Expanding Your Toolkit for the Treatment of Anxiety in the Pediatric Population

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Learning Objectives

- At the conclusion of this session, learners will be able to:
  - Identify common anxiety disorders in the pediatric population
  - Better understand psychopharmacological treatment options for the treatment of anxiety disorders in the pediatric population
  - Understand non-pharmacological treatment options for the treatment of anxiety disorder in the pediatric populations
  - Understand the effects of trauma on pediatric patients and the development of anxiety disorders

Epidemiology

- Anxiety Disorders are the most common childhood-onset psychiatric disorders
- Prevalence between 10% to 30%
- Rates of anxiety disorders increased to 20.5% following COVID-19 pandemic

What is anxiety?

Selective Mutism

Generalized Anxiety Disorder

Social Anxiety Disorder

Post Traumatic Stress Disorder

Specific Phobia

Separation Anxiety Disorder

Agoraphobia

Panic Disorder

Illness Anxiety Disorder

Substance/Medication-Induced Anxiety Disorder

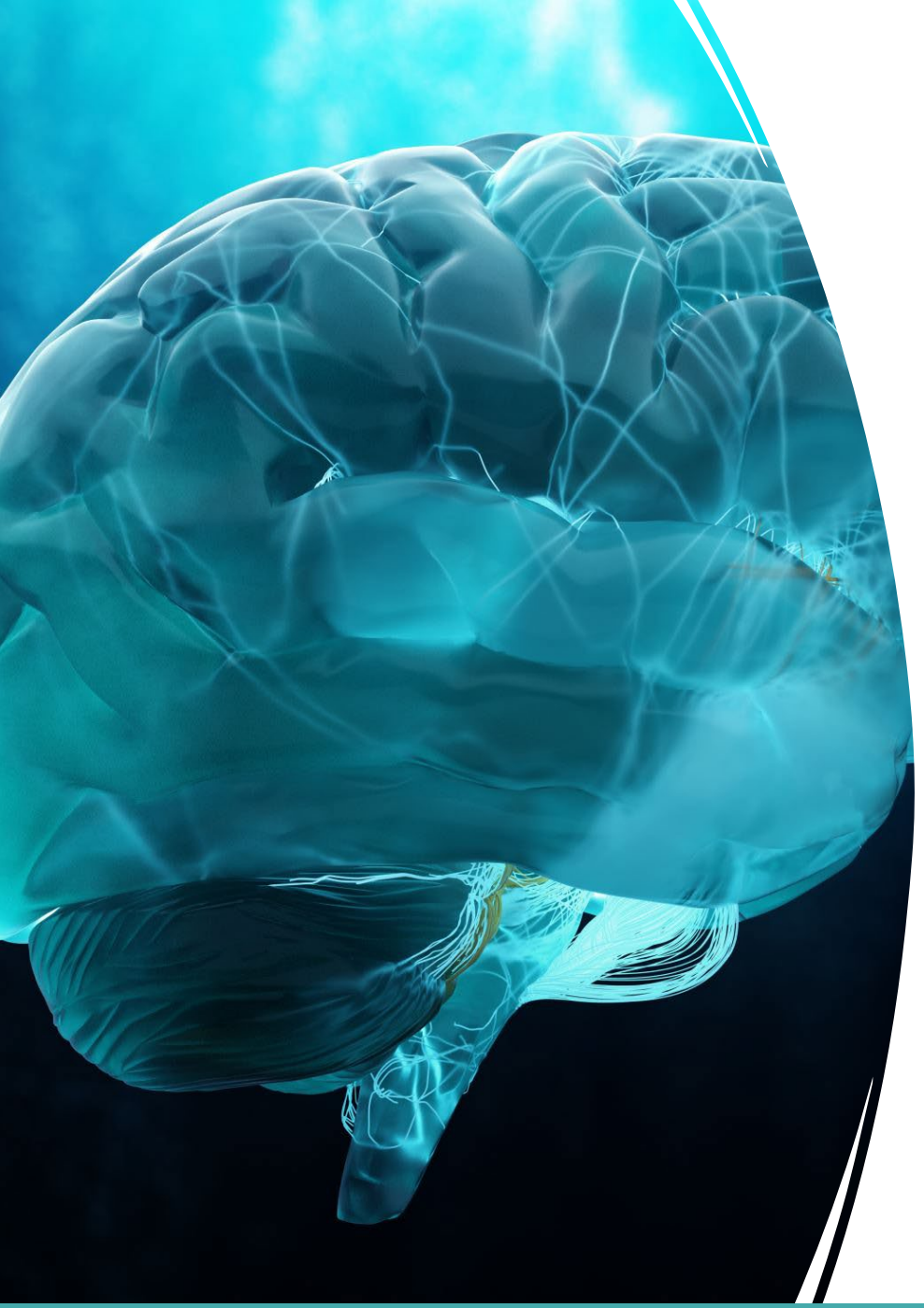
Obsessive Compulsive Disorder

What is anxiety?

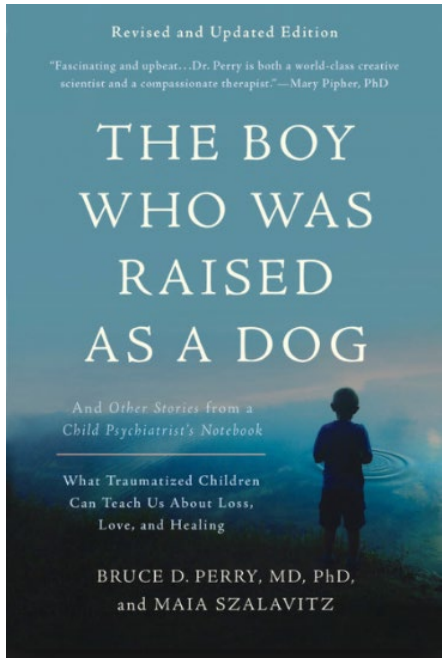
- According to the DSM-5-TR:
  - ***Fear*** *is the emotional response to real or perceived imminent threat*
  - ***Anxiety*** *is the anticipation of future threat*

What is anxiety?

- Anxiety Can Look Like:
  - Avoidance
  - Somatic symptoms
  - Sleep problem
  - Excessive need for reassurance
  - Poor school performance
  - Eating problems
  - Suicidal thoughts or behavior (22-55% of patients with anxiety will report SI)



But what about the brain?

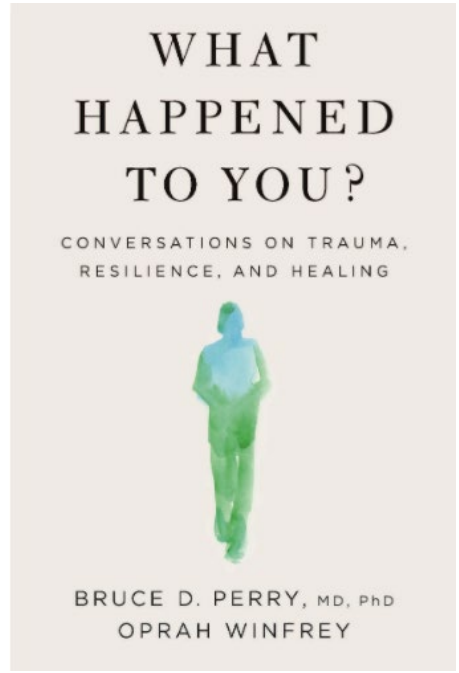


WHAT IS NMT?

The Neurosequential Model of Therapeutics is a neuroscience-informed, developmentally-sensitive, approach to the clinical problem solving process.

It is not a therapy – and does not specifically imply, endorse or require – any single therapeutic technique or method.

NEUROSEQUENTIAL NETWORK™



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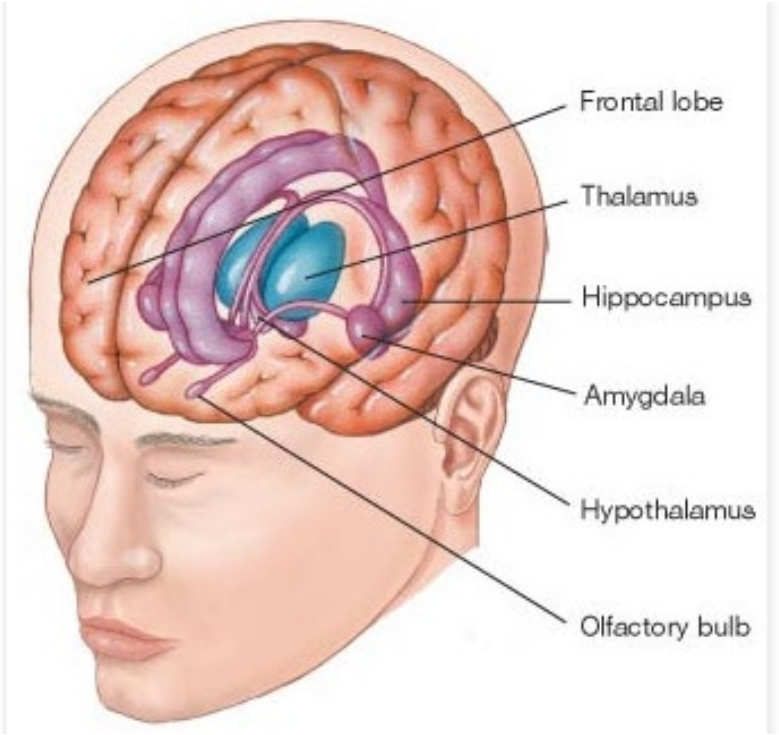
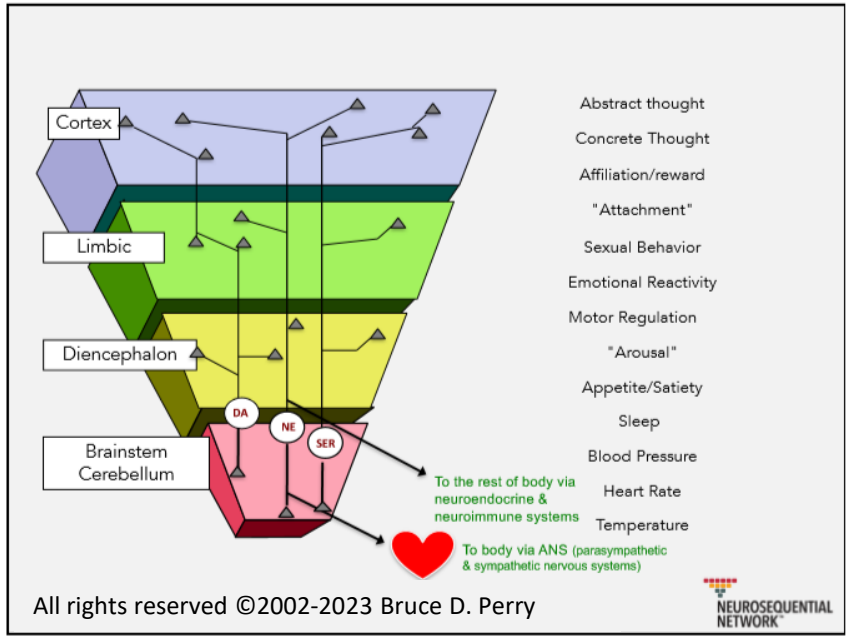
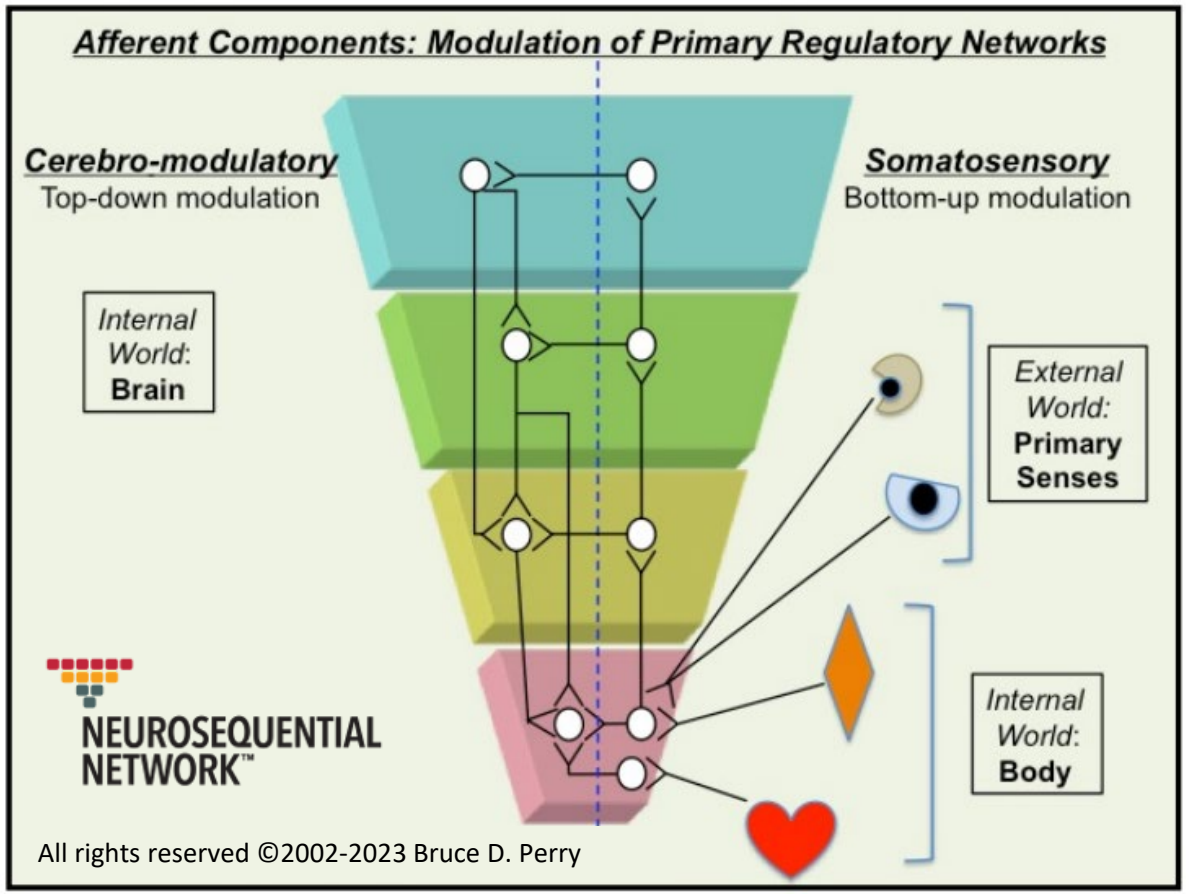
Typical Brain Organization and Childhood Development

