disorder

The Bell Curve of Anxiety



The Yerkes-Dodson Law and Performance

- When stress gets too high, performance decreases. To add more nuance, the shape of the stress-performance curve varies based on the complexity and familiarity of the task.



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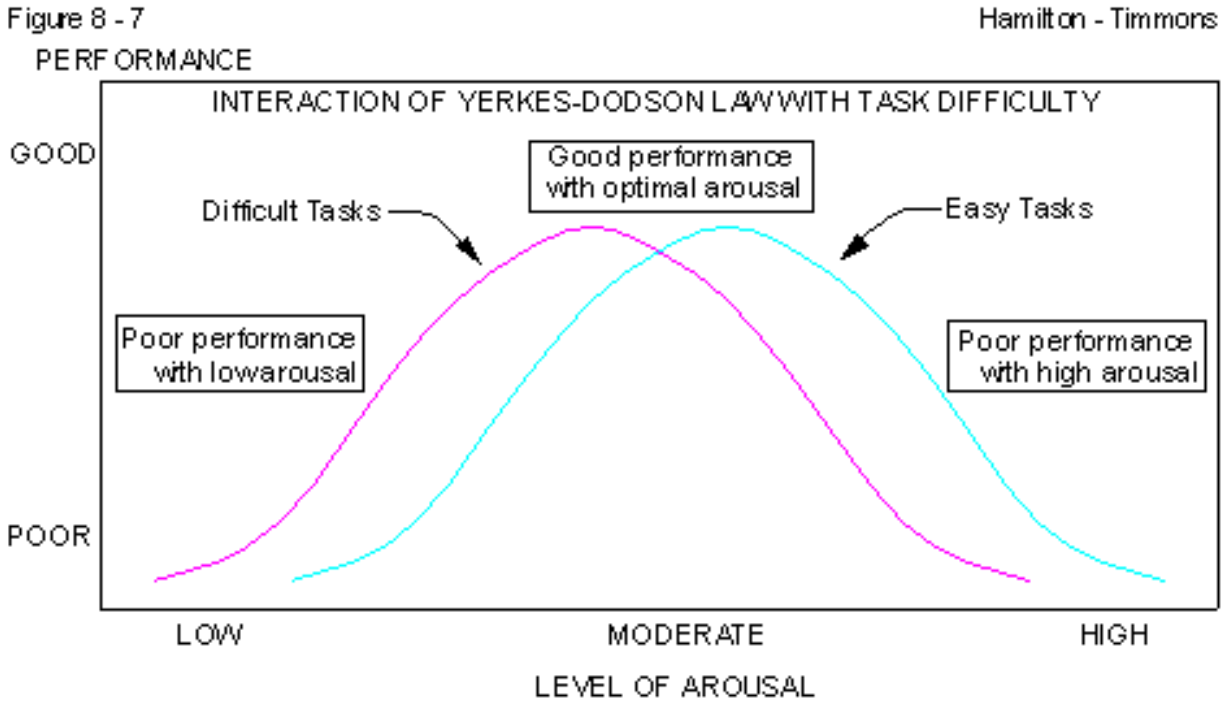
Another Bell Curve- Courtesy of Our Good Buddies Yerkes-Dodsen



How Does This Science Tell us About Anxiety and Learning?

