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Editor-in-Chief

Volume 12 Issue 3&4
April/May/June 2021
www.thecarlatchildreport.com

IN THIS ISSUE

Autism in Children and Adolescents

Learning Objectives

After reading these articles, you should be able to:

1. Describe current pharmacological and non-pharmacological interventions for children and adolescents with autism spectrum disorder.
2. Identify best practices for applying the 21st Century Cures Act ("Cures Act").
3. Summarize some of the findings in the literature regarding psychiatric treatment for children and adolescents.

Approaches to Autism Intervention

Diane Cullinane, MD. Developmental pediatrician. Co-founder and Executive Director Emerita of Professional Child Development Associates (PCDA), Pasadena, CA.

Dr. Cullinane has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Your patient is a young child who has recently been diagnosed with autism. Her parents are asking about the available treatments, and in particular, they want to know whether they should pursue the 40-hour-per-week program recommended by the local autism society.

As clinicians, we are often faced with questions from families about the "best" program for autism intervention. While children with autism may receive a range of services including speech and language

Highlights From This Issue

- Research support for autism treatment is far less robust than typically advertised, and traditional behavioral approaches lack actual effect size.
- Clinicians need to be able to advise families on the three main branches of autism treatment: applied behavioral analysis, developmental relationship-based intervention, and naturalistic developmental-behavioral intervention.
- Risperidone remains the best-supported medication for treating irritability in autism.
- Clinicians need to efficiently respond to patient requests for records and document their considered judgment in decisions about restricting records to patients and families.

Continued on page 4

Q&A With the Expert

Effect Size Matters: The Seismic Shift Toward Naturalistic and Developmental Interventions in Autism

Micheal P. Sandbank, PhD

Assistant professor of special education at the University of Texas, Austin.

Dr. Sandbank has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CCPR: Welcome, Dr. Sandbank. Tell us about your work.

Dr. Sandbank: My current research is in social communication and language interventions for young children with disabilities, including those on the autism spectrum. I am lead researcher on Project AIM, a vast systematic review and meta-analysis of all group design studies of interventions for young children with autism (www.tinyurl.com/dda6pzpv).

CCPR: What's the state of research in autism?

Dr. Sandbank: Autism treatment is a huge industry, and yet randomized controlled trials (RCTs) have been rare in the autism field, making it hard to show that treatment is effective. Despite a tidal wave of low-quality studies, RCTs were almost nonexistent in the early 2000s. In 2011, a systematic review in *Pediatrics* found only two high-quality RCTs. Then in 2017, another

Continued on page 2

Expert Interview—Effect Size Matters: The Seismic Shift Toward Naturalistic and Developmental Interventions in Autism

Continued from page 1

systematic review found 48. That's a major change in just six years.

CCPR: What is the purpose of a meta-analysis?

Dr. Sandbank: Studies that show "significant change" do not tell you if that change is meaningful for patients. Meta-analysis allows you to compute an effect size across multiple studies to get a sense of the magnitude of the clinical impact. With so many kinds of autism treatment, people are looking at many different outcomes. We used a recently developed technique that lets us compare all the effect sizes for the different outcome measures. In our 2019 Project AIM study, we sorted interventions and outcomes into broad domains and calculated effect sizes across outcomes (Sandbank M et al, *Psychol Bull* 2019;146(1):1–29).

CCPR: What population did you look at in the study, and what were the categories of interventions?

Dr. Sandbank: We looked at studies of children 8 years and under because that's the defining age range of early childhood. Most of the studies focused on three categories: traditional applied behavioral analysis (ABA), developmental relationship-based interventions (DRBI or "developmental"), and naturalistic developmental behavioral intervention (NDBI).

CCPR: So what did you find?

Dr. Sandbank: For the developmental interventions and NDBI, we found moderate effect sizes for improving social communication, which is the central problem area in autism. But by far the most interesting finding of our study was that we couldn't find compelling evidence for traditional applied behavioral analysis (ABA) interventions. There weren't enough RCTs to compute summary effects on any outcome for traditional ABA interventions. This is concerning because traditional ABA interventions are far and away the most commonly recommended approach in the field.

CCPR: This could change how we look at autism treatment.

Dr. Sandbank: Yes. And even the few positive findings we computed were based on the rare very high-quality studies. The majority of studies were impacted by potential bias, largely when participants were aware of what group they were assigned to. When we excluded those studies, we saw no significant effects on any intervention approach for any outcome for any treatment.

CCPR: Can you talk more about the outcomes you were looking at in these studies?

Dr. Sandbank: Sure. When a child learns a skill and then can use it in several contexts, we call that generalization. When a child learns a skill and then builds on that to develop other new skills, we call that distal development. We wanted to see whether interventions were causing meaningful change in generalized and distal outcomes, or if the child had simply acquired a very discrete skill that they could only use in the exact circumstances where they were taught. If you teach the child 10 words, you may not see growth in general communicative ability. On the other hand, teaching social communication may cascade into language development not just within the intervention, but across multiple contexts.

CCPR: How does this relate to the different categories of treatment?

Dr. Sandbank: The traditional ABA behavioral approaches teach specific skills. The developmental approaches work on foundational skills, such as emotional regulation and reciprocal communication, that support both generalization across domains and cascading distal development. NDBI marries the two theories. *(Editor's note: For a succinct tutorial on the differences between these three approaches, see Dr. Diane Cullinane's article in this issue.)*

CCPR: Why have behavioral approaches dominated treatment?

Dr. Sandbank: It is far easier to do research in traditional ABA approaches that teach specific skills such as new phrases. These are narrow proximal outcomes. It has been harder to conduct research on developmental or NDBI approaches. You need to measure change across a whole domain on a validated, standardized assessment administered by a naïve assessor. That would be a distal effect. Proximal effects appear large, even though they may not generalize nor result in distal growth. Distal and generalized effects are more clinically meaningful but likely to appear smaller.

