Anxiety In Children and Adolescents with Autism Spectrum Disorders: Therapeutic and Psychopharmacological Interventions

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Wednesday, February 27th, 2013
Agenda:

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<td>7:20– 7:45pm</td>
<td>Q &amp; A</td>
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<td>7:45 – 8pm</td>
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Anxiety In Children and Adolescents with Autism Spectrum Disorders: Therapeutic & Psychopharmacological Interventions

Eugene D’Angelo, Ph.D.
Katherine Driscoll, Ph.D.
Kerim Munir, MD, MPH, DSc
Goals For This Evening’s Presentation

- Provide an Overview of Anxiety in Children with ASD (Dr. D’Angelo)
- Review of Psychosocial Interventions for Anxiety in Children with ASD (Dr. Driscoll)
- Description of Psychopharmacological Treatment Options and Their Considerations (Dr. Munir)
Anxiety In Children and Adolescents with Autism Spectrum Disorders: An Overview

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Disclosures

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  - SAMSHA/CMHS #03M00026501D
  - R01: R01 MH64717
  - John and Geraldine Weil Foundation

Conflicts of Interest: None
I Am A New York Yankees Fan!!!
Normative Anxiety: 4 years – 8 years

- Visual and auditory stimuli (fire engines, sirens, noises, scary pictures)
- Small animals
- The dark and imaginary creatures
- Separation from caregivers, parents leaving at night
- Personal harm or harm to others
- Medical procedures
- Frightening dreams and movies
Normative Anxiety: 9 years – 12 years

- School evaluation------ failure and criticism
  - Tests, oral reports, answering questions out loud
- Peer bullying and teasing
- Rejection
- Death and dying of others
- Personal harm and harm to others
- Illness
Normative Anxiety: 13 years – 18 years

- Evaluation, Social fears, Social Alienation
- Embarrassment or humiliation
- Personal inadequacy and Performance
- Worries about appearance
- Future events
- Injury or illness
- Natural or human made disasters (e.g. economic and political concerns)
- Death and Danger
Anxiety Disorders in Children and Adolescents

- When normative fears lead to uncontrollable worry, avoidance, physiological arousal, interfere with social, home, family functioning
- Anxiety Disorders most prevalent mental health problems children in the U.S.
- Prevalence estimates range between 6-20%
- Age of onset and prevalence roughly corresponds to developmental fears
Characteristics of Anxiety Disorders in Youth

- **Behavioral**: avoidance, outbursts, freezing
- **Cognitive**: negative self-talk, attributions, expectations, less positive self-talk
- **Physiological Arousal**: HR, stomachaches, headaches
- **Social**: impaired peer relationships, social withdrawal
- **Emotion regulation and coping**: poorer understanding of ability to hide or change emotions, fewer/less mature methods
- **Functional Limitations**: school, social, family problems, withdrawal from activities
Prevalence of Anxiety Problems in Youth Diagnosed with ASD

- Prevalence rates range from 30 to 80% of the ASD population
- Second greatest concern reported by their parents
- Additional problems can also emerge, namely, attentional problems, oppositionality, and depression
Types of Anxiety Problems Frequently Experienced by Youth with Autism Spectrum Disorders

- Generalized Anxiety
- Phobias
- Obsessive-Compulsive Symptoms
- Panic
- Social Anxiety
- Separation Anxiety
- Trauma Symptoms
The Comprehensive Evaluation Schema

Parental Diagnostic Interview

Child Diagnostic Interview
Medical Reports

Behavioral Rating Scales

Careful Review of DSM IV Criteria

Teacher Interview
School Reports
Efforts to Reduce Stress For Youth

- Promote Awareness of Stress in Your Child
- Help Your Child Develop Stress-Reduction Skills
- Teach Your Child In-the-Moment Stress Coping Techniques

Promote Awareness of Stress in Your Child

- Help to educate your child to identify “stress signals” that are experienced in his/her body, thought, and action—*Feelings, thoughts, and behaviors go together.*