The Brain's Main Directive is Survival!!





The Brain's Main Directive is SURVIVAL!



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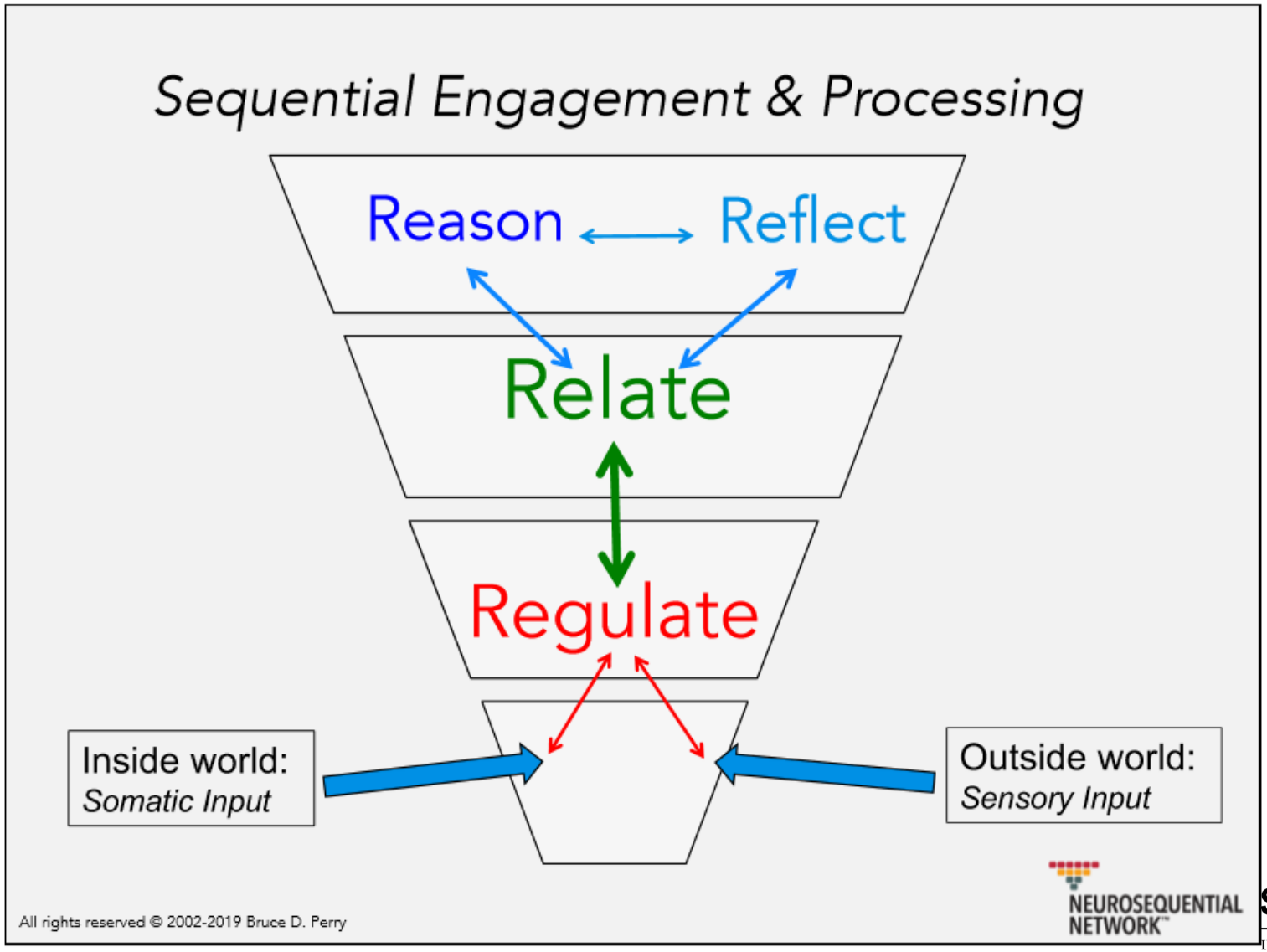
Sequential Engagement & Processing
Reason
Reflect
Relate
Regulate
Inside world:
Somatic Input
Outside world:
Sensory Input
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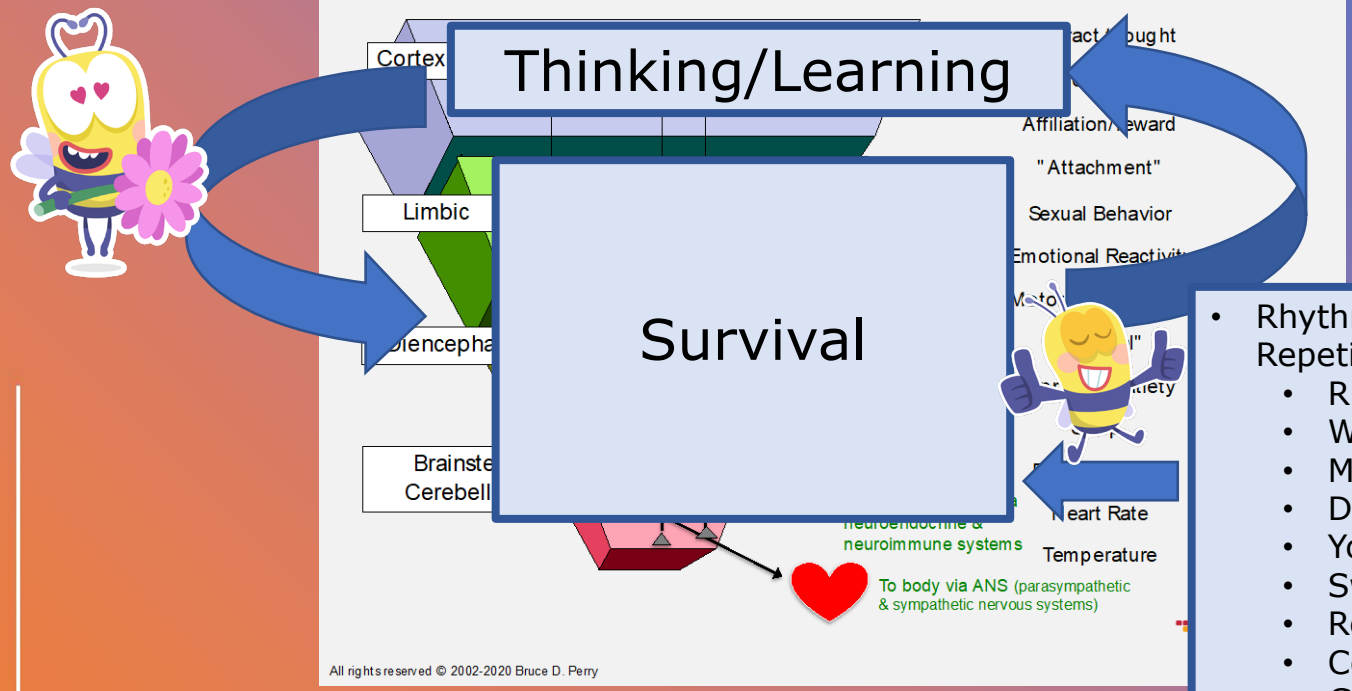
NEUROSEQUENTIAL NETWORK™



- Rhythmic, Patterned, Repetitive Activities:
  - Running
  - Walking
  - Music
  - Dance
  - Yoga
  - Swinging
  - Rocking
  - Coloring
  - Gardening
- Safe, regulating relational experiences

Understanding the Response to Threat

Flock, Freeze, Flight, Fight Continuum

Traditional Fight/Flight	Reflect	Flock	Freeze	Flight	Fight
Primary *secondary* Brain Areas	NEOCORTEX *Subcortex*	SUBCORTEX *Limbic*	LIMBIC *Midbrain*	MIDBRAIN *Brainstem*	BRAINSTEM *Autonomic*
Cognition	Abstract	Concrete	Emotional	Reactive	Reflexive
Mental State	CALM	ALERT	ALARM	FEAR	TERROR

NEUROSEQUENTIAL NETWORK™

- Anxiety Can Look Like:
  - Avoidance
  - Somatic symptoms
  - Sleep problem
  - Excessive need for reassurance
  - Poor school performance
  - Eating problems
  - Suicidal thoughts or behavior (22-55% of patients with anxiety will report SI)