CCPR: What are the implications for treatment?

Dr. Sandbank: Since the traditional ABA approaches have seemed to be more effective, they have dominated treatment and also insurance reimbursement. And when therapists are trained, they tend to be trained in behavioral approaches. Students train in traditional ABA approaches to become Board Certified Behavioral Analysts (BCBAs). These are BA or MA certifications that are separate from usual mental health specialties and focused on autism treatment without training in more broad mental health conditions or treatments. Therapists learn

Continued on page 3

Expert Interview—Effect Size Matters: The Seismic Shift Toward Naturalistic and Developmental Interventions in Autism

Continued from page 2

to teach autistic children specific skills. For instance, they learn to teach children to point to specific objects, a common activity in these treatments. It turns out from our research that this is unlikely to generalize to new kinds of pointing nor other communication. Developmental and NDBI approaches have certifications provided by the training institutions but no central board like the BCBA. Still, NDBI and developmental interventions may have better outcomes. For the same example, the child may learn to use pointing better because they learn it in the context of meaningful interactions. The newer research supports this.

CCPR: The recent American Academy of Pediatrics (AAP) guidelines seem to favor the traditional behavioral approaches.

Dr. Sandbank: Current practice is typically the use of an Autism Diagnostic Observation Schedule (ADOS) as a chief diagnostic tool, which is taken to a psychiatrist, psychologist, or pediatrician who often doesn't have expertise in autism but recommends 40 hours per week of intensive behavioral intervention. We just wrote an opinion piece in *JAMA Pediatrics* that urges clinicians to learn about the entire range of treatments and collaborate with families to figure out what might work best for them rather than routinely recommending just the one approach (Sandbank M et al, *JAMA Pediatr* 2020. Epub ahead of print). Clinicians are gatekeepers who need to know about the different intervention approaches, particularly those supported by RCTs.

"By far the most interesting finding of our study was that we couldn't find compelling evidence for traditional applied behavioral analysis (ABA) interventions. There weren't enough RCTs to compute summary effects on any outcome for traditional ABA interventions."

Micheal P. Sandbank, PhD

CCPR: Can you comment on the recommended intensity of treatment?

Dr. Sandbank: We did an analysis of intensity to see if more hours of intervention was associated with greater effect sizes. We did this for behavioral, developmental, and NDBI studies and found no association between the total hours of intervention received in the study and the size of the effect. That doesn't mean the amount of intervention doesn't matter, but it means that we lack the kind of evidence needed to support recommendations for the very high-intensity treatments. It may be problematic to recommend that a toddler receive 40 hours of intervention. This is quite taxing for children and families and it may not be necessary.

CCPR: Families often come to us asking for 40 hours of ABA.

Dr. Sandbank: They hope that this will result in the best outcomes, and yet mere access to these hours is not what the research suggests. About a third of kids with autism who are preverbal at 2 are not likely to develop phrase speech by the end of elementary school, and this is related to effective intervention—not access to traditional ABA (Anderson DK et al, *J Consult Clin Psychol* 2007;75(4):594–604). Sadly, when kids haven't made progress, it is common for parents to feel guilty and ask, "Why isn't my child speaking? Was it because I didn't start intervention early enough? Was it because I didn't do the 40 hours?"

CCPR: Does the research support any particular time commitment for these interventions?

Dr. Sandbank: For many treatments, the intensity and duration of intervention really depends on the intervention. There's a parent-mediated communication-focused treatment called PACT, a developmental approach, that is only 18 one-hour sessions—no more, no less. But we have a really high-quality study that shows it improves the core challenges related to autism and development over time. There are few RCTs comparing intervention intensity. My former advisor, Paul Yoder, just completed a study comparing the Early Start Denver Model (ESDM, a form of NDBI) and a traditional ABA intervention, where children were randomly assigned to receive either 15 or 25 hours per week, and they showed no differences in outcomes by intervention or intensity across the whole group (Rogers SJ et al, *J Am Acad Child Adolesc Psychiatry* 2020;S0890-8567(20):31350–31352). It is the first study to ask this question in this way. We need more studies like that. A more recent paper found that more hours of intervention led to better outcomes for higher-functioning children. This is interesting since most of the time, it is the children with more severe challenges who are offered higher numbers of hours.

CCPR: How do we decide what kind of approach to recommend? Can we predict which child responds to which intervention?

Dr. Sandbank: It's not one size fits all. We need to look within the groups for mediators. Maybe kids with better social attention do better with developmental interventions or NDBI. And maybe kids who don't have that social awareness need more formal, explicit instruction in how to do these things. A lot of families feel that their ABA therapy has been very helpful, in which case we should let that support continue. Does it depend on study-entry autism symptomology, social communication skills, or age? Those are the kinds of studies that we need.

CCPR: What should we say to families about how to choose among the various options for autism treatment?

Dr. Sandbank: We certainly have more high-quality evidence supporting developmental and naturalistic approaches as our research is improving. Autism is a spectrum, and different kids have different abilities and strengths. Some families prefer certain interventions, and some kids improve with certain interventions. I recommend that clinicians describe the different approaches, which means you have to be familiar with them and what's available in your community; you can't recommend an intervention that a family cannot access. Identify the family's priorities. Do they want direct structured intervention from a clinician, or do they think that won't fit into their life? You have to have buy-in from the family, and it has to be something that the child experiences positively.

To learn more, listen to our podcast, "Effect Size Matters." Search for "Carlat" on your podcast store.

CCPR: Thank you for your time, Dr. Sandbank.

Continued from page 1

therapy, occupational therapy, and social skills help, some in the community, the anchor to most programs is some form of behavioral health treatment. This article will help you understand the main options for this kind of care and help you advise families on how to proceed.