- Help your child to identify signs of stress that he/she might experience

  **Examples of “Stress Spikes”**

  **Body Signals**
  --*Increased breathing, tense muscles, heart rate*

  **Thought Signals**
  --*“I hate you.” “I can’t do it.” “I give up.” “I’m going to hit him.”*

  **Behavior Signals**
  --*Avoiding, threatening, hitting, threatening, running, withdrawing, yelling, crying*
Help Your Child Develop Stress-Reduction Skills

- Promote healthy habits (*exercise, periodic relaxation, getting enough sleep, socializing more, develop a routine, keep up with your homework*)

- Discuss the development of specific stress producing activities that the child may engage in with the belief that they reduce stress but actually can promote it:
  - *Avoiding Behaviors, Withdrawing Behaviors, Overthinking*

- Create a plan with your child to reverse the stress promoting actions
Teach Your Child In-the-Moment Stress-Coping Skills

- Recognition of Stress Spikes
- Introduction of child relaxation techniques (e.g., diaphragmatic breathing, muscle tension-release, visualization)
- Teach Your Child to Use Calming Self-Talk
- Teaching Your Child to Take Effective Action
- Being a Good Role Model for Stress-Coping Skills
An Example of A Structured Approach to Staying Calm

1. What am I stressed, angry, or nervous about?

   - Not at all
   - A little
   - Somewhat
   - A lot
   - Very much

2. How stressed, or angry, or nervous am I?

3. Calm down my body with slow breathing, muscle relaxation, and visualization.

   - Tense
   - Cooling down
   - Relaxed

4. Use calming self-talk.

5. Take some action to solve the problem.

From Skills Training for Struggling Kids. Copyright 2013 by The Guilford Press.
An Example of A Self-Evaluation Worksheet for Older Youth

<table>
<thead>
<tr>
<th>Staying Calm Worksheet</th>
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<tbody>
<tr>
<td><strong>Name:</strong> ___________________ <strong>Date:</strong> ___________________</td>
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A child/teen and/or parent can complete this worksheet. It's best to fill out the worksheet while you are upset, but it's also okay to fill it out afterward.

1. What am I stressed, angry, or nervous about?

2. How stressed, angry, or nervous am I? (Circle one.)

<table>
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<th>2</th>
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<th>4</th>
<th>5</th>
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<tbody>
<tr>
<td>Not at all</td>
<td>A little</td>
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<td>A lot</td>
<td>Very much</td>
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3. What are the signals that tell me I am stressed out?

   a. Body signals:

   b. Thought signals:

   c. Behavior signals:

4. What can I do to slow my breathing and relax my body?

5. What calming self-talk can I use to cope?

6. What action can I take to deal with the situation or solve the problem?

   **How Well Did It Work?**
   (Circle 1, 2, 3, or 4.)
   1. I didn’t really try too hard.
   2. I sort of tried, but it didn’t really work.
   3. I tried hard, and it kind of worked.
   4. I tried really hard, and it really worked.

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Treatment of Anxiety in Children with Autism Spectrum Disorders

Katherine Driscoll, Ph.D.
Topics to Cover

- Presentation of anxiety
- Treatment options
- Considering treatment fit
- Resources
Framework for Understanding Anxiety

- Considering a developmental approach to understanding how anxiety develops and how anxiety may interact with the core features of ASD
- Age effects, cognitive/IQ effects, and ASD diagnostic subgroup differences
Why are Kids Vulnerable to Anxiety?

- Social difficulties can lead to increased anxiety
- Tendency to engage in “black and white” or rule-based thinking
- More difficulty identifying early cues and triggers for anxiety
Presentation of Anxiety

- Acting out behaviors
- Increased withdrawal
- Irritability
- Repetitive behaviors
- Intensity of restricted interests
- Sleep/appetite disturbance
- Physical symptoms: stomachaches, sweating, tension, racing heart
Treatment Options

- Psychopharmacological interventions
- Psychosocial interventions
- There are presently no empirically supported treatments that target the behavioral and emotional concerns presented by children with ASD, including anxiety.
What is an Empirically Supported Treatment?