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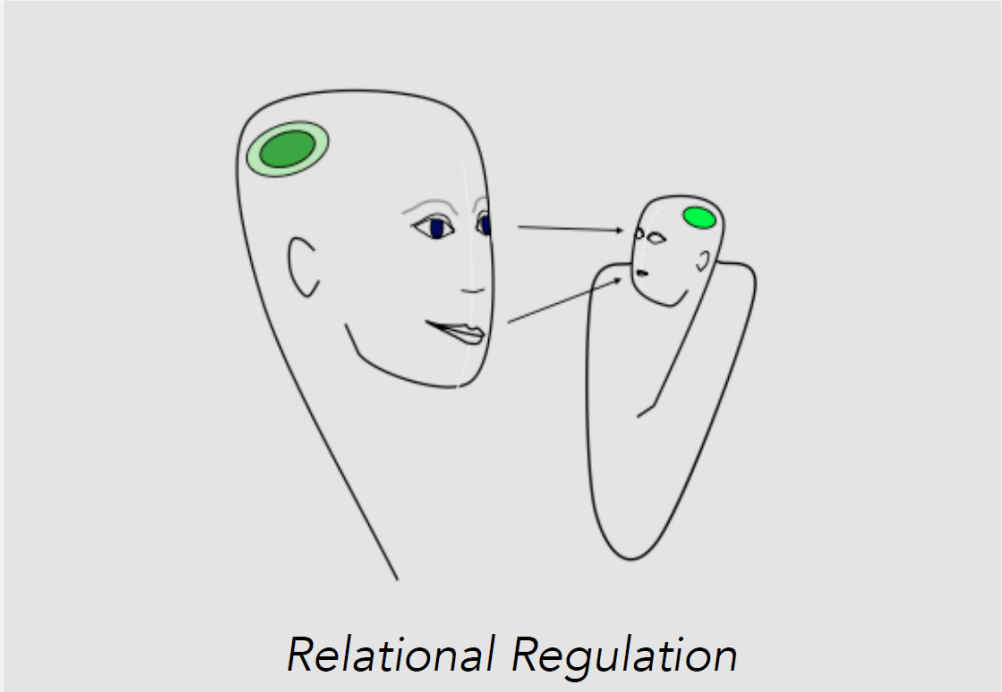
Relational Experience Matters—forming relational "templates"

The Magical Moments

Weaving Together the Neurobiology of Relationship, Reward and Regulation



Relational Regulation

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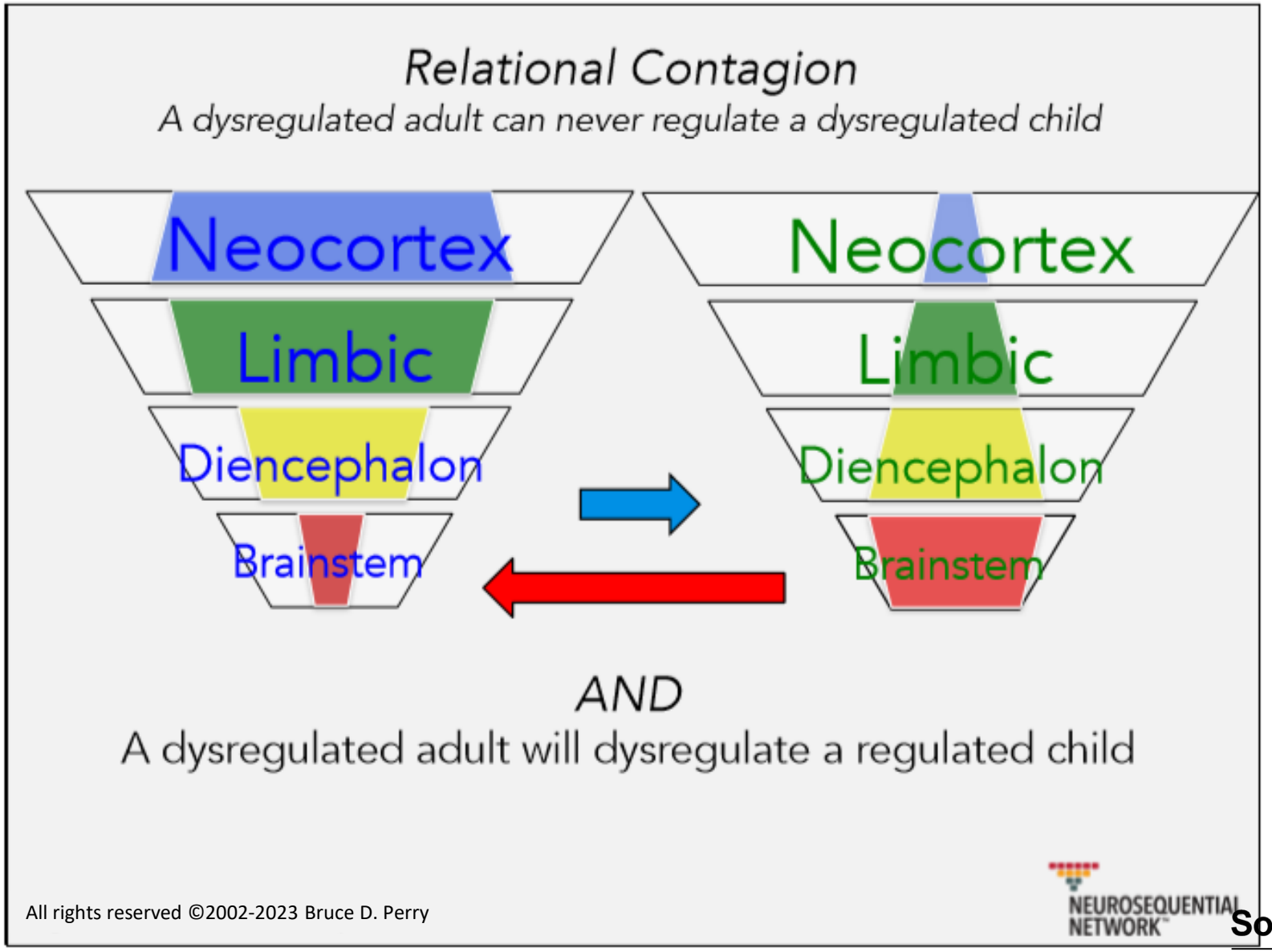


NEUROSEQUENTIAL NETWORK™

Case:
The *(not yet)* strong and (too) silent type

- J is a 7yo boy who is brought in by his mother who reports that he has been having increasing difficulty with talking at school and now is saying no words in school. He has been sleeping well and will talk to his parents and siblings at home. He does have some intermittent generalized worries that he expresses to his family, but these worries do not cause impairment at home. He does worry about what people think about him at school.

Case: Bothered Belly

- S is a 9yo girl who has been having recurrent episodes of abdominal pain. The belly pain occurs most commonly in the mornings on weekdays and subsides in the evenings and on the weekends. She has missed several days of school and has presented to the pediatrics office 5 times in the past month. She does admit to having difficulty making friends and feeling nervous at school, particularly after returning to school following the COVID-19 pandemic.

Case: Can't Stop, Won't Stop

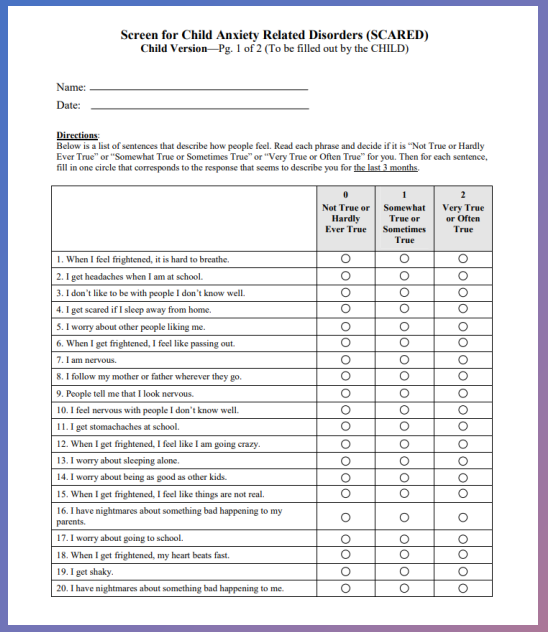
- Z is a 14yo girl who has been having intrusive thoughts that she is contaminated with germs. She has been engaging in repetitive handwashing to the point that her hands have been bleeding. When asked if she is having other intrusive thoughts, she admits that she has intrusive thoughts about dying, which has been terrifying for her and has resulted in decreased sleep.

Identifying Anxiety

- When is it a disorder?
  - When typical developmental tasks illicit anxiety
  - Impairment in functioning
  - Emotional/behavioral changes
  - Differentiating anxiety versus anxiety disorder

Anxiety

Anxiety Disorder



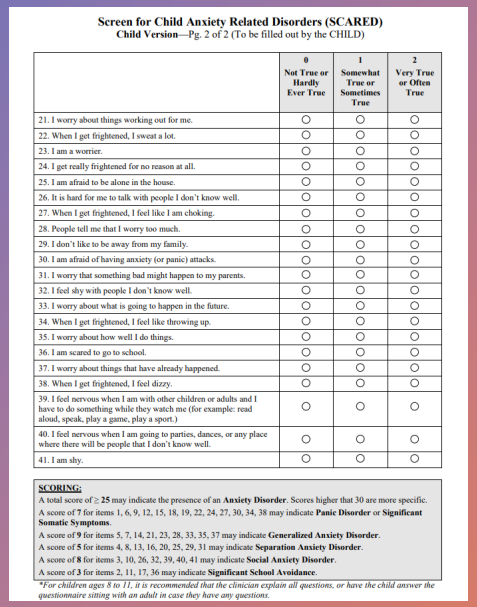
Screen for Child Anxiety Related Disorders (SCARED)
Child Version—Pg. 1 of 2 (To be filled out by the CHILD)

Name: _____

Date: _____

Directions:
Below is a list of sentences that describe how people feel. Read each phrase and decide if it is "Not True or Hardly Ever True" or "Somewhat True or Sometimes True" or "Very True or Often True" for you. Then for each sentence, fill in one circle that corresponds to the response that seems to describe you for the last 3 months.

	0 Not True or Hardly Ever True	1 Somewhat True or Sometimes True	2 Very True or Often True
1. When I feel frightened, it is hard to breathe.	○	○	○
2. I get headaches when I am at school.	○	○	○
3. I don't like to be with people I don't know well.	○	○	○
4. I get scared if I sleep away from home.	○	○	○
5. I worry about other people liking me.	○	○	○
6. When I get frightened, I feel like passing out.	○	○	○
7. I am nervous.	○	○	○
8. I follow my mother or father wherever they go.	○	○	○
9. People tell me that I look nervous.	○	○	○
10. I feel nervous with people I don't know well.	○	○	○
11. I get stomachaches at school.	○	○	○
12. When I get frightened, I feel like I am going crazy.	○	○	○
13. I worry about sleeping alone.	○	○	○
14. I worry about being as good as other kids.	○	○	○
15. When I get frightened, I feel like things are not real.	○	○	○
16. I have nightmares about something bad happening to my parents.	○	○	○
17. I worry about going to school.	○	○	○
18. When I get frightened, my heart beats fast.	○	○	○
19. I get shaky.	○	○	○
20. I have nightmares about something bad happening to me.	○	○	○

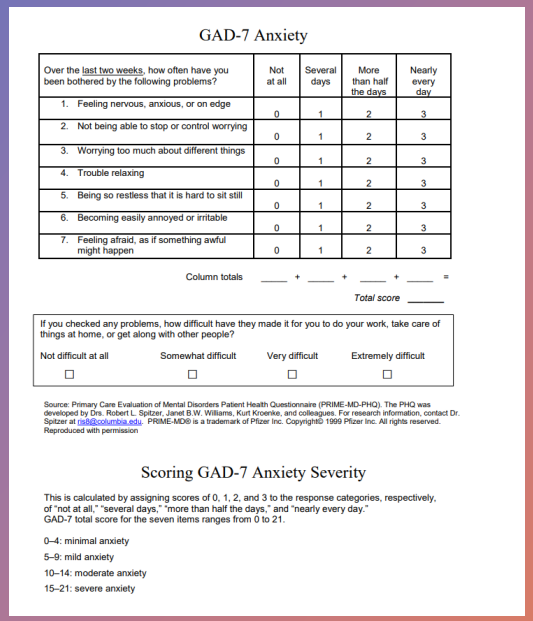


Screen for Child Anxiety Related Disorders (SCARED)
Child Version—Pg. 2 of 2 (To be filled out by the CHILD)