Three main approaches to autism intervention

In the past couple of decades, the field of autism intervention has evolved into three main evidence-based approaches. Here's a brief synopsis of each:

1. *Applied behavioral analysis (ABA).* ABA is the best-known type of intervention. It is based on operant learning theory, meaning that behavior is learned based on what happens before the behavior (antecedent) and what happens after it (reward). Since the groundbreaking 1987 study by Dr. Ole Ivar Lovaas that indicated a positive relationship between individual behavior modification and "normal intellectual and educational functioning," many additional studies have shown the effectiveness of ABA to help children learn a wide variety of specific behaviors (Lovaas OI, *J Consult Clin Psychol* 1987;55(1):3–9; Tews L, *Developmental Disabilities Bulletin* 2007;35:148–168). Some drawbacks of the ABA approach include poor maintenance of skills, poor generalization of learning to new situations, and prompt dependency: reliance on adults to tell the child what to do (Mace FC and Critchfield TS, *J Exp Anal Behav* 2010;93(3):293–312). See www.bacb.com/about-behavior-analysis for more information.

2. *Developmental relationship-based intervention (DRBI).* In contrast to behavioral intervention, DRBI is a parent-mediated intervention where the primary focus is on training parents and other caregivers to build and use warm, meaningful interactions to help the child function better in communicating, learning, and problem solving. The best-known model is DIRFloortime® or simply Floortime®, which came from the work of Dr. Stanley Greenspan and Dr. Serena Wieder (Greenspan SI, Wieder S. *Engaging Autism: Using the Floortime Approach to Help Children Relate, Communicate, and Think.* Boston, MA: Da Capo Lifelong Books; 2006). The strategies of developmental interventions are distinct from behavioral intervention approaches in that they are less structured and emphasize free play without direct instruction or contingent rewards. An adult takes a child's interest and builds on it, while making the activity an emotionally meaningful experience. These fun reciprocal interactions help the child extend their capacities for creating and working with ideas, communicating, and social connection. See www.profectum.org/about/dir and www.icdl.com/dir for more information.

3. *Naturalistic developmental behavioral intervention (NDBI).* In an effort to address some of the drawbacks of traditional ABA, NDBI incorporates more choices for children to gain their buy-in to the treatment. The learning is carried out in natural situations such as play or daily routines and involves parents, and the rewards given are related to the child's interest. For example, if a child performs the desired behavior, they get the toy they want, rather than a sticker or other reward that other children may prefer. Some goals in NDBIs are chosen based on developmental abilities, such as pointing to share interest (joint attention), eye contact, and having the child imitate an adult, rather than a specific behavior, such as increasing vocabulary. See www.ncbi.nlm.nih.gov/pmc/articles/PMC4513196/pdf/10803_2015_Article_2407.pdf for more information.

In addition, see page 5 for a summary table of these interventions, meant as a start at understanding these different treatments. We recommend that clinicians learn more from the organizations that train and deliver these treatments.

Evidence of efficacy

The most recent edition of The National Clearinghouse on Autism Evidence and Practice supports specific practices that fall within all three of these main branches of autism intervention (Steinbrenner JR, Hume K, Odom SL, et al. *Evidence-Based Practices for Children, Youth, and Young Adults With Autism.* Chapel Hill, NC: National Clearinghouse on Autism Evidence and Practice; 2020). The American Academy of Pediatrics also endorsed all three interventions in their recent guidelines (Hyman S et al, *Pediatrics* 2020;145(1):e20193447). While there are thousands of studies on ABA, recent reviews recognize the growing body of research legitimizing DRBI and NDBI and showing that both of these have demonstrable effect sizes for social communication, while these effect sizes have not been shown for ABA (Sandbank M et al, *Psychol Bull* 2020;146(1):1–29).

Time investment

While mostly focused on younger children, ABA and DRBI approaches are used for children of all ages and abilities and any behavioral challenge. NDBI is more narrowly focused on children 12 and younger. Direct DRBI is usually provided for fewer hours per week than ABA, with parents implementing the model throughout the week, which naturally extends the child's engagement in the therapeutic process. While DRBI may also employ some additional hours with an interventionist to expand the range of people and experiences the child is exposed to, on balance DRBI requires less time and cost in most cases.

Cost and availability of treatment

The Affordable Care Act mandates that all commercial insurance companies and Medicaid must provide "behavioral health treatment" for autism. Many insurance companies interpret this to mean ABA; however, all evidence-based treatments are included. Though you should direct families to go to their insurance company and ask for the treatment they desire, keep in mind that the choice of intervention approach may be dictated by the available funding source and options available in their community, rather than the best fit for the child and family. Traditional ABA has been easier to obtain with insurance, but developmental options are becoming more available. Good informed consent means the family knows their options. Advocate for their preferred treatment.

Questions from families

As the child's clinician, your biggest task will most likely be helping the family sort

Continued on page 5

Approaches to Autism Intervention
Continued from page 4

through available treatment options to try and find the best fit for their needs. These common questions and answers should help you respond in a helpful manner.

1. *Which kind of treatment is best for us?*
Parents may be baffled by the autism treatment options and the various opinions that they hear. Review the basics of the three types of treatments and help them decide what fits their style and values. For instance, a family that prioritizes learning specific facts and following directions may do better with traditional ABA, and a family that is more free flowing in their interactions may do better with DRBI.

2. *What's the main difference between how these different programs work?*
Behavioral programs are more structured, and the interventionist will work directly with the child to teach them specific skills. They may also teach parents how to use some of these strategies. Developmental programs use natural interactions such as play, focusing on parents' relationships with their child and on building better communication and learning.

3. *I am getting different advice from different people—what do I do?*
Acknowledge that there are many opinions about the "right" treatment for kids with autism. Emphasize the need to figure out what might work best for each family. They can try a treatment out and see how it works. Families often try different styles as their needs change.