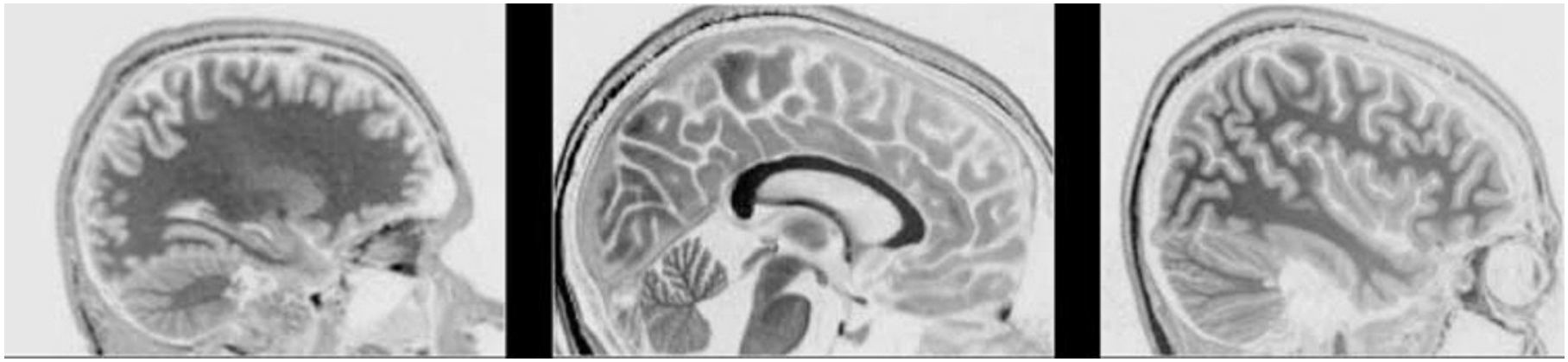
- **Raising arousal levels can cause a state of readiness to perform**.
- This is largely a positive aspect and can enhance performance.
- **High arousal or over arousal can cause us to worry and become anxious , which can be negative if not controlled**.

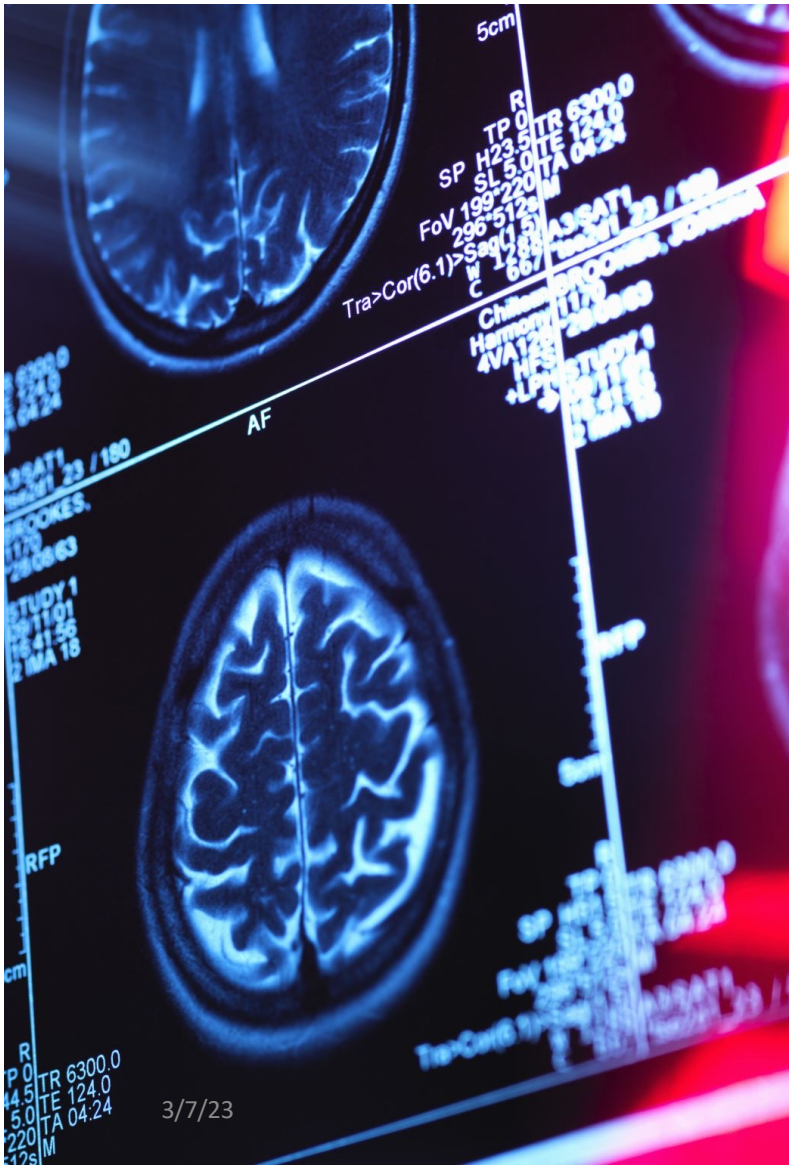
The Neuroscience of Anxiety

- Research on the neurocircuitry of anxiety disorders has its roots in the study of fear circuits in animal models and the study of brain responses.
- Anxiety disorders are marked by excessive fear (and avoidance), often in response to specific objects or situations and in the absence of true danger, and they are extremely common in the general population.