	0 Not True or Hardly Ever True	1 Somewhat True or Sometimes True	2 Very True or Often True
21. I worry about things working out for me.	○	○	○
22. When I get frightened, I sweat a lot.	○	○	○
23. I am a worrier.	○	○	○
24. I get really frightened for no reason at all.	○	○	○
25. I am afraid to be alone in the house.	○	○	○
26. It is hard for me to talk with people I don't know well.	○	○	○
27. When I get frightened, I feel like I am choking.	○	○	○
28. People tell me that I worry too much.	○	○	○
29. I don't like to be away from my family.	○	○	○
30. I am afraid of having anxiety (or panic) attacks.	○	○	○
31. I worry that something bad might happen to my parents.	○	○	○
32. I feel shy with people I don't know well.	○	○	○
33. I worry about what is going to happen in the future.	○	○	○
34. When I get frightened, I feel like throwing up.	○	○	○
35. I worry about how well I do things.	○	○	○
36. I am scared to go to school.	○	○	○
37. I worry about things that have already happened.	○	○	○
38. When I get frightened, I feel dizzy.	○	○	○
39. I feel nervous when I am with other children or adults and I have to do something while they watch me (for example: read aloud, speak, play a game, play a sport.)	○	○	○
40. I feel nervous when I am going to parties, dances, or any place where there will be people that I don't know well.	○	○	○
41. I am shy.	○	○	○

SCORING:
A total score of ≥ **25** may indicate the presence of an **Anxiety Disorder**. Scores higher that 30 are more specific.
A score of **7** for items 1, 6, 9, 12, 15, 18, 19, 22, 24, 27, 30, 34, 38 may indicate **Panic Disorder** or **Significant Somatic Symptoms**.
A score of **9** for items 5, 7, 14, 21, 23, 28, 33, 35, 37 may indicate **Generalized Anxiety Disorder**.
A score of **5** for items 4, 8, 13, 16, 20, 25, 29, 31 may indicate **Separation Anxiety Disorder**.
A score of **8** for items 3, 10, 26, 32, 39, 40, 41 may indicate **Social Anxiety Disorder**.
A score of **3** for items 2, 11, 17, 36 may indicate **Significant School Avoidance**.

**For children ages 8 to 11, it is recommended that the clinician explain all questions, or have the child answer the questionnaire sitting with an adult in case they have any questions.*



GAD-7 Anxiety

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

Column totals ____ + ____ + ____ + ____ = ____

Total score ____

If you checked any problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people?

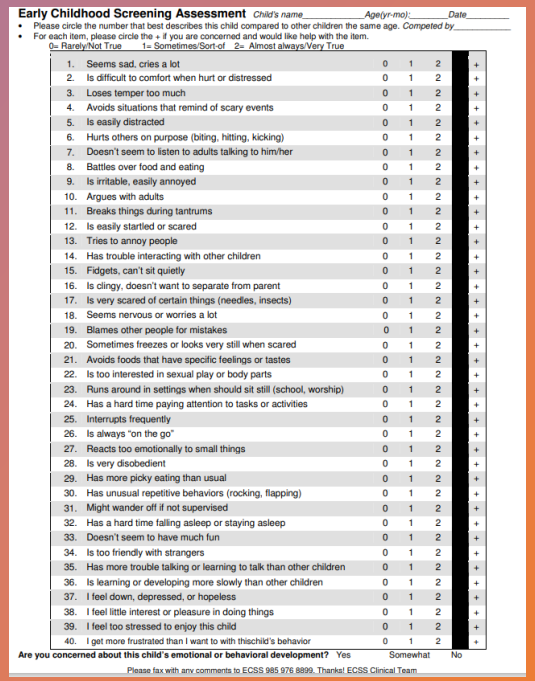
Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult ☐

Source: Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MD-PHQ). The PHQ was developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke, and colleagues. For research information, contact Dr. Spitzer at rls8@columbia.edu. PRIME-MD® is a trademark of Pfizer Inc. Copyright© 1999 Pfizer Inc. All rights reserved. Reproduced with permission

Scoring GAD-7 Anxiety Severity

This is calculated by assigning scores of 0, 1, 2, and 3 to the response categories, respectively, of "not at all," "several days," "more than half the days," and "nearly every day."
GAD-7 total score for the seven items ranges from 0 to 21.

0–4: minimal anxiety
5–9: mild anxiety
10–14: moderate anxiety
15–21: severe anxiety



Early Childhood Screening Assessment *Child's name_____Age(yr-mo):_____Date_____*

- Please circle the number that best describes this child compared to other children the same age. *Competed by*_____
- For each item, please circle the + if you are concerned and would like help with the item.

0= Rarely/Not True 1= Sometimes/Sort-of 2= Almost always/Very True

1.	Seems sad, cries a lot	0	1	2	+
2.	Is difficult to comfort when hurt or distressed	0	1	2	+
3.	Loses temper too much	0	1	2	+
4.	Avoids situations that remind of scary events	0	1	2	+
5.	Is easily distracted	0	1	2	+
6.	Hurts others on purpose (biting, hitting, kicking)	0	1	2	+
7.	Doesn't seem to listen to adults talking to him/her	0	1	2	+
8.	Battles over food and eating	0	1	2	+
9.	Is irritable, easily annoyed	0	1	2	+
10.	Argues with adults	0	1	2	+
11.	Breaks things during tantrums	0	1	2	+
12.	Is easily startled or scared	0	1	2	+
13.	Tries to annoy people	0	1	2	+
14.	Has trouble interacting with other children	0	1	2	+
15.	Fidgets, can't sit quietly	0	1	2	+
16.	Is clingy, doesn't want to separate from parent	0	1	2	+
17.	Is very scared of certain things (needles, insects)	0	1	2	+
18.	Seems nervous or worries a lot	0	1	2	+
19.	Blames other people for mistakes	0	1	2	+
20.	Sometimes freezes or looks very still when scared	0	1	2	+
21.	Avoids foods that have specific feelings or tastes	0	1	2	+
22.	Is too interested in sexual play or body parts	0	1	2	+
23.	Runs around in settings when should sit still (school, worship)	0	1	2	+
24.	Has a hard time paying attention to tasks or activities	0	1	2	+
25.	Interrupts frequently	0	1	2	+
26.	Is always "on the go"	0	1	2	+
27.	Reacts too emotionally to small things	0	1	2	+
28.	Is very disobedient	0	1	2	+
29.	Has more picky eating than usual	0	1	2	+
30.	Has unusual repetitive behaviors (rocking, flapping)	0	1	2	+
31.	Might wander off if not supervised	0	1	2	+
32.	Has a hard time falling asleep or staying asleep	0	1	2	+
33.	Doesn't seem to have much fun	0	1	2	+
34.	Is too friendly with strangers	0	1	2	+
35.	Has more trouble talking or learning to talk than other children	0	1	2	+
36.	Is learning or developing more slowly than other children	0	1	2	+
37.	I feel down, depressed, or hopeless	0	1	2	+
38.	I feel little interest or pleasure in doing things	0	1	2	+
39.	I feel too stressed to enjoy this child	0	1	2	+
40.	I get more frustrated than I want to with thischild's behavior	0	1	2	+

Are you concerned about this child's emotional or behavioral development? Yes Somewhat No

Please fax with any comments to ECSS 985 976 8899, Thanks! ECSS Clinical Team

Screening

- Screen for Childhood Anxiety Related Disorders (SCARED)
- GAD-7
- Early Childhood Screening Assessment (ECSA)

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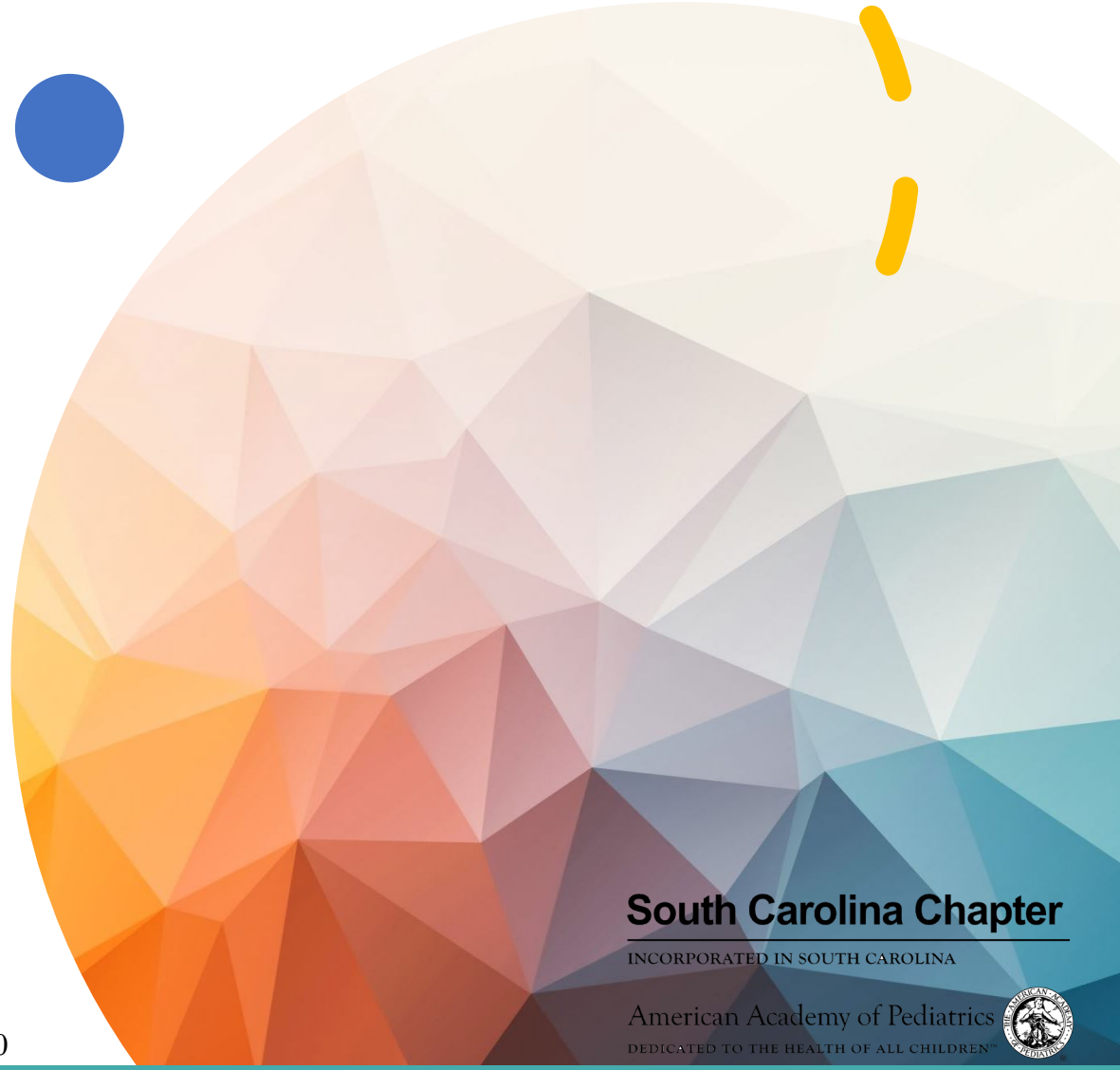
2023 ANNUAL MEETING

Treatment Stats:
According to the CAMS*

Treatment goal is REMISSION! (not symptom improvement)