4. *Can we do both ABA and DRBI together?*
Many children receive some ABA services at school, and developmental services, such as Floortime after school, or other combinations of services. This can be successful if there are clear distinctions about the developmental areas to be addressed. For example, behavioral intervention can focus on specific language or cognitive skills, activities of daily living, or other routines. Floortime could focus on play skills and on interactions with parents and peers. However, confusion can arise if both developmental and behavioral approaches address the same activity, such as feeding, sleep, or behavioral issues. If a child is receiving both types of intervention, work with providers to coordinate their efforts and avoid conflict.

5. *Where can I get more information?*
For ABA and NDBI, a good resource is www.bacb.com. For DRBI, good resources include www.icdl.com and www.profectum.org.

CCPR VERDICT: Choice of autism intervention is not a one-time decision. It's an ongoing process of monitoring and evaluation. Any program may be more or less effective depending on the skills of the particular interventionist as well as the match to the family and the developing child. Together, you can guide families in navigating these complex decisions.

To learn more, listen to our podcast, "Approaches to Autism Intervention." Search for "Carlat" on your podcast store.

Three Main Categories of Autism Treatment Approaches

Traditional Behavioral Approaches	Developmental Approaches aka Developmental Relationship-Based Interventions (DRBI)	Naturalistic Developmental Behavioral Interventions (NDBI)
Types of interventions		
Applied behavioral analysis (ABA) Discrete trial training (DTT) Intensive behavioral intervention (IBI)	Developmental individual differences relationship-based approach (DIR/Floortime) Relationship development intervention (RDI) Parent-mediated communication-focused treatment (PACT) Focused playtime intervention (FPI) Responsive teaching (RT)	Pivotal response training (PRT) Early Start Denver Model (ESDM) Joint attention, symbolic play, and engagement regulation (JASPER) Project ImPACT Social communication, emotional regulation, and transactional support (SCERTS)
General description		
Behavioral changes as the result of environmental antecedents and rewards	Child improves when we support pleasurable, developmentally supportive interactions between child and parent	Mix of behavioral and developmental with some shared control between child and parent
Goals of treatment		
Compliance, correct responses on a wide variety of behaviors	Calm and regulated, engagement, reciprocal interactions, shared problem solving, logical and reflective thinking	Calm and regulated, with discrete goals for specific behaviors
Characteristics of treatment		
Therapist directs child while both are sitting Reward for correct response Extinction (ignoring) or replacing a tantrum or repetitive behavior High intensity and time intensive	Parent coaching supplemented with additional staff Following the child's lead, often on the floor Building on the child's responses and adding new concepts rather than judging behavior as correct or incorrect Providing empathy and support during a tantrum	Parent coaching Following the child's lead, often on the floor Giving the child choices, some open-ended play Some forms of NDBI look nearly identical to IBI but with some choices (eg, PRT) while others can look nearly identical to DRBI (eg, Project ImPACT)

Welcome to the 21st Century Cures Act Information Sharing Rules

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Dr. Levy has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

The 21st Century Cures Act (or the "Cures Act" for short) was a federal law passed in 2016 that included various mental health provisions (www.healthit.gov/curesrule). One of them is a law prohibiting what's now called "information blocking." In short, information blocking means preventing your patient from accessing information in their medical record. As of April 5, 2021, the law stipulates that patients must be able to access nearly all of the information we have in their electronic chart, on demand. This article focuses on how the Cures Act applies to child psychiatrists, how it impacts what we record in charts, what happens to that information, and how to best work with patients and families as they gain more access to their information.

Impact of information blocking

As of April 5, 2021, all clinicians are expected to respond to patient requests to view clinical data such as treatment notes, laboratory results, and medical problems without delay. For most of us, this means 1–2 business days after receiving a request. Intentional or unnecessary delays in fulfilling patient requests are also considered information blocking. An example of this kind of delay is requiring a patient or family member to sign a document, often erroneously referred to as a "HIPAA form," before transmitting their health records to another provider. This has been common practice, but now it might be considered information blocking unless certain exceptions can be demonstrated. Charging a fee for electronic access to records can also be information blocking.

What do you have to share with patients? Just about everything in your chart—including clinical notes, medication lists, vital signs, lab results, and assessments and treatment plans.

Exceptions to the rule

Worried about releasing sensitive information? You can restrict requests for data only when doing so is reasonable and necessary, and addresses a significant risk (www.tinyurl.com/4ssfee8h).

While the definition of "significant risk" is not clear, we need to clearly document our reasons for restricting access and fulfill as much of the request as we can. And keep in mind that this law pertains to requests for information; there is no requirement that we proactively share health data with patients or guardians who have not requested access to the information. There are eight recognized exceptions where it might be permissible to not honor a patient's request to view their information, two of which pertain directly to our work. See table below.

What about teens?

Can teens see their records? The short answer is yes. Can parents and other guardians see them? That depends on whether the teen grants them access as proxies, but also on state laws about the limits of adolescent confidentiality. Some teens do not want their parents actively involved in their treatment. You should review your state's laws about what data can be shared with parents, and when consent is needed.

Many EHRs have a multitiered access system where less sensitive clinical data are available to parents, while other data such as clinical notes and certain laboratory results are available only to the teen. A teen can choose to go onto the EHR portal and add their parent or guardian as a proxy if they wish for that parent or guardian to have electronic access to notes or more sensitive data.

Help your teen patient think through the risks and benefits when deciding whether to allow other people to access their records, and at what level (ie, medical vs therapy notes). Remind teens not to share their password with anyone. Help them understand the long-term risks of sharing their data such as cybersecurity risks and possible ramifications if future employers see the data (Pageler NM et al, *Pediatrics* 2021;147(3):e2020034199).

Planning for the age of open notes

Your notes will be open to patients, families, and colleagues alike. Here are some guidelines for writing notes in this new age:

1. Assume that everything you write in the EHR will be viewed by the patient. This includes comments and messages to other doctors that are transmitted through the EHR.