- An intervention that has been found to be efficacious for one or more psychological conditions
- Interventions have been studied enough, following rigorous guidelines, to conclude that treatment is effective
- 16 total, for example CBT for major depression or exposure response prevention for OCD
- Other treatments are “probably efficacious”
Psychosocial Interventions

- Cognitive-Behavior Therapy (CBT)
- Social stories
- Social skills training
- School consultation
What is CBT?

- CBT is a fairly general term
- Emphasizes the role of thoughts in how we feel and what we do
- Treatment tends to be structured, directive, and time-limited
Various CBT Treatments

- Coping Cat (Philip Kendall, Ph.D.)
- Cool Kids Anxiety Program (Ronald Rapee, Ph.D.)
- Treatments have been adapted to address anxiety in children with ASD.
Example of Being Brave CBT protocol

- Being Brave treatment developed by Dina Hirshfeld-Becker, Ph.D. at MGH
- 20-week treatment
- 6 weeks of parent training about anxiety, child-directed play, and exposure
- Child-directed play component
- Techniques of active coping and gradual exposure
Being Brave (cont)

- Relaxation exercises
- Planning, rehearsing, and practicing coping with anxiety-provoking situations through exposure exercises

- **Notion that avoidance increases anxiety**
Sample Hierarchy for Fear of Dogs

- 1. Listen to someone read a book about dogs aloud.
- 4. Stand outside a pet shop and look at dogs through the window.
Dogs (cont.)

5. Visit a friend who has a dog and watch the dog playing outside while standing inside.
6. Stand outside and watch the dog while it is on a leash.
7. Pat a dog on a leash.
8. Play catch with a dog for two minutes with help from an adult.
9. Play with a relative’s dog for 10 minutes.
Social Stories

- Limited research on effectiveness of Social Stories to treat anxiety
- Social Stories were developed by Carol Gray to model appropriate social interaction by describing a situation with relevant social cues, other’s perspectives, and suggested response.
- Blood draw intervention program at Children’s
- Case example: flip book for separation anxiety
Social Skills Training

- One study found reduced anxiety in adolescents with ASD who received social skills training or vocational training.
- Lunch bunch, friendship group, social skills group can be tailored to address anxiety.
School Consultation

- Particularly helpful for children with limited language
- Observation a key component
- Request a Functional Behavior Analysis (FBA)
- Case examples: ABA to support affect recognition, Child experiences changes to PECS program
Sources of Anxiety for Parents of Children with ASD

- Managing challenging behavior
- Making decisions
- Adjusting expectations at each stage, whether positive or negative
Strategies for Parents

- Praise brave behavior
- Acknowledge the worry one time
- Notion of “planned ignoring”
- Modeling brave behavior and self-talk
- Allow and encourage mistakes
- Schedule “worry time”
Exploring Feelings: Cognitive Behaviour Therapy to Manage Anxiety by Tony Attwood
FRIENDS for Life is a school-based anxiety prevention program (www.friendsinfo.net)
Worried No More by Aureen Pinto Wagner
What to Do When You Worry Too Much by Dawn Huebner
When My Worries Get Too Big by Kari Dunn Buron
Managing Anxiety in People with Autism by Anne Chalfant
www.worrywisekids.org Dr. Tamar Chansky
Functional Behavior Assessment for People with Autism by Beth Glasberg
Treatment of Anxiety in Autism Spectrum Disorder: Psychopharmacological Approaches

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The Children’s Hospital Boston
Presentation CASD Forum, February 27, 2013
Judah Folkman Auditorium, Enders Research Building
NIH Support / No other disclosures
Intersection of Anxiety and Autism Spectrum Disorders in children and adolescents
Anxiety as Symptom
Anxiety as Disorder
ASD broad variation in core and comorbid features
Review of psychopharmacological approaches
Two caveats

- Despite being very common in all children and adolescents anxiety disorders are often under-diagnosed and under-treated

- Anxiety symptoms and disorders are the most common co-morbid conditions in children and adolescents with autism spectrum disorders
In ASD children often lack verbal skills to communicate concerns.

However, all children, irrespective of diagnosis of ASD, exhibit anxiety through behavioral (tantrums, crying, clinging, freezing) and physical symptoms (aches and pains, etc.).