Brain Areas That Are Involved With Fear and Anxiety

A Hippocampus Amygdala **B. Anterior Cingulate** **C. Insula Cortex**



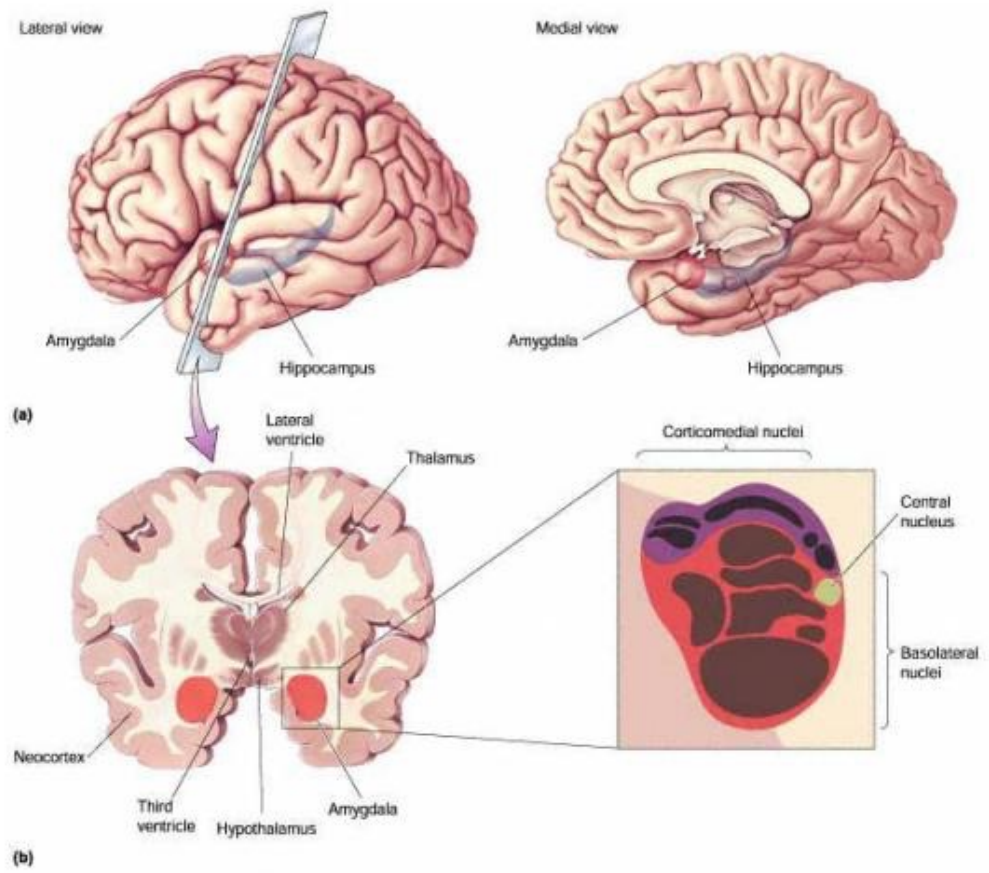


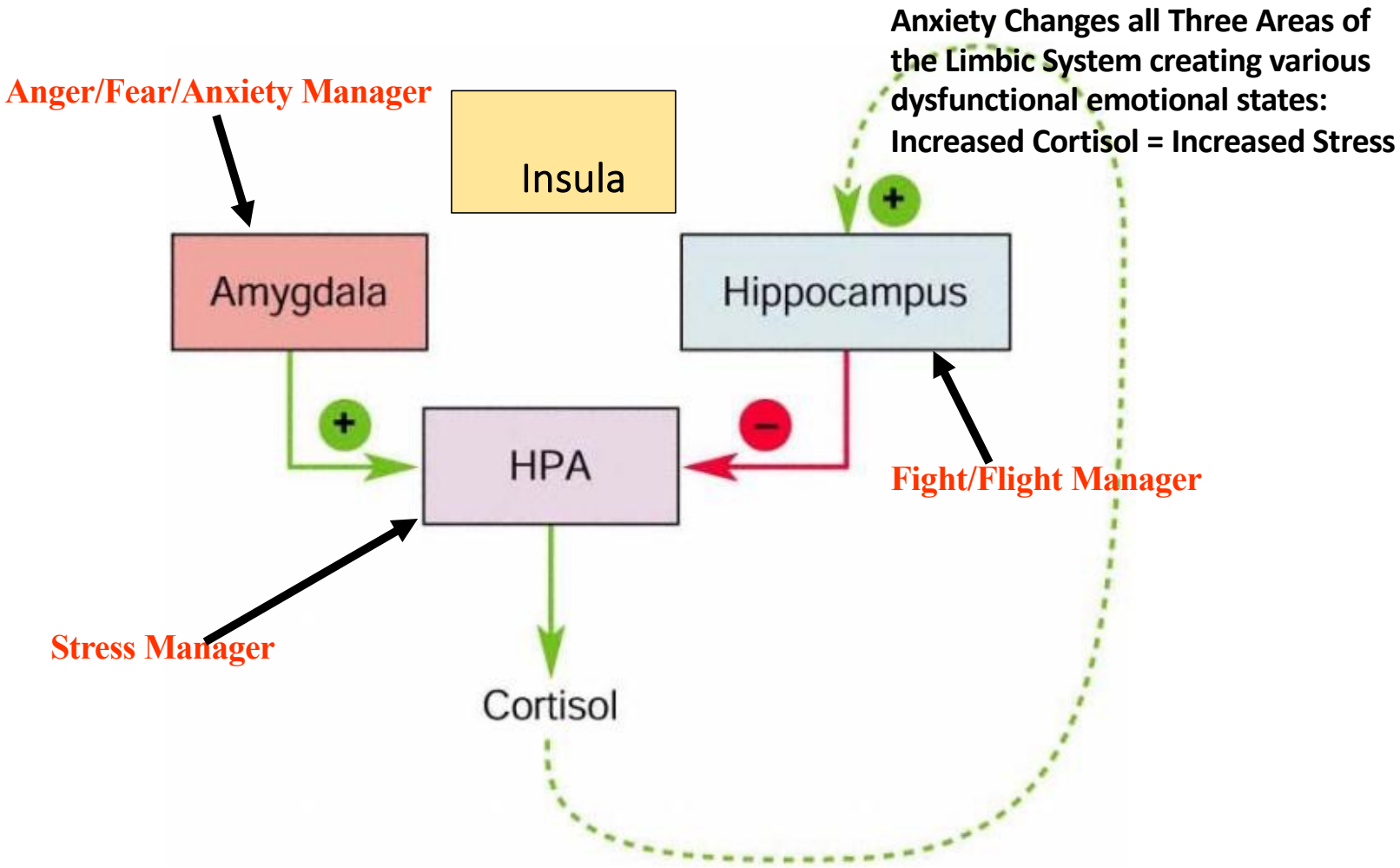
A Theory of Basic Emotional Circuits

- **According to Panksepp, there are at least 4 basic, distinct emotion circuits in the mammalian brain**
  - **Fear**
  - **Anger or Rage**
  - **Anticipation or Seeking Behavior**
  - **Social Bonding**

Panksepp, J. 1998. Affective Neuroscience: The foundations of human and animal emotions. New York, Oxford University Press.