Continued on page 7

Exceptions to the Rule Requiring Release of Information to Patients and Families

Exceptions	Comment
1. Preventing harm	Clinicians should document specifically why release of the information might harm the patient.
2. Privacy	Clinicians do not need to release psychotherapy notes or substance use treatment history (the latter still requires a patient's written consent). If a patient asks you not to release information, you can respect their wishes and not release it.
3. Security	Clinicians may (and should) avoid release of information when there is a legitimate digital security threat.
4. Infeasibility	Clinicians are not required to release information when it is essentially impossible to do so. Examples include public health emergencies and cases where requested data cannot be segmented from data that should not be shared.
5. Health IT performance	Clinicians do not need to release data during a downtime needed to maintain or upgrade technology until system is up and running. (Not releasing data during downtime is not considered information blocking.)
6. Content and manner	For the first two years of implementation, the Cures Act allows some tolerance for providing less than all the data to give systems a chance to catch up to the new rules.
7. Licensing	Royalties paid to health IT developers do not need to be disclosed.
8. Fees	It is permissible to charge reasonable fees, including a profit margin, for accessing, exchanging, or using electronic health information.

Source: www.healthit.gov/cures/sites/default/files/cures/2020-03/InformationBlockingExceptions.pdf

Welcome to the 21st Century Cures Act Information Sharing Rules

Continued from page 6

2. Be polite and respectful in notes and in correspondence to colleagues.

3. Make sure your notes are written in a neutral perspective. Where possible, use patient quotes rather than making an assumption about a patient's motivations. For example, if a patient reports multiple symptoms of depression since a breakup, consider noting this in the patient's own words: "I'm so depressed. I can't sleep or eat." vs generalizing: "Patient is severely depressed due to the breakup."

4. Maintain cultural sensitivity. Avoid broad statements that deride an individual for engaging in a culturally sanctioned practice. For example, rather than writing "The child is up all night and tired during the day because the mother has the children all in the family bed." consider "The mother reports the child is waking 2–3 times per night and waking others in the family bed, which she notes is an uncommon problem among her cultural community."

5. Protect the privacy of LGBTQIA+ youth who may use names or pronouns that parents disagree with. Privately discuss names or pronouns to use in your notes ahead of time in case the patient is concerned about a parent seeing them. If you are unsure, consider gender-neutral pronouns such as "they" instead of "he" or "she."

6. Take care when documenting unflattering things about patients. Say we document our thought that a patient does not seem to have the ability to complete an educational program that is deeply important to their future plans. Upon reading this "conclusion," our patient may feel despondent, lose sleep, have trouble concentrating, or perhaps experience suicidal thinking. If you suspect a patient will be harmed or put at risk based on something you write, be proactive and document why you believe your patient will be harmed by accessing the data.

7. Make sure your pager or cell number is not listed in your progress notes unless you want patients to have it.

If your patient or family encounters data that they find inaccurate or troubling, listen to their concerns. Have a procedure to correct errors brought to your attention. Consult a lawyer or your malpractice provider if there is evidence of harm to a patient after viewing data in the chart.

Remember that open notes also provide new opportunities for patient engagement. For instance, when written in plain language, your notes can double as patient instructions. I often start follow-up visits by reading out loud the salient points from the patient's last progress note. I find this to be a great way to frame our conversation at follow-up time and remind patients why we chose to proceed as we did.

CCPR VERDICT: Like it or not, the new norm will soon be for patients to have on-demand access to their electronic charts. Although these reforms affect all specialties, we in child psychiatry face unique challenges in opening our notes to patients and their families. We can adapt by being thoughtful, respectful, and proactive in our documentation.

News of Note

Viloxazine (Qelbree): A Faster Strattera?

On April 2 viloxazine, brand name Qelbree, received an FDA indication for the treatment of attention-deficit hyperactivity disorder (ADHD) in children and adolescents ages 6–17 years. Viloxazine is a norepinephrine reuptake inhibitor, similar to atomoxetine (Strattera), which was approved in 2008. Atomoxetine, while approved for ADHD, has some disadvantages when compared with stimulants. It is generally less effective, with response rates only about 50%–75% of typical stimulants. And it is slow, usually taking 2–4 weeks to kick in, as opposed to a day or two for stimulants. Does viloxazine have the same disadvantages? Let's look at the data that have been reported so far.

Viloxazine has been studied for various indications since the 1970s. It originally received an FDA orphan drug designation (less rigorous than approval) for narcolepsy and was studied for nocturnal enuresis and depression, though it did not gain approval for either indication.

For their Phase III studies of viloxazine in ADHD, Supernus Pharmaceuticals (Qelbree's manufacturer) performed four short-term, six- to eight-week randomized controlled trials (Nasser A et al, *Clin Ther* 2020;42(8):1452–1466). 1,013 children and adolescents (ages 6–17) were randomly assigned to various doses of viloxazine (100–600 mg per day) or placebo. Measures included the ADHD Rating Scale-5 (ADHD-RS-5) and the Weiss Functional Impairment Rating Scale-Parent (WFIRS-P): assessments of symptom severity and functional impairment, respectively. In one of the studies, patients taking viloxazine 400 mg daily improved significantly more than those assigned to placebo; however, the 600 mg dose did not reach statistical significance.

What about speed of response? In one study, patients assigned to viloxazine 400 mg began to show improvement over placebo by week 1—more quickly than most studies of atomoxetine, which generally separates from placebo around week 3. Viloxazine has not been compared head-to-head with stimulants or with atomoxetine, so its comparative efficacy is unknown, but it's clearly slower than stimulants, with a clinically meaningful onset similar to atomoxetine beginning at 2–4 weeks.

The viloxazine studies have been criticized because the researchers completed the study then used a crossover mapping from the original outcome scales—the ADHD-RS-5 and WFIRS-P—to the Clinical Global Impression Scale. Such "post hoc" analyses often find positive results that may not be valid.