- Combination treatment: 80.7%
- CBT alone: 59.7%
- Sertraline alone: 54.9%
- Placebo: 23.7%

*Child/Adolescent Anxiety Multimodal Study (CAMS): rationale, design, and methods 2010



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Environment

- How can you change the environment to decrease anxiety?
  - Decrease Stimulation
  - Create Schedule
  - Give Opportunities for Control

Quick Skills

Breathing:

- Square breathing
- Cookie breathing
- Bubbles: who could make the biggest bubble
- Pinwheels

Thought Stopping:

- Visualizing a stop sign to stop negative thoughts
- Changing the channel

Mindfulness

- Progressive Muscle Relaxation
- Guided Imagery

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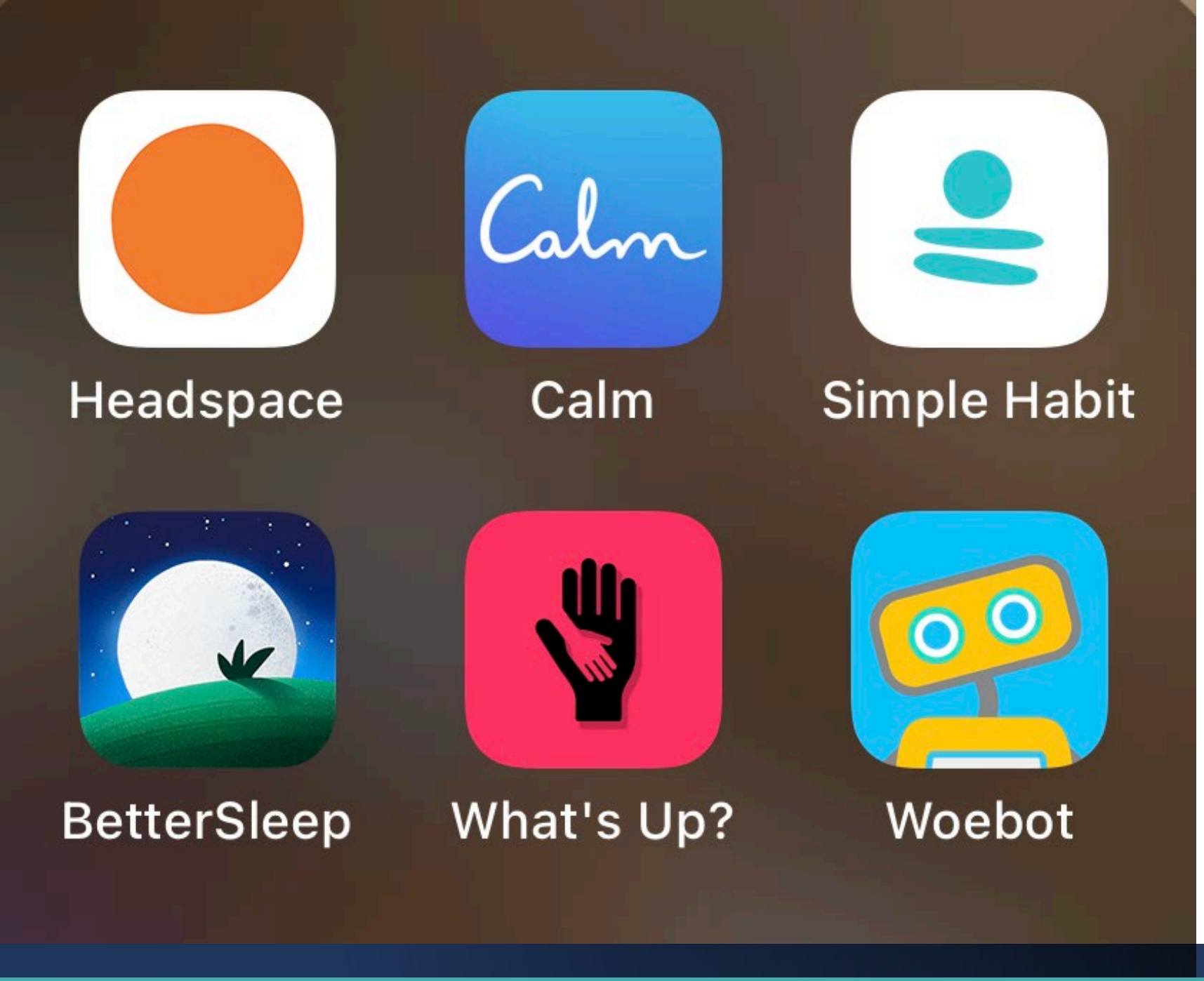

Multimedia Resources

- Sesame Street Monster Meditations
- Woebot
- Calm
- What's Up?
- Headspace
- Simple Habit
- BetterSleep

Psychotherapy

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ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *Childhood Onset Developmental Disorders*

Treatment of pediatric anxiety disorders

Amy Rapp,[1] Alice Dodds,[2] John T. Walkup,[3] and Moira Rynn[1]

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- The Coping Cat
- Camp Cope-A-Lot (CCAL)
- BRAVE-ONLINE
  - Body signs, Relax, Activate helpful thoughts, Victory over fears, Enjoy yourself
- Social Effectiveness Therapy (SET-C)
- Exposure and Response Prevention
- Trauma-Focused Cognitive Behavioral Therapy (TF-CBT)
- Cognitive-Behavioral Intervention for Trauma in Schools (CBITS)
- Structured Psychotherapy for Adolescents Responding to Chronic Stress (SPARCS)
- Combined Parent-Child Approach for Children and Families At-Risk for Child Physical Abuse (CPC-CBT)

Treatment for Anxiety Disorders in the Pediatric Primary Care Setting

Jennifer B. Blossom, PhD[a,*], Nathaniel Jungbluth, PhD[b], Erin Dillon-Naftolin, MD[b,c,d], William French, MD[b,c,d]

KEYWORDS

• Integrated care • Pediatric primary care • Anxiety • Cognitive-behavioral therapy
• Pharmacotherapy

KEY POINTS

- Pediatric anxiety can be effectively managed in integrated pediatric primary care.
- Exposure-based cognitive behavioral therapy is the first-line behavioral intervention for youth anxiety.
- Pharmacotherapy can be effective as a stand-alone treatment or in conjunction with cognitive behavioral therapy.

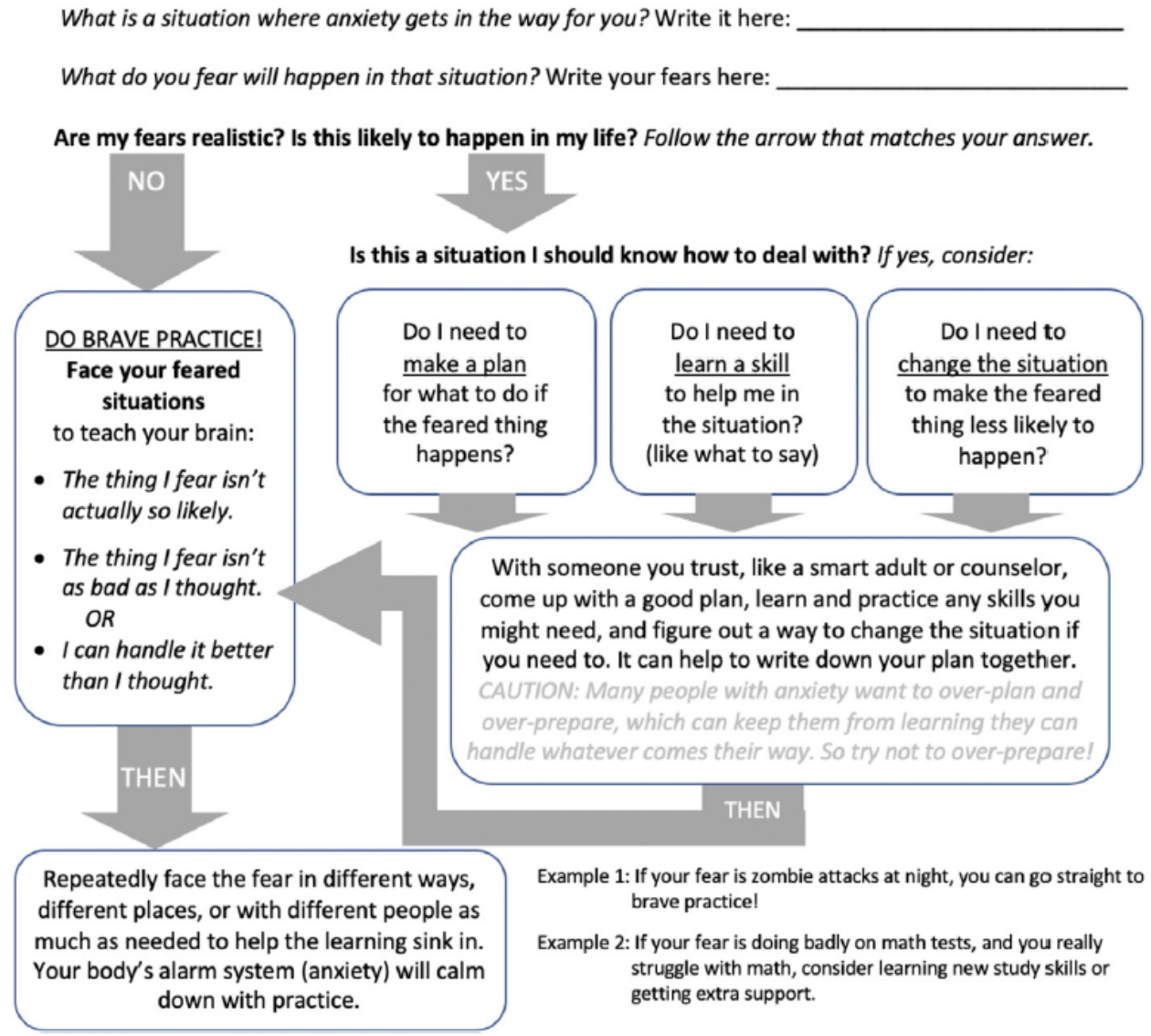

Fig. 1. Decision tree for using exposure to address fear of normal risk, age-appropriate situations.[37]

It's a Family Affair

- Courage, avoiding avoidance
- Staying active
- Family history discussion early (Dr. Walkup says 1st WCC)
- Personalized screening for your child based on family history
  - Screen for anxiety ages 4-6 yo
  - ADHD 3-4 yo
  - MDD screen in adolescent years
- Continued discussion about anxiety and anxiety treatment as the child develops

Is it time to consider medications?

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Time for medication, now what?

- Family history
  - What worked?
  - What did not work?
- Anticipatory guidance
  - Onset time
  - Follow up
  - Addition of therapy
- Previous medication trials

Selective Serotonin Reuptake Inhibitors (SSRIs)

Name (Brand Name)	Starting dosage		Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use
Fluoxetine (Prozac)	≤12yo	13+	Increase by 5-10 mg/day every 7-14 days Max: 60mg (80mg)	GI, headache, activation, SI, sexual dysfunction, agitation, insomnia	MDD: 8+ OCD: 7+	MDD: <8 Other anxiety d/o: 6+ Selective mutism
	5mg* *(PI states 10-20mg)	10mg* *(PI states 10-20mg)				
Escitalopram (Lexapro)	≤12yo	13+	Increase by 2.5 - 5mg/day every 7-14 days Max: 20mg (30mg)	GI, headache, activation, SI, sexual dysfunction, insomnia	GAD: 7+ MDD: 12+	MDD: 6 – 11
	2.5mg* *(PI states 10mg)	5mg* *(PI states 10mg)				
Sertraline (Zoloft)	≤12yo	13+	Increase by 12.5 - 25mg/day every 7-14 days Max: 200/300mg	GI, headache, activation, SI, sexual dysfunction, agitation, insomnia	OCD: 6+	Other anxiety d/o: 6+ MDD: 6+
	12.5mg-25mg	25mg-50mg				
Fluvoxamine (Luvox)	≤12yo	13+	Increase by 12.5 - 25mg/day every 4-7 days Max: 200mg	GI, headache, activation, SI, sexual dysfunction, sedation	OCD: 7+	Other anxiety d/o: 6+ MDD: 7+
	12.5mg daily/BID	25mg daily/BID				
Citalopram (Celexa)	≤12yo	13+	Increase by 5 - 10mg/day every 7 – 14 days Max: 40mg	GI, headache, activation, SI, sexual dysfunction, **QTC prolongation**	NONE	MDD: 7+ Other anxiety d/o: 7+
	5mg	10mg				
Paroxetine (Paxil)	☹		☹	☹	NONE	☹

This table is used for guidance purposes only. The information contained here is compiled from multiple references including the package inserts, child and adolescent pharmacology textbooks (McVoy and Findling), and clinical practice.