Furthermore, unlike adults, children, irrespective of co-occurring diagnosis of ASD, are not required to recognize that anxious thoughts or fears are unreasonable or excessive.
Childhood Fear and Phobias

- Lapouse and Monk (1959)
- Survey of 6-12 year-old children
- 43% had 7+ fears
- Specific objects (e.g., animals, strangers, storms, flying) to those that are more abstract (e.g., monsters)
Anxiety Disorders in Children and Adolescents

- Specific Phobia
- Separation Anxiety Disorder
- Generalized Anxiety Disorder
- Social Phobia
- Panic Disorder
- Selective Mutism
- Obsessive Compulsive Disorder*
- Acute Stress Disorder*
- Post Traumatic Stress Disorder*

*Will be moved to their own diagnostic categories in DSM-5 – May 2013
Changes in DSM-5

- Trauma-related and obsessive-compulsive spectrum disorders will be classified separately in DSM-5 (different outcomes, comorbidities, familial aggregations and underlying biology)
- Disorders under the Anxiety Category will include: specific, social phobias, separation and generalized anxiety and panic disorders
Separation, Generalized Anxiety Disorders, Social Phobia

- Separation Anxiety - anticipation of something bad happening to primary attachment figure)
- Generalized Anxiety - excessive worry of a calamitous event, persistent trait rather than state, often co-occurs with separation anxiety)
- Social Phobia: avoidance or refusal of situations, e.g., school, social activities, as child will have to face others, speak, eat, drink in front of them, participate in groups)
Some Initial Questions

- **Question 1**: Is anxiety as symptom part of ASD? Cf., sensory-difficulties [DSM5]? (inclusive of ASD symptoms)

- **Question 2**: Is anxiety distinct from ASD but sub-threshold for anxiety disorder? (exclusive of ASD symptoms)

- **Question 3**: Is a specific, definable anxiety disorder a comorbid subtype with ASD, e.g., SAD, GAD, Social Phobia? (specific comorbid anxiety disorder)

- **Question 4**: Is anxiety as a general category (or set of disorders) comorbid with ASD? (comorbid category with ASD)
Was anxiety ever part of the definition of autism?

- According to Kanner (1943): “Anxious desire to maintain sameness” was described as a core characteristic

- DSM-III (1980) that revolutionized the definition noted, “intense and unusual anxieties”, “sudden excessive anxiety”. “unexplained panic attack”

- DSM-IV and proposed criteria for DSM-5: anxiety is not essential for ASD diagnosis
“Anxious children are in tune with their bodies”

- Aches and pains (stomach, head)
- Frequently sick in the morning
- Frequent visits to the bathroom
- Baseline high breathing and pulse rates
- Sensitive gag, fear of choking, difficulty swallowing, vomiting
- Shaky, dizzy, tense, easily exhausted
What are some interfering symptoms of anxiety in ASD?

- Sleep difficulties, frequent visits to parents’ room
- Excessive need for reassurance
- Avoidance of activities, clingingness
- Fearfulness, startle
- Inattention (may in fact be misclassified as ADHD inattentive type)
- Inconsolable tantrums
Multimodal Psychopharmacological Treatment: *Autism Spectrum Disorder*

**Core Symptoms:**
- No pharmacotherapy for social interaction and reciprocity at this time
- *Interfering* stereotyped repetitive behaviors, obsessive thoughts, compulsions*
- Regulatory, transitional, sensory difficulties*

*It is important to address these concerns with a multimodal behavioral modification and augmentative pharmacological approach in appropriate educational setting but evidence base is limited (Melmed, Munir, Tanguay, 2006)*
Autism Spectrum Conditions: Co-occurring conditions

- Disruptive, aggressive behaviors
- Self-injurious behaviors (SIB)
- Anxiety
- Inattention
- Sleep difficulties
- Seizures
- Depression and Mood Disorders
- Psychosis
Multimodal Treatment: Some barriers to care

- Limited availability of behavioral therapists
- Presence of a behavioral program is necessary but not sufficient
- Lack of communication among caregivers
- Limited behavioral data collection or limited use of data when available
- Legacy of failure various medication trials
Multimodal Treatment: Obstacles