Side effects

Viloxazine's side effects, like other norepinephrine reuptake inhibitors, included

Continued on page 8

News of Note

Continued from page 7

sedation, mania, increased blood pressure and heart rate, and suicidal ideation. Six out of the 1,013 patients reported suicidal ideation, 1 reported suicidal behavior, and 2 patients reported both suicidal ideation and behavior for a total of 9 patients (0.9%). Two control patients reported suicidal ideation (0.4%), though there were no completed suicides in either group. Irritability and insomnia were more common in the viloxazine group, with 4% reporting insomnia (vs 1% in placebo) and 3% reporting irritability (1% in placebo). Viloxazine is a potent inhibitor of CYP1A2 and is contraindicated with duloxetine, ramelteon, tasimelteon, tizanidine, and theophylline.

Dosing

Viloxazine is supplied in dosages of 100, 150, and 200 mg extended-release capsules. It takes 2 days for this preparation to reach steady-state blood levels, and there is a ~10% reduction in absorption if viloxazine is taken with a high-fat meal or if the capsules are opened and sprinkled on applesauce. The recommended dosage for children 6–11 years old is 100 mg once daily, titrated as needed weekly by 100 mg increments to a maximum of 400 mg. For 12- to 17-year-olds, the starting dosage is 200 mg and can be titrated weekly in 100 mg increments up to 400 mg.

Any advantages over atomoxetine?

The preliminary data reported in press releases show that viloxazine may work a little bit faster than atomoxetine. But there's no reason to expect it to be any more effective in the long run, nor do we expect it to compare favorably to stimulants.

Cost

Supernus has not released the price of Qelbree as of this writing; however, they claim that it will be competitively priced.

CCPR'S TAKE

Viloxazine is the second norepinephrine reuptake inhibitor to be approved for ADHD. It's not clear if it has any advantage over atomoxetine, though if its reputed faster onset of action is better substantiated, it may be advantageous. As with atomoxetine, you should monitor patients for suicidality, mania, and drug interactions.

—Joshua Feder, MD, and Talia Puzantian, PharmD, BCPP. Dr. Feder and Dr. Puzantian have disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Q&A With the Expert

Pharmacotherapy for Autism Spectrum Disorder

Matthew Krause, DO

Child psychiatrist with Primary Health Network, Latrobe, PA.

Dr. Krause has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CCPR: Welcome, Dr. Krause. Tell us a little bit about the recent paper you coauthored called *Pharmacologic Management of Autism Spectrum Disorder: A Review of Seven Studies* (Kothadia RJ et al, *Current Psychiatry* 2021;20(1):33–38).

Dr. Krause: Our study was a review of reviews. The aim was to see if we could find any new insights into medication treatment in autism. Medication is a supplemental intervention in autism. We reserve it for challenging situations due to neurologic, metabolic, behavioral, and other side effects. Still, medications can be very beneficial when implemented appropriately. Our AACAP practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder emphasizes the developmental assessment screening, a thorough diagnostic evaluation, multidisciplinary assessment, and structured educational and evidence-based behavioral health treatment, all ahead of pharmacotherapy.

CCPR: What do you see as the main goals in treating autism with medications?

Dr. Krause: The main goal is to target secondary symptoms, such as irritability, anger, self-injurious behavior, anxiety, and depressed mood. Because of the heterogeneity of autism, we need to look at the associated symptoms and comorbid diagnoses before electing which direction to go with medication. Medications for autism are not curative, but they can alter the trajectory of the outcomes, quiet things down so patients can reach their goals. Often medication resets that baseline to get them to function to the best of their capabilities.

CCPR: What did you learn in your review of reviews?

Dr. Krause: The big news is sort of no news. Antipsychotics have the most data, and risperidone outperformed aripiprazole, lurasidone, and placebo on the Autism Behavior Checklist-Iceberg (ABC-I). This supports what most of us are already doing. But the other news is that SSRIs show mixed results. Fluoxetine worked for 75% of patients with positive changes on the Autism Behavior Checklist (ABC), Autism Treatment Evaluation Checklist (ATEC), Clinical Global Impression scale (CGI), and Yale-Brown Obsessive Compulsive checklist (YBOC) but with frequent behavioral activation. Sertraline, on the other hand, was well tolerated but ineffective on measures of expressive language or any other outcomes. Donepezil plus choline helped expressive language in 5- to 10-year-olds but not older children, who also had worse behavior on the treatment. And in the supplement realm, both Vitamin D and omega-3 fatty acids each separately reduced hyperactivity and were well tolerated.

Continued on page 9

Expert Interview—Pharmacotherapy for Autism Spectrum Disorder

Continued from page 8

CCPR: What else was interesting?

Dr. Krause: There is a wide variety of medications and natural supplements employed for the management of autism-related symptoms. I was intrigued by all the neurotransmitter and biological targets, including dopamine and serotonin, but also GABA-glutamate pathways. The bumetanide trial could represent a potential breakthrough. It is one of the first of its kind to study the core feature deficits in social communication and restricted range of interests.

CCPR: Tell us more about bumetanide.

Dr. Krause: It could be a game-changer. Bumetanide is actually a loop diuretic similar to furosemide that acts by antagonizing ion channel transporter systems in renal tissue but also in the central nervous system. Low-dose bumetanide improved social communication as well as restricted interests. The three trials included 208 patients ages 2–18 years in randomized controlled trials, but used different outcome measures including CARS, CGI, the ABC, the Social Responsiveness Scale, and the ADOS, making it difficult to draw specific conclusions (James BJ et al, *Ann Pharmacother* 2019;53(5):537–544). So, based on that alone, am I ready to recommend bumetanide? Probably not.

CCPR: It still sounds hopeful. Were there side effects with bumetanide?

Dr. Krause: With higher doses, there was hypokalemia and polyurea. Apart from that, it was pretty well tolerated.

CCPR: What's the message of your paper for everyday clinical practice?

Dr. Krause: Begin where we have the most evidence and branch out from there to options with limited or anecdotal evidence. Off-label prescribing is OK; however, we should have a low threshold to discontinue treatment at the first sign of significant side effects or clinical worsening.