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) & Norepinephrine-Dopamine Reuptake Inhibitors (NDRIs)

Name (Brand Name)	Starting dosage	Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use	Mechanism of Action
Venlafaxine ER (Effexor ER)	37.5mg/day	Increase by 37.5mg/day every 4-7 days Max: 75mg (300mg)	GI, headache, activation, SI, sexual dysfunction, **HTN, Taper slowly, "electric-shock" sensations**	NONE	MDD: >8 GAD: 7+	SNRI
Desvenlafaxine (Pristiq) (Khedezla)	25mg/day *(PI states 50mg/day for adults)	Start 50mg/day >50mg unlikely to help Max 200mg for neuropathic pain	GI, headache, activation, SI, sexual dysfunction, **HTN, Taper slowly**	NONE	NONE Some safety and tolerability studies in pediatrics	SNRI
Duloxetine (Cymbalta)	20mg/day* *(PI states 30mg/day)	Increase by 20-30mg*/day every 14 days Max: 120mg *(PI states 30mg/day)	GI, headache, activation, SI, sexual dysfunction, **Taper slowly**	GAD (7+)	MDD: 6+ Pain	SNRI
Bupropion XL (Wellbutrin XL)	150mg* (may use IR for lower dosages) *Also SR has 100mg option	Increase by 150mg/day every 14 days Max: 300mg* *(PI states 450mg)	GI, headache, activation, SI, **HTN, contraindicated in seizure and eating disorders**	NONE	MDD: 6+ ADHD: 6+ Smoking cessation	NDRI Nicotinic receptor antagonist

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Alpha Agonists and Antagonists

Name (Brand Name)	Starting dosage	Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use	Mechanism of Action
Clonidine (Catapres)	0.05mg – 0.1mg divided q day or BID* *(PI will recommend TID-QID)	Increase by 0.05mg/day every 7 days Max: 0.4mg/day	Sedation, hypotension, bradycardia, **rebound hypertension**	ADHD (6+)	Tourette syndrome Anxiety PTSD-related nightmares ODD/CD	Alpha-2 agonist
Guanfacine (Tenex)	0.5mg – 1mg q day or divided BID-TID	Increase by 0.5mg/day every 7 days Max: 3mg/day and 1mg/dose	Sedation, hypotension, bradycardia, **rebound hypertension**	ADHD (6+)	Tourette's syndrome Anxiety	Alpha-2 agonist
Guanfacine ER (Intuniv)	1mg q day	Increase by 1mg/day every 7 days Max: 4mg/day* *(PI states 7mg/day (91+kg))	Sedation, hypotension, bradycardia, **rebound hypertension**	ADHD (6+)	Tourette's syndrome Anxiety	Alpha-2 agonist
Prazosin	1mg q day	Increase by 1mg/day every 7 days Max: 4-5mg/day* *(PI states 20mg for HTN)	Hypotension (AM), syncope, sedation	HTN	PTSD-related nightmares	Alpha-1 antagonist

This table is used for guidance purposes only. The information contained here is compiled from multiple references including the package inserts, child, and adolescent pharmacology textbooks (McVoy and Findling), and clinical practice.

Other Options

- Hydroxyzine
- Buspirone
- Propranolol
- Hypnotics
- Second-generation antipsychotics* (severe symptoms)
- Benzodiazepines* (procedural anxiety)

Hypnotic Agents*

Name (Brand Name)	Starting dosage	Titration Recommendation	Common Side Effects	Indications	Mechanism of Action
Melatonin	3mg	Increase by 3-5mg every 2-3 days as needed for sleep Max: 10mg	sedation	Insomnia	Acts on melatonin receptors in the SCN to regulate sleep cycle
Hydroxyzine (Vistaril) (Atarax)	2mg/kg/day divided q 6-8prn <44kg: 25mg >44kg: 50mg	Increase by 12.5-25mg/dose as needed (also, can use 10mg formulation) Max: 200mg/day	Sedation, dry mouth, weight gain?	Insomnia Anxiety Agitation Pruritus	1st generation antihistamine
Mirtazapine (Remeron)	7.5mg	Increase by 7.5mg. Dosages greater than 15mg are not as effective for sleep Max: 45mg	Sedation, dry mouth, **weight gain**, increased appetite, abnormal dreams,	Anorexia Insomnia Depression	Presynaptic alpha-2 antagonist 5-HT2A/C, 5-HT3, H2 antagonist
Diphenhydramine (Benadryl)	2-5yo: 6.25mg 6-11yo: 12.5-25mg 12+: 25mg-50mg 1-2mg/kg/dose	Increase by 6.25-25mg per dose (depending on starting dose) Max: age dependent (50mg/dose)	Sedation, dry mouth, weight gain, increased appetite, urinary retention	Allergies Insomnia Allergies	1st generation antihistamine

* Can also consider alpha-agonists or second-generation antipsychotics for sleep and nighttime anxiety

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Antipsychotics

Name (Brand Name)	Starting dosage		Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use	Mechanism of Action
Risperidone (Risperdal)	0.25mg – 0.5mg divided q day or BID		Increase by 0.25mg – 0.5mg per day every 4 days Max: 6mg	Increased appetite, weight gain, EPS/TD, akathisia, sedation, hyper-prolactinemia, gynecomastia	Irritability +ASD (5+) BPAD—manic/mixed (10+) Schizophrenia (13+)	Aggression Tourette's syndrome	D2/5-HT2A antagonist 5-HT2A>D2
Aripiprazole (Abilify)	2mg* – 5mg q day *(Can use 1mg in young patients)		Increase by 2.5mg – 5mg/day every 2-7 days Max: 30mg	Increased appetite, weight gain, EPS/TD, **akathisia**, activation	Irritability +ASD (5+) BPAD—manic/mixed (10+) Schizophrenia (13+)	Aggression Tourette's syndrome MDD adjunct (on label for adults)	D2/5-HT2A partial agonist 5-HT2A antagonist
Olanzapine (Zyprexa)	2.5mg – 5mg divided qHS or BID		Increase by 2.5mg – 5mg every 2-7 days Max: 20mg (30mg)	Increased appetite, **weight gain, metabolic syndrome,** less EPS/TD, **sedation**	Schizophrenia (13+) BPAD—manic/mixed (13+) BPAD—depression (10+)	Aggression Tourette's syndrome **Delirium**	D2/5-HT2A antagonist
Quetiapine (Seroquel)	12.5mg – 25mg q day or BID* *(PI states 25mg BID)		Increase by 12.5mg – 25mg up to every day* Max: 800mg *(PI states increase by 50-100mg/day)	Increased appetite, **weight gain,** less EPS/TD, **sedation, metabolic syndrome**	Schizophrenia (13+) BPAD—mania (10+)	Aggression Tourette's syndrome **Delirium**	D2/5-HT2A antagonist
Haloperidol (Haldol)	3-12yo	12+	Increase by 0.5mg/day every 5-7 days Max: 0.15mg/kg/day or 15-20mg/day	**EPS/TD**, akathisia, hyper-prolactinemia	Psychosis (3+) Tourette's syndrome Hyperactivity Severe behavioral problems	**Delirium**	D2 antagonist
	0.05-0.15mg/kg/day divided BID or TID	0.5mg – 5mg divided BID or TID					

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Side Effects

- Most common side effects:
  - Headache
  - GI distress
  - Sleep disturbance (insomnia or somnolence, vivid dreams)
  - Restlessness
  - Diaphoresis
  - Akathisia
  - Appetite change (increase or decrease)
- 3-8% of youths may show increased impulsivity, agitation, irritability, silliness, and “behavioral activation”
  - These symptoms need to be differentiated from mania or hypomania

- Less common side effects:
  - Serotonin syndrome
  - Increased bleeding
  - Increased suicidality
- Venlafaxine:
  - Hypertension
  - Tachycardia
- Bupropion:
  - Seizures (in doses higher than 400mg/day in non-XL preparations)
  - This was increased in patients with bulimia

Things to Consider

Lower starting doses for patients with anxiety

Be mindful of cytochrome P-450 metabolism and drug-drug interactions

Ask about other serotonergic agents

Nonlinear response to medication

Up to 60% of adolescents respond to placebo

Half life may be shorter in adolescents and children; consider BID dosing for withdrawal symptoms* or side effects

"Is this going to make my child suicidal?"

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Clinical response and risk for reported suicidal ideation and suicide attempts in a pediatric antidepressant treatment: a meta-analysis of randomized control trials Bridge et al 2007 in JAMA

Diagnosis	NNT	NNH	Response Rate	SI Rate
MDD	10	112	61%	3%
OCD	6	200	52%	1%
Non-OCD Anxiety Disorders	3	143	69%	1%

SSRIs and Suicide

Figures

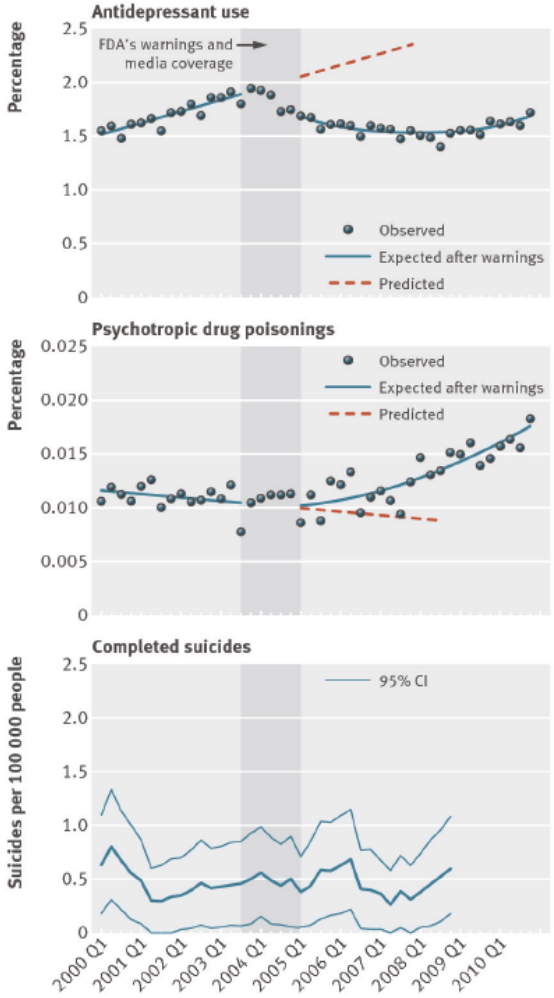

Fig 1 Rates of antidepressant use, psychotropic drug poisonings, and completed suicides per quarter before and after the warnings among adolescents enrolled in 11 health plans in nationwide Mental Health Research Network

Follow-up Recommendations

- The FDA recommends that patients started on antidepressants
  - Should be seen every week x 4 weeks
  - Then every 2 weeks x 8 week
  - Then monthly after the first 12 weeks of treatment
  - If face-to-face appointments are not possible, it is recommended to have brief telephone evaluations
- No data supports that this monitoring has any impact on suicide rate
- Patients are often engaged in weekly therapy (which helps with monitoring)

Learning Objectives

- At the conclusion of this session, learners will be able to:
  - Identify common anxiety disorders in the pediatric population
  - Better understand psychopharmacological treatment options for the treatment of anxiety disorders in the pediatric population
  - Understand non-pharmacological treatment options for the treatment of anxiety disorder in the pediatric populations
  - Understand the effects of trauma on pediatric patients and the development of anxiety disorders

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Q & A

Megan Zappitelli, MD, FAAP
Prisma Health University of South Carolina
School of Medicine Greenville
Department of Psychiatry

THANK YOU!