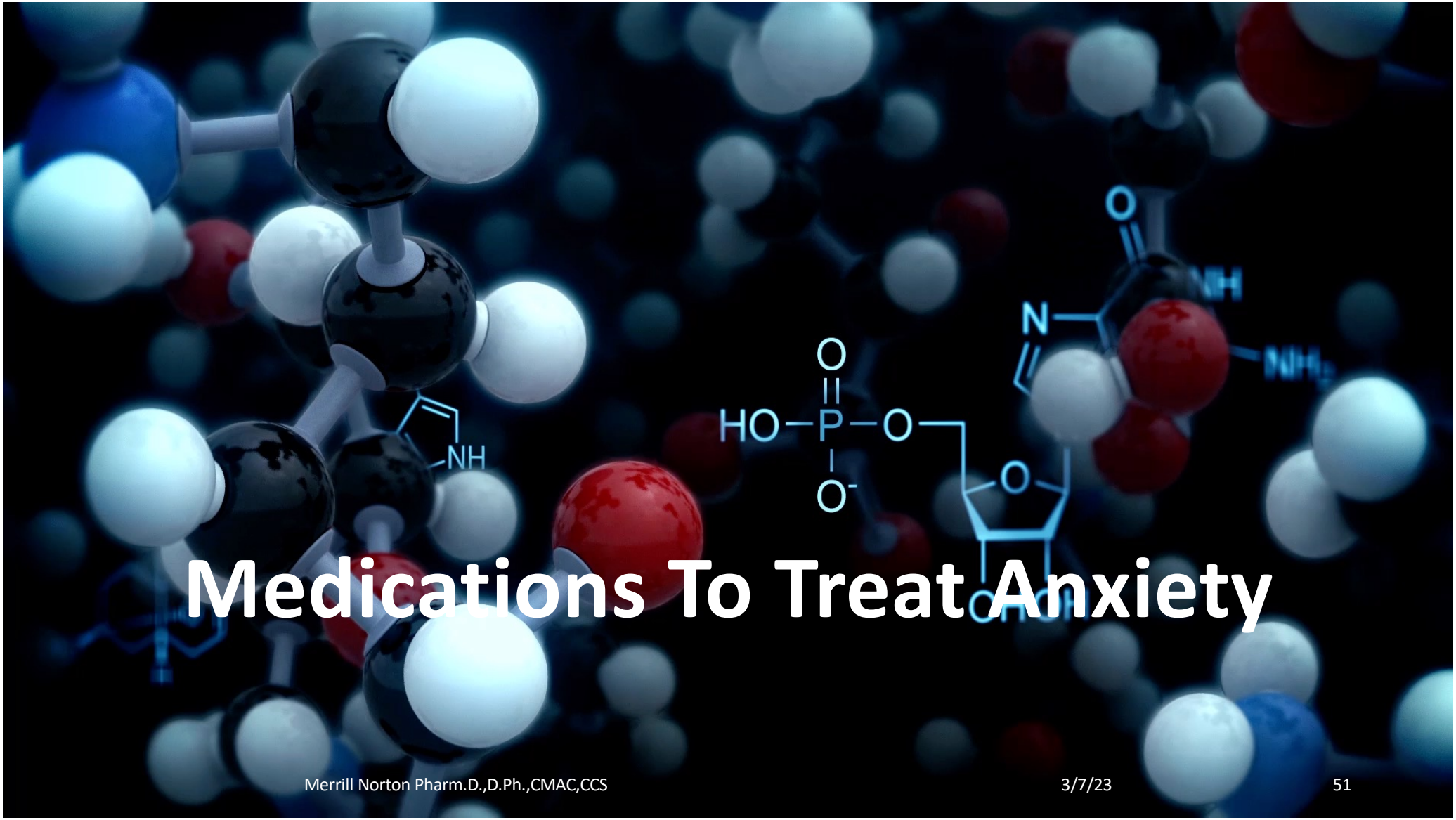
Amygdala is a key structure in fear and anxiety




Anxiety Changes all Three Areas of the Limbic System creating various dysfunctional emotional states:
Increased Cortisol = Increased Stress
Anger/Fear/Anxiety Manager
Insula
Amygdala
Hippocampus
HPA
Fight/Flight Manager
Stress Manager
Cortisol