"The big news is sort of no news. Antipsychotics have the most data, and risperidone outperformed aripiprazole, lurasidone, and placebo on the Autism Behavior Checklist-Iceberg (ABC-I)."

Matthew Krause, DO

CCPR: What should we tell patients and families about the use of medications for autism?

Dr. Krause: Medication is a tool that should be used when it might help. Tell them how it may help some problems, such as irritability and perhaps attention, but is unlikely to help the core problems with social communication and the narrow range of interests. Talk about the available evidence in a way that families can understand. I talk about the goal to strengthen the quality of life and mental well-being of patients and perhaps lessen the burden on parents and guardians, educators, and others involved in the day-to-day life of the child.

CCPR: What do you tell them about side effects?

Dr. Krause: We need to monitor closely because medications in this population often do not have the expected and desired effects. One example is that SSRIs have a higher likelihood of behavioral activation. Medications don't work the same in the autism population as they do in others, and so close follow-up and psychoeducation are important.

CCPR: Parents often want to use medication only as a last resort, pursuing things that have less evidence such as herbals, acupuncture, and chiropractic. How do you respond to this?

Dr. Krause: I use the AACAP practice parameters to offer what we know of the evidence for various treatments (www.tinyurl.com/kd6mwxss). At the same time, you have to respect families' wishes. I always say: "We want to try whatever we can and if there's newer options, it's intriguing." Don't discount it completely. Some families will come in and say they've started something—for example, CBD—and they feel it's working. I will say: "I hear you that you are finding it useful. I can't recommend a certain product or a certain dose." Then I offer the AACAP stance. There are ethical nuances in not recommending or recommending against a "treatment," and in not interfering with parents' choices for their children. We have to find ways to work safely with families.

CCPR: What cultural or equity impacts do you see at play in the use of medication for kids with autism?

Dr. Krause: Racial and socioeconomic disparities are particularly problematic for autism when considering the importance of early detection, screening, identification, and treatment. African American children are diagnosed a year and a half later than the general population, and minority children tend to receive fewer services, which really puts them at a disadvantage. They are also more likely to be given medications as first-line options because prescribing trends for autism increase with age. Furthermore, more Medicaid-insured children are prescribed medication relative to those who have a commercial payer source. Taken together, a delay in diagnosis plus limited access to resources results in increased pressure on psychiatrists to play catch-up in the form of medication management, which often leads to polypharmacy (Constantino JN et al, *Pediatrics* 2020;146(3):e20193629).

CCPR: Any thoughts on how to get earlier diagnosis and access to treatment for minority populations?

Dr. Krause: We need to ensure minority and underserved populations have appropriate access to primary care. Going back a step, we also need to ensure that women receive timely prenatal and perinatal care, especially when autism risk factors may already be present within the family. A key component as well is education of personnel at childcare/school, where kids spend so much of their time and where their social interactions and play tendencies can be closely observed from a very young age.

CCPR: What's your bottom-line message about medication treatment for kids with autism spectrum disorder?

Dr. Krause: As psychiatrists, we need to be compassionate but up front with families about the indications and expectations of medication treatment for autism spectrum disorder.

CCPR: Thank you for your time, Dr. Krause.

Research Updates IN PSYCHIATRY

MOOD DISORDERS

ECT in Severe Adolescent Mood Disorders

REVIEW OF: Ghaziuddin N et al, *J Child Adolesc Psychopharmacol* 2020;30(4):235–243

ECT is the gold standard for treatment of severe unipolar depression in adults, with remission rates of 70%–90% in randomized trials. In bipolar depression, response rates are 50%–75%. A 2020 retrospective chart study reviewed ECT's utility in adolescents with severe mood disorders.

The study consisted of 54 adolescents, mean age 15.8, with treatment-resistant mood disorders (two-thirds unipolar, one-third bipolar), who received ECT at the University of Michigan Medical Center from 1996 to 2010. Treatment resistance was defined as failure to respond to 3 or more mood-stabilizing medications combined with psychotherapy. The patients averaged 4 hospitalizations, 2 suicide attempts, and 7 failed medication trials (4 antidepressants, 3 antipsychotics and mood stabilizers), each of at least 6 weeks duration, with adequate dosage and good compliance.

The patients received a mean of 13.7 ECT treatments, almost all with bilateral electrode placement. The primary outcome measure was Clinical Global Impressions (CGI) score; response was defined as a CGI score of 2 (much improved), while remission was defined as a score of 1 (very much improved).

The response rate at the end of the index ECT treatment was 52.8%, while the remission rate was 15%, both lower than typical findings in adults. While rates increased at 6 and 12 months, this improvement occurred only with observed cases (OC) data, and with dropouts removed. There was minimal improvement at later time points when looking at last observation carried forward (LOCF) data. There was no difference in response or remission rates between unipolar and bipolar patient groups. Still, by the end of index treatment, suicidal ideation declined from roughly 80% to 40%; self-injurious behavior declined from about 50% to 18%; and school attendance increased threefold, from 20% to 60%. Side effects were minimal.

The limitations of this study included its relatively small size for a chart review, the use of non-blinded raters, the use of the CGI as the measure of treatment outcome (due to missing depression rating scale data), obtaining data from retrospective chart review, and diagnoses made without the use of standardized instruments.

CCPR'S TAKE

While ECT in adolescents appears less effective than in adults, it did produce clinically meaningful changes in these treatment-resistant patients for a year after the index ECT course. Keep it in mind as a possible tool.

—John Raiss, MD. Dr. Raiss has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

GENDER

The Effect of Age and Pubertal Stage on Mental Health in Gender-Incongruent Youths

REVIEW OF: Sorbara JC et al, *Pediatrics* 2020;146(4):e20193600

Gender incongruence means that a young person identifies with a gender that's different from the one they were born with. These youths have an elevated risk of suicide and other psychiatric problems. Gender-affirming medical care (GAMC), such as hormonal therapies, can reduce those risks, but when is it best to start those treatments?