QTIP Monthly Call: Anxiety Disorders

Megan Zappitelli, MD
October 11, 2023

Epidemiology

- Anxiety Disorders are the most common childhood-onset psychiatric disorders
- Prevalence between 10% to 30%
- Rates of anxiety disorders increased to 20.5% following COVID-19 pandemic

What is anxiety?

Selective Mutism

Generalized Anxiety Disorder

Social Anxiety Disorder

Post Traumatic Stress Disorder

Specific Phobia

Separation Anxiety Disorder

Agoraphobia

Panic Disorder

Illness Anxiety Disorder

Substance/Medication-Induced Anxiety Disorder

Obsessive Compulsive Disorder

What is anxiety?

- According to the DSM-5-TR:
  - ***Fear*** *is the emotional response to real or perceived imminent threat*
  - ***Anxiety*** *is the anticipation of future threat*

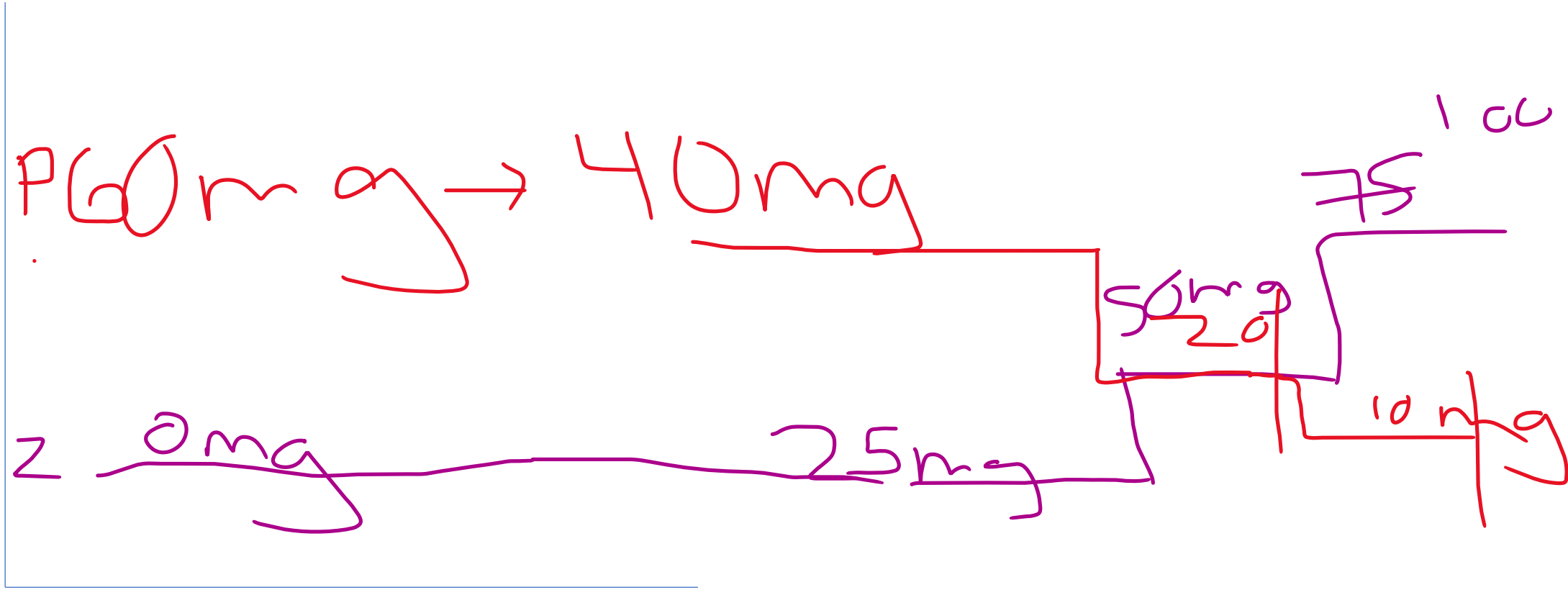
What is anxiety?

- Anxiety Can Look Like:
  - Avoidance
  - Somatic symptoms
  - Sleep problem
  - Excessive need for reassurance
  - Poor school performance
  - Eating problems
  - Suicidal thoughts or behavior (22-55% of patients with anxiety will report SI)

Transitioning Between Medications

Things to Consider

- Half Life
- Starting Dose
- Medication formulation: (ie. dose, capsule/tablet, etc).
- Availability of follow up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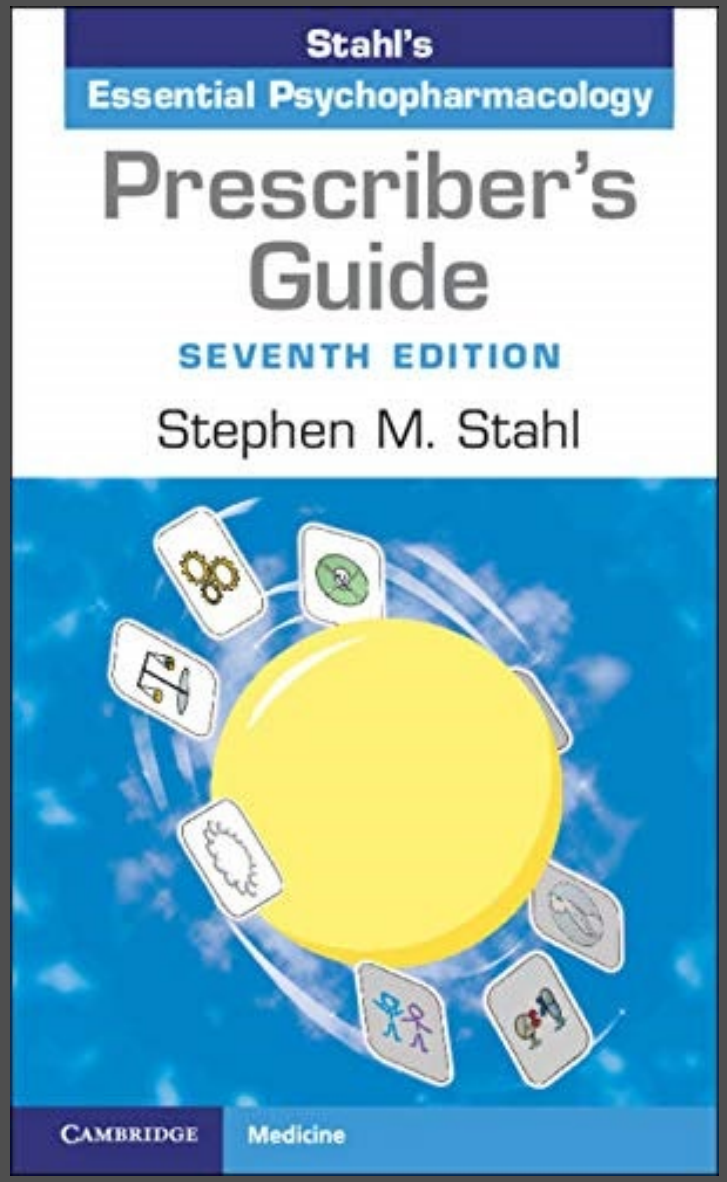
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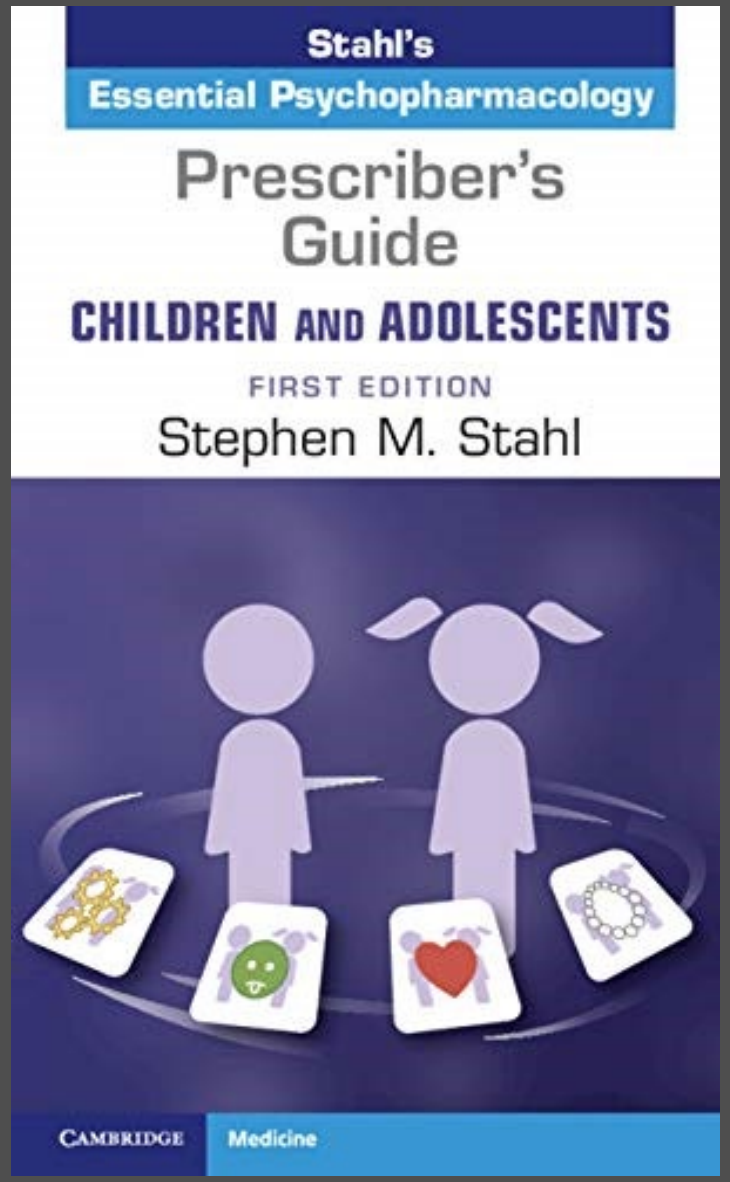
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Are there specific medications you like for specific ages/genders/concerns?

Time for medication, now what?