Treatment of Anxiety

- **Cognitive-Behavioral Therapy**
- **Behavioral Therapy**
- **Relaxation Therapy**
- **Medication (SSRIs – Prozac, Paxil, Celexa, Zoloft, Luvox; Tricyclics – Desiprimine, Imiprimine; Benzodiazapines – Xanax, Ativan, Valium)**



Medications To Treat Anxiety

SSRIs

- Mechanism of action: Selective 5-HT reuptake inhibitor

Name	FDA Approvals for Anxiety Disorder	Off-label Uses	Dose Ranges (mg/day)
Fluoxetine	PD	GAD, SAD	20-60
Sertraline	PD, SAD	GAD	50-200
Citalopram	None	GAD, PD, SAD	20-40
Escitalopram	GAD	PD, SAD	10-20
Paroxetine	PD, SAD, GAD	None	20-60
Paroxetine ER	PD, SAD	GAD	27-75
Fluvoxamine	None	GAD, PD, SAD	100-300

SNRIs

- Mechanism of Action: 5-HT (serotonin), Norepinephrine (and dopamine) reuptake inhibitor

Name	FDA Approvals for Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Duloxetine	GAD	PD, SAD	30-60
Venlafaxine	GAD	PD, SAD	75-300
Desvenlafaxine	None	GAD, PD, SAD	100-300

TCAs

- Mechanism of Action: Norepinephrine and 5-HT (serotonin) reuptake inhibitors

Name	FDA Approvals for Anxiety Disorders	Off-label uses	Dose Ranges (mg/day)
Clomipramine	None	GAD, PD, SAD	100-250
Imipramine	None	GAD, PD, SAD	100-300
Desipramine	None	GAD, PD, SAD	100-200
Nortriptyline	None	GAD, PD, SAD	50-150

MAOIs

Name	FDA Approvals for Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Phenelzine	None	GAD, PD, SAD	30-90

- Mechanism of Action: MAO inhibitor

Mechanism of Action: 5-HT_2, 5-HT_3, a_2, H_1 antagonist

Mixed Antidepressants

Name	FDA Approvals for Anxiety Disorders	Off-Label Uses	Dose Ranges (mg/day)
Mirtazapine	None	Anxiety, GAD, PD, SAD	15-45

GABAergic

- Mechanism of Action: Unclear, may modulate calcium channels

Name	FDA Approvals for Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Pregabalin	None	GAD, SAD	150-600
Gabapentin	None	GAD, SAD PD	600-2,400

Benzodiazepines

- Mechanism of Action: GABA-A agonist

Name	FDA Approvals for Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Clonazepam	PD	Anxiety, GAD, PD, SAD	1-2
Alprazolam	Anxiety, PD	GAD, PD, SAD	1-4
Lorazepam	Anxiety	GAD, PD, SAD	2-6
Chlordiazepoxide	Anxiety	GAD, PD, SAD	20-100
Oxazepam	Anxiety	GAD, PD, SAD	30-60

Antipsychotics

Name	Mechanism of Action	FDA Approvals of Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Trifluoperazine	D_z antagonist	Anxiety	GAD, PD, SAD	2-6
Olanzapine	D_2, 5-HT_2, H_1 antagonist	None	Anxiety, GAD	5-15
Quetiapine	D_2, 5-HT_2, H_1 antagonist	None	Anxiety, GAD	50-300

Beta-blockers

- Mechanism of Action: B-1, B-2 antagonist

Name	FDA Approvals for Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Propranolol	None	Anxiety, PD, SAD	60-120

Antihistamines

- Mechanism of Action: H_1 antagonist

Name	FDA Approvals for Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Hydroxyzine	Anxiety	GAD, PD, SAD	25-100

Other anxiolytics

Name	Mechanism of Action	FDA Approvals for Anxiety Disorders	Off-label Uses	Dose Ranges (mg/day)
Buspirone	5-HT_{1a} partial agonist	Anxiety	GAD	15-60

Novel Medications

Name	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
Vilazodone	MDD	GAD, SAD	SAD
Vortioxetine (& 5-HT_2 antagonist)	MDD	GAD, PD	Comorbid SAD, MDD