- Misclassification of co-occurring symptoms and co-morbid disorders (e.g., calling problems with inattention – ADHD, labeling transitional difficulties – overanxious, poor frustration tolerance and irritable mood – bipolar, etc.)
- Prescribing for extended period of time with limited consideration of concurrent change in the child’s environment and availability (or lack thereof) of supports
- Use of “poly-pharmacy” med-regimens with little or no attempts over time to consolidate or reduce dose
General Approaches to Psychopharmacology

- Adequate diagnostic assessment
- Adequate medical assessment
- Good therapeutic agreement
- Well defined target symptoms
- Safety/efficacy review
- Benefits outweigh risks
General Approaches to Psychopharmacology*

- Multimodal approach essential: psychosocial, behavioral, educational:
- Single med trial at a time
- Start low, increase slowly
- Taper cautiously
- Monitor side effects/labs/VS/growth
- Consider discontinuation

*Prescribing Guidelines Pediatrics 2001; 107:1221-1226
Psychopharmacology of Anxiety in ASD

- Paucity of studies
- Difficulties in rating anxiety in ASD
- Grouping symptoms and sub-threshold presentations and disorders

Need for:
- Family history
- Genetics
- Longitudinal course/outcome
- Larger/representative sample sizes
Brief Overview of Psychotropic Medication Categories

- Stimulants
- Antidepressants
- Central adrenergic agonists
- Mood stabilizers
- Antianxiety agents
- Antipsychotics
- Other
Psychotropics Appropriate for use in Anxiety in ASD

- **Serotonin reuptake inhibitors**
  - Fluvoxamine (Luvox®)
  - Fluoxetine (Prozac®)
  - Citalopram (Celexa®)
  - Escitalopram (Lexapro®)
  - Sertraline (Zoloft®)

- **Trazedone**

- **Benzodiazepines**
  - Clonazepam (Klonopin®)
  - Lorazepam (Ativan®)

- **Other antidepressants**

- **Antihistamines**

- **Buspirone**
SSRI - Activation

- May lead to increased irritability, may induce hypomania/mania in predisposed individuals
- Care when giving to individuals with a strong family history of Bipolar Disorder
- Individuals with ASD are susceptible to activation, irritability and mood instability; should be used at low doses and with appropriate caution
Benzodiazepines

- Effective in the treatment of anxiety related problems
- Tolerance
- Somnolence, memory difficulties
- Active metabolites of some may lead to prolonged effects
- Useful as an adjunct in managing a panic situation (need to clarify its specific use)
- Useful as a sedative hypnotic
Children’s Health Act (2000) and NIH: Studies to Advance Autism Research and Treatment (STAART) for research in causation, diagnosis, early detection, prevention, and treatment

- BU, Kennedy Krieger, Mt. Sinai, UCLA, UNC, Rochester, U Washington, Yale (8 sites)
- 2 studies on medications in autism:
  - A double-blind, placebo-controlled trial of fluoxetine in pre-school children with autism (ages 30-58 months) to examine if it enhances developmental processes in “core areas” impacted by the disorder (no publications have been recorded)
  - A double-blind, placebo-controlled clinical trial of citalopram for children with autism and repetitive behaviors
Studies To Advance Autism Research and Treatment (STAART) - relevance to Anxiety in ASD

- N=149, ages 5-17 y (128 boys, 21 girls); mean age 9.3 y, Autistic Disorder (88.6%), Asperger (4.7%), PDD-NOS (6.7%)
- Less than half with ID (of these 78.5% with moderate or severe)
- Citalopram, (N=73) vs. Placebo (N=79) for ostensibly examined repetitive behavior (RB)
- 12-wk, mean dose 16.5 mg, no benefit for RB
STAART Trial - Some kids with anxiety improved on citalopram but unclear if they had anxiety disorder!

Research Units in Pediatric Psychopharmacology (RUPP) Autism Network Trials – Some important conclusions

- Need for improved rating scales!
- Need for extensive cross-site training!
- Subject groups highly heterogeneous across sites!
- Parent-defined ‘target’ symptoms, e.g., disruptive behaviors respond to atypical neuroleptics (risperidone first to be selected to target impaired social and interfering repetitive and aggressive behaviors)
- Parent training improves long-term medication efficacy and child adaptive functioning
So, what do we really know?