- Family history
  - What worked?
  - What did not work?
- Anticipatory guidance
  - Onset time
  - Follow up
  - Addition of therapy
- Previous medication trials

Selective Serotonin Reuptake Inhibitors (SSRIs)

Name (Brand Name)	Starting dosage		Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use
Fluoxetine (Prozac)	≤12yo	13+	Increase by 5-10 mg/day every 7-14 days Max: 60mg (80mg)	GI, headache, activation, SI, sexual dysfunction, agitation, insomnia	MDD: 8+ OCD: 7+	MDD: <8 Other anxiety d/o: 6+ Selective mutism
	5mg* *(PI states 10-20mg)	10mg* *(PI states 10-20mg)				
Escitalopram (Lexapro)	≤12yo	13+	Increase by 2.5 - 5mg/day every 7-14 days Max: 20mg (30mg)	GI, headache, activation, SI, sexual dysfunction, insomnia	GAD: 7+ MDD: 12+	MDD: 6 – 11
	2.5mg* *(PI states 10mg)	5mg* *(PI states 10mg)				
Sertraline (Zoloft)	≤12yo	13+	Increase by 12.5 - 25mg/day every 7-14 days Max: 200/300mg	GI, headache, activation, SI, sexual dysfunction, agitation, insomnia	OCD: 6+	Other anxiety d/o: 6+ MDD: 6+
	12.5mg-25mg	25mg-50mg				
Fluvoxamine (Luvox)	≤12yo	13+	Increase by 12.5 - 25mg/day every 4-7 days Max: 200mg	GI, headache, activation, SI, sexual dysfunction, sedation	OCD: 7+	Other anxiety d/o: 6+ MDD: 7+
	12.5mg daily/BID	25mg daily/BID				
Citalopram (Celexa)	≤12yo	13+	Increase by 5 - 10mg/day every 7 – 14 days Max: 40mg	GI, headache, activation, SI, sexual dysfunction, **QTC prolongation**	NONE	MDD: 7+ Other anxiety d/o: 7+
	5mg	10mg				
Paroxetine (Paxil)	☹		☹	☹	NONE	☹

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How High Can Lexapro Go?

Selective Serotonin Reuptake Inhibitors (SSRIs)

Name (Brand Name)	Starting dosage		Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use
Fluoxetine (Prozac)	≤12yo	13+	Increase by 5-10 mg/day every 7-14 days Max: 60mg (80mg)	GI, headache, activation, SI, sexual dysfunction, agitation, insomnia	MDD: 8+ OCD: 7+	MDD: <8 Other anxiety d/o: 6+ Selective mutism
	5mg* *(PI states 10-20mg)	10mg* *(PI states 10-20mg)				
Escitalopram (Lexapro)	≤12yo	13+	Increase by 2.5 - 5mg/day every 7-14 days Max: 20mg (30mg)	GI, headache, activation, SI, sexual dysfunction, insomnia	GAD: 7+ MDD: 12+	MDD: 6 – 11
	2.5mg* *(PI states 10mg)	5mg* *(PI states 10mg)				
Sertraline (Zoloft)	≤12yo	13+	Increase by 12.5 - 25mg/day every 7-14 days Max: 200/300mg	GI, headache, activation, SI, sexual dysfunction, agitation, insomnia	OCD: 6+	Other anxiety d/o: 6+ MDD: 6+
	12.5mg-25mg	25mg-50mg				
Fluvoxamine (Luvox)	≤12yo	13+	Increase by 12.5 - 25mg/day every 4-7 days Max: 200mg	GI, headache, activation, SI, sexual dysfunction, sedation	OCD: 7+	Other anxiety d/o: 6+ MDD: 7+
	12.5mg daily/BID	25mg daily/BID				
Citalopram (Celexa)	≤12yo	13+	Increase by 5 - 10mg/day every 7 – 14 days Max: 40mg	GI, headache, activation, SI, sexual dysfunction, **QTC prolongation**	NONE	MDD: 7+ Other anxiety d/o: 7+
	5mg	10mg				
Paroxetine (Paxil)	☹		☹	☹	NONE	☹

This table is used for guidance purposes only. The information contained here is compiled from multiple references including the package inserts, child and adolescent pharmacology textbooks (McVoy and Findling), and clinical practice.

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) & Norepinephrine-Dopamine Reuptake Inhibitors (NDRIs)

Name (Brand Name)	Starting dosage	Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use	Mechanism of Action
Venlafaxine ER (Effexor ER)	37.5mg/day	Increase by 37.5mg/day every 4-7 days Max: 75mg (300mg)	GI, headache, activation, SI, sexual dysfunction, **HTN, Taper slowly, "electric-shock" sensations**	NONE	MDD: >8 GAD: 7+	SNRI
Desvenlafaxine (Pristiq) (Khedezla)	25mg/day *(PI states 50mg/day for adults)	Start 50mg/day >50mg unlikely to help Max 200mg for neuropathic pain	GI, headache, activation, SI, sexual dysfunction, **HTN, Taper slowly**	NONE	NONE Some safety and tolerability studies in pediatrics	SNRI
Duloxetine (Cymbalta)	20mg/day* *(PI states 30mg/day)	Increase by 20-30mg*/day every 14 days Max: 120mg *(PI states 30mg/day)	GI, headache, activation, SI, sexual dysfunction, **Taper slowly**	GAD (7+)	MDD: 6+ Pain	SNRI
Bupropion XL (Wellbutrin XL)	150mg* (may use IR for lower dosages) *Also SR has 100mg option	Increase by 150mg/day every 14 days Max: 300mg* *(PI states 450mg)	GI, headache, activation, SI, **HTN, contraindicated in seizure and eating disorders**	NONE	MDD: 6+ ADHD: 6+ Smoking cessation	NDRI Nicotinic receptor antagonist

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Alpha Agonists and Antagonists

Name (Brand Name)	Starting dosage	Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use	Mechanism of Action
Clonidine (Catapres)	0.05mg – 0.1mg divided q day or BID* *(PI will recommend TID-QID)	Increase by 0.05mg/day every 7 days Max: 0.4mg/day	Sedation, hypotension, bradycardia, **rebound hypertension**	ADHD (6+)	Tourette syndrome Anxiety PTSD-related nightmares ODD/CD	Alpha-2 agonist
Guanfacine (Tenex)	0.5mg – 1mg q day or divided BID-TID	Increase by 0.5mg/day every 7 days Max: 3mg/day and 1mg/dose	Sedation, hypotension, bradycardia, **rebound hypertension**	ADHD (6+)	Tourette's syndrome Anxiety	Alpha-2 agonist
Guanfacine ER (Intuniv)	1mg q day	Increase by 1mg/day every 7 days Max: 4mg/day* *(PI states 7mg/day (91+kg))	Sedation, hypotension, bradycardia, **rebound hypertension**	ADHD (6+)	Tourette's syndrome Anxiety	Alpha-2 agonist
Prazosin	1mg q day	Increase by 1mg/day every 7 days Max: 4-5mg/day* *(PI states 20mg for HTN)	Hypotension (AM), syncope, sedation	HTN	PTSD-related nightmares	Alpha-1 antagonist

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Other Options

- Hydroxyzine
- Buspirone
- Propranolol
- Hypnotics
- Second-generation antipsychotics* (severe symptoms)
- Benzodiazepines* (procedural anxiety)

Hypnotic Agents*

Name (Brand Name)	Starting dosage	Titration Recommendation	Common Side Effects	Indications	Mechanism of Action
Melatonin	3mg	Increase by 3-5mg every 2-3 days as needed for sleep Max: 10mg	sedation	Insomnia	Acts on melatonin receptors in the SCN to regulate sleep cycle
Hydroxyzine (Vistaril) (Atarax)	2mg/kg/day divided q 6-8prn <44kg: 25mg >44kg: 50mg	Increase by 12.5-25mg/dose as needed (also, can use 10mg formulation) Max: 200mg/day	Sedation, dry mouth, weight gain?	Insomnia Anxiety Agitation Pruritus	1st generation antihistamine
Mirtazapine (Remeron)	7.5mg	Increase by 7.5mg. Dosages greater than 15mg are not as effective for sleep Max: 45mg	Sedation, dry mouth, **weight gain**, increased appetite, abnormal dreams,	Anorexia Insomnia Depression	Presynaptic alpha-2 antagonist 5-HT2A/C, 5-HT3, H2 antagonist
Diphenhydramine (Benadryl)	2-5yo: 6.25mg 6-11yo: 12.5-25mg 12+: 25mg-50mg 1-2mg/kg/dose	Increase by 6.25-25mg per dose (depending on starting dose) Max: age dependent (50mg/dose)	Sedation, dry mouth, weight gain, increased appetite, urinary retention	Allergies Insomnia Allergies	1st generation antihistamine

* Can also consider alpha-agonists or second-generation antipsychotics for sleep and nighttime anxiety

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Antipsychotics

Name (Brand Name)	Starting dosage		Titration Recommendation	Common Side Effects	FDA approved indications	Off-label Use	Mechanism of Action
Risperidone (Risperdal)	0.25mg – 0.5mg divided q day or BID		Increase by 0.25mg – 0.5mg per day every 4 days Max: 6mg	Increased appetite, weight gain, EPS/TD, akathisia, sedation, hyper-prolactinemia, gynecomastia	Irritability +ASD (5+) BPAD—manic/mixed (10+) Schizophrenia (13+)	Aggression Tourette's syndrome	D2/5-HT2A antagonist 5-HT2A>D2
Aripiprazole (Abilify)	2mg* – 5mg q day *(Can use 1mg in young patients)		Increase by 2.5mg – 5mg/day every 2-7 days Max: 30mg	Increased appetite, weight gain, EPS/TD, **akathisia**, activation	Irritability +ASD (5+) BPAD—manic/mixed (10+) Schizophrenia (13+)	Aggression Tourette's syndrome MDD adjunct (on label for adults)	D2/5-HT2A partial agonist 5-HT2A antagonist
Olanzapine (Zyprexa)	2.5mg – 5mg divided qHS or BID		Increase by 2.5mg – 5mg every 2-7 days Max: 20mg (30mg)	Increased appetite, **weight gain, metabolic syndrome,** less EPS/TD, **sedation**	Schizophrenia (13+) BPAD—manic/mixed (13+) BPAD—depression (10+)	Aggression Tourette's syndrome **Delirium**	D2/5-HT2A antagonist
Quetiapine (Seroquel)	12.5mg – 25mg q day or BID* *(PI states 25mg BID)		Increase by 12.5mg – 25mg up to every day* Max: 800mg *(PI states increase by 50-100mg/day)	Increased appetite, **weight gain,** less EPS/TD, **sedation, metabolic syndrome**	Schizophrenia (13+) BPAD—mania (10+)	Aggression Tourette's syndrome **Delirium**	D2/5-HT2A antagonist
Haloperidol (Haldol)	3-12yo	12+	Increase by 0.5mg/day every 5-7 days Max: 0.15mg/kg/day or 15-20mg/day	**EPS/TD**, akathisia, hyper-prolactinemia	Psychosis (3+) Tourette's syndrome Hyperactivity Severe behavioral problems	**Delirium**	D2 antagonist
	0.05-0.15mg/kg/day divided BID or TID	0.5mg – 5mg divided BID or TID					

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Patient case examples?

Patient case example

- A 14yo female patient without past psychiatric history presents with symptoms of increased worry that bad things are going to happen to her loved ones. She also worries that she will fail tests, and notes that she will have episodes of increased heart rate, sweating, feelings of dread and feelings like she cannot breathe. These episodes last about 15-30 minutes. She also reports that she is missing school about 1 day per week for feeling that she is going to throw up and is having diarrhea in the mornings with severe abdominal cramping. She notes that she does not have these symptoms on the weekends, and they are commonly on Monday morning, most frequently.
- What's next?

Fluox 10mg → 20mg → 40mg

hydroxy 10mg–50mg TID PRN

4–6°

ID → 25 / 50

Esc 20mg (10-20mg) "Max"

Escitalopram 20mg (10-20mg) Max 30mg "Max" (10mg/20mg)
Want to change to sertraline (50mg-200mg) (presumed goal around 150-200mg) (25mg, 50mg)

Escitalopram 20mg → 10mg x 7 days (1/2 of Max)
Day 2: Wait one day. sertraline 25mg → x 6 days. (1/8 of Max)

Then:
Escitalopram 10mg → 5mg x 7 days (or stop)
Day 2: sertraline 50mg → x 6 days (pause for a month—or not) and then increase by 25-50mg until 100mg (and then pause).

Akathisia
agitated more likely with SSRIs/anticholinergics