- Selective 5-HT reuptake inhibitor and 5-HT_{1A} partial agonist

Novel Medications

Name	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
Gepirone ER	None	None	GAD
Tandospirone	None	None	GAD
PRX-00023	None	None	None
TGFK08AA	None	None	GAD
TGW00AA	None	None	GAD, SAD

- 5-HT_{1A} partial agonist

Other Serotonergic Agents

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
AVN-101	5-HT_6 receptor antagonist	None	None	Anxiety disorders
Ondansetron	5-HT_3 antagonist	Nausea/vomiting	GAD	None
Agomelatine	melatonin-½ agonist, 5-HT_{2c} antagonist	None	GAD	None
Psilocybin	5-HT_{2A}, 5-H_{1A}, 5-HT_{2C} agonist	None	"Life-Threatening anxiety"	Cancer-related anxiety
Lysergic Diethylamide	Unclear	None	None	"Life-Threatening anxiety"

Glutamate

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
LY354740	mGluR2-3 agonist	None	PD	None
LY544344	mGluR2-3 agonist	None	GAD	None
JNJ40411813	mGluR2 allosteric modulator	None	Anxious depression	None
Ketamine	NMDA Receptor antagonist	MDD	SAD	NOne
Riluzole	Inhibits glutamate release	Amyotrophic lateral sclerosis	GAD	None

Glutamate Cont.

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
Troriluzole	Reduces synaptic Glutamate	None	GAD	None
D-cycloserine	NMDA partial agonist	Tuberculosis	PD, SAD, and specific phobias	None
Memantine	NMDA receptor antagonist	Alzheimer's dementia	GAD	None
Nitrous Oxide	NMDA receptor antagonist	Inhaled anesthetic	None	None

GABAergic

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
AZD7325	GABA-A alpha 2-3 modulator	None	GAD	None
PF-06372865	GABA-A allosteric modulator	None	GAD	None
BNC-210	A_7 nicotinic ach allosteric modulator GABA modulator	None	GAD	NOne
SAGE-17	GABA-A allosteric modulator	None	None	GAD

Neurosteroids

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
Mifepristone	Progesterone Inhibitor	Early pregnancy termination	PTSD, GAD, PD, or anxiety NOS	None
PH94B	Binds to nasal chemosensory receptors to trigger neural circuits	None	SAD	Adjustment disorder with anxiety symptoms

Neuropeptides

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
Oxytocin	Unclear	Labor induction	SP, SAD	Anxiety and Depression
LY686017	Neurokinin-1 antagonist	None	SAD	None
LY-759274	Neurokinin-1 antagonist	None	GAD	None
Neuropeptide Y	Y1 agonist	None	PTSD	None
SSR 149145	V1b antagonist	None	MDD + GAD	None
SRX246	V1a antagonist	None	None	Experimental anxiety

Neuropeptides Cont.