- Prevalence of Anxiety is high: Girls > Boys
- But this is different for Anxiety in ASD (more common in Boy > Girls)
- Impairments common even with sub-threshold symptoms
- Long-term course unknown
- Severe symptoms and older youth predict poorer treatment response
- Parent/family integration in treatment plus social skills training improve outcomes
- Parent involvement is especially critical when parent is anxious
- SSRIs are the medications of choice
- Controlled trials have established safety and efficacy of short term treatments of SSRIs in anxiety and depression in children
- Other medications include: benzodiazepenes, TCA (no longer used), beta blockers, SNRIs, trazedone, buspirone, antihistamines
New studies confirm these observations

- Anxiety is highly prevalent in children and adolescents with ASD (in particular without ID) – 42% (Montpellier study, France)

- Parent-rated anxiety symptoms in children with ASD was 43% with higher levels of anxiety in (Sukhodolsky et al, 2008) children with:
  - Better functional language
  - IQ above 70
  - Higher level of repetitive behaviors
  - 40% children with ASD met criteria for anxiety disorder
  - 84% children with ASD had impairing symptoms of anxiety
Hallett et al (2013) RUPP Autism Multisite Treatment Trials

- N=415, 4-17 y, 4 “mixed” groups
- RUPP1 (N=101) Double-blind trial of risperidone vs. placebo in children with ASD and serious behavioral problems
- RUPP2 (N=66) Methylphenidate vs. placebo in children with ASD and hyperactivity
- RUPP3 (N=124) Risperidone vs. risperidone plus parent management training in children with ASD and severe behavioral diagnosis
- RUPP4 (N=149) Citalopram vs. placebo in children with ASF with moderate or greater repetitive behaviors

- N=336 autism (81%) (139 with IQ > 70); N=20 Asperger (5%) (18 with IQ >70)
- N=59 PDD (14%) (44 with IQ > 70)
- N=200 IQ ≥ or = 70
- N=94 Nonverbal

Participants in trials selected for specific behavioral difficulties, convenience samples, although relatively large, findings not applicable to wider ASD population
Anxiety occurs across the full range of IQ
- Children with an IQ below 70 have lower scores, in part because the items that rely on language are rarely endorsed and do not contribute to the anxiety total score.
- Anxiety measurements in children with ASD, especially for those with ID, will benefit from greater emphasis on observable behavior.
- Most common disorders endorsed included: Specific phobia 30%; Social anxiety 17%; OCD 17%; Generalized anxiety 15%.
- It is still unclear if these were separate conditions separate or aligned with core symptoms of ASD (cf., Social-Anxiety, social avoidance scales), further research is needed.
- Study identified four underlying factors: 1) Generalized Anxiety; 2) Separation Anxiety; 3) Social-Anxiety; and 4) Over-arousal.
Challenges

- Limitation of STAART and RUPP was that they were simple placebo controlled clinical trials, unlike the MTA ADHD Study or the TADS Adolescent Depression Study the STAART and RUPP were not multisite mixed-design randomized treatment trials with: 1) behavioral; 2) medication; 3) combined; and 4) community arms.

- There were also unique challenges in that ASD core symptoms (i.e., social interaction, RB) were target of medication treatment rather than comorbid disorders (e.g., anxiety, ADHD, sleep, etc). The argument was that there was no available rating scales to effectively measure or diagnose these co-morbid conditions in ASD.
Recommendations

- NIH should consider funding mixed-design treatment arms and outcome studies involving with careful ascertainment of patients and assessment of co-occurring conditions

- Stronger inter-site collaborations are needed

- From a clinical perspective, children ought to have access to EBT with an individualized approach

- Policymakers must enable access to combined treatment modalities in collaborative centers

- Families and communities must be educated
Resources

- Practice Parameters for Use of Stimulants in the Treatment of Children, Adolescents and Adults [www.aacap.org](http://www.aacap.org)
- Practice Parameters for Assessment and Treatment of Children and Adolescents with Depressive Disorders