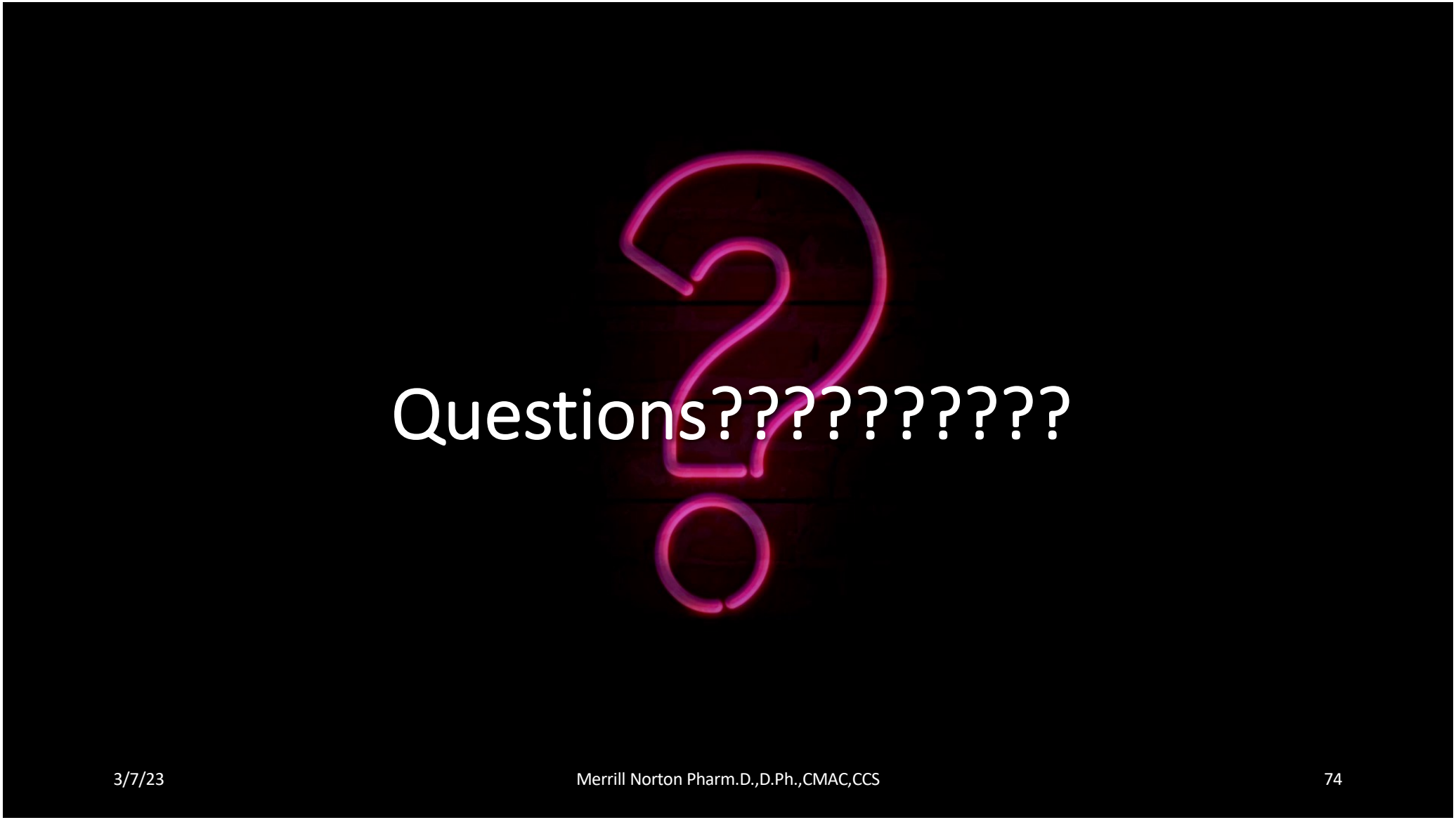
Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
Pexacerfont	CRF-1 antagonist	None	GAD	None
Verucerfont	CRF-1 antagonist	None	GAD	None
Emicerfont	CRF-1 antagonist	None	GAD	None
Suvorexant	Orexin 1,2 antagonist	Primary insomnia	PD	None

Cannabinoids

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
Cannabidiol	CB1 allosteric modulator, CB2 antagonist-inverse agonist, $5HT_{1A}$ agonist	None	SAD	PD, GAD, SAD agoraphobia
Delta-9-tetrahydrocannabinol	CB1, CB2 partial agonist	None	None	None
Dronabinol	CB1 agonist	Chemo-related NV	None	None
Nabilone	CB1, CB2 agonist	Chemo-related NV	GAD, “anxiety neuroses”	None

Natural Remedies

Name	Medication Class	FDA Approvals	Past RCTs in anxiety	Ongoing/future trials in anxiety
KAVA	Unclear	None	GAD	None
Galphimine-B	Unclear	None	GAD	Anxiety
Chamomile	Unclear	None	GAD	None
Lavender	Inhibition of voltage-gated Ca channels	None	GAD	Dental Anxiety, Pre-op anxiety
Saffron	Unclear	None	Anxiety symptoms	GAD


Questions??????????