An earlier study found that psychiatric outcomes were better when youths began GAMC before age 12 compared to those who transitioned in adolescence. This newer study builds on this literature by examining the association of both age and pubertal stage at presentation for GAMC on mental health.

The researchers undertook a chart review of 300 patients at a Canadian clinic for transgender youths. They compared outcomes for two groups: those presenting before age 15 (n = 116, median age 14) and those presenting after age 15 (n = 184, median age 16). Most were assigned female at birth (75%), and the majority were Caucasian (72%). The rate of autism (6%) was higher than that of the general population.

Youths who started treatment after age 15 had higher rates of depression (46% vs 30%), self-harm (40% vs 28%), suicide attempts (17% vs 9%), and psychiatric medication use (36% vs 23%). They also recognized their gender incongruence later (median age 9 vs 6) and socially transitioned later (15 vs 13).

Stage of puberty at the time of starting hormones was even more predictive of problems than age. Late pubertal youths (Tanner Stage 4 or 5) were 4–5 times more likely to report depressive or anxiety disorders. The gender assigned at birth was also predictive, with those transitioning from female to male reporting a threefold higher rate of self-harm than those transitioning male to female. Older teens were more likely to be taking psychotropic medications.

The study's main limitation is its uncontrolled design, which leaves open the possibility that the youths who presented later were already at risk for psychiatric problems. It may be that youths with more secure identities and supportive families are simply more likely to seek these services at a younger age.

CCPR'S TAKE

This field is complex. We have a lot to learn about such things as possible differences between patients who experience gender dysphoria earlier in life vs at or around puberty. Still, this study brings reassuring data for families who are considering gender-affirming hormones before the onset of puberty. Outcomes are apparently better when treatment is started before secondary sexual characteristics begin to develop.

—John Raiss, MD.

CME Post-Test

To earn CME or CE credit, log on to www.TheCarlatReport.com to take the post-test. You will be given 2 attempts to pass the test. You must answer 75% of the questions correctly to earn credit. Tests must be completed within a year from each issue's publication date.

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1. A demonstrable effect size for social communication is associated with which autism spectrum disorder intervention(s) (LO #1)?
   - [ ] a. ABA and NDBI
   - [ ] b. DRBI and NDBI
   - [ ] c. NDBI
   - [ ] d. ABA and DRBI

2. The parents of your adolescent patient want access to their child's clinical data. However, there's some information that he doesn't want to share with his parents. In accordance with the Cures Act, what advice should you give your patient (LO #2)?
   - [ ] a. "You can either share all or none of your clinical data with your parents."
   - [ ] b. "You can give your parents access to your more sensitive clinical data by making them a proxy through your EHR, but only if you want to."
   - [ ] c. "You can tell your parents to call me if they want access to your more sensitive clinical data."
   - [ ] d. "You are required to share all of your clinical data with your parents if you're a minor."

3. In a recent study, ECT improved suicidal ideation, self-injurious behavior, and school attendance in adolescents with treatment-resistant mood disorders (LO #3).
   - [ ] a. True
   - [ ] b. False

4. According to a study by Dr. Sandbank and colleagues, what was concluded about the effectiveness of ABA interventions for autism spectrum disorder (LO #1)?
   - [ ] a. ABA interventions have a moderate effect size for improving social communication
   - [ ] b. ABA interventions have a smaller effect size than that of DRBI and NDBI for improving social communication
   - [ ] c. ABA interventions are superior to DRBI and NDBI on all outcomes
   - [ ] d. There aren't enough RCTs to compute the effect size of traditional ABA interventions on social communication

5. In a recent study of gender-affirming medical care for youths with gender incongruence, how did the mental health of those who started treatment after age 15 differ from those who started treatment before age 15 (LO #3)?
   - [ ] a. They had lower rates of depression and suicide attempts
   - [ ] b. They had higher rates of self-harm but lower rates of suicide attempts
   - [ ] c. They socially transitioned earlier and had lower rates of psychiatric medication use
   - [ ] d. They had higher rates of depression, self-harm, suicide attempts, and psychiatric medication use

6. Your patient sends you a request to view their clinical data. According to the Cures Act, which of the following is NOT considered information blocking (LO #2)?
   - [ ] a. Responding to your patient's request after a month
   - [ ] b. Charging your patient a fee for electronic access to their medical records
   - [ ] c. Having your patient sign a HIPAA form
   - [ ] d. Providing your patient with all of the information present in your chart without delay

7. What is the relationship between outcome improvement and the intensity of a specific intervention for autism spectrum disorder (LO #1)?
   - [ ] a. There's no evidence supporting an association between the 15-hour or 25-hour intensities of NDBI or traditional ABA interventions and outcome improvements for either of these approaches
   - [ ] b. More hours of any intervention are associated with better outcomes
   - [ ] c. Only more hours of ABA interventions are associated with greater effect sizes
   - [ ] d. Only more hours of NDBI and DRBI interventions are associated with better outcomes

8. In a recent study of adolescents, how did those with unipolar depression respond to ECT compared to those with bipolar depression (LO #3)?
   - [ ] a. There was no difference in response or remission rates between those with unipolar and those with bipolar depression
   - [ ] b. Bipolar patients had higher remission rates than unipolar patients
   - [ ] c. Unipolar patients had higher response and remission rates than bipolar patients
   - [ ] d. Bipolar patients had higher response rates but equal remission rates compared to unipolar patients

THE CARLAT REPORT
CHILD PSYCHIATRY
P.O. Box 626
Newburyport, MA 01950

This Issue:
Autism in Children and Adolescents
April/May/June 2021

Next Issue:
Substance Use in Children and Adolescents
July/August/Sept 2021

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Note From the Editor-in-Chief

When I was a kid, I was a junior member of the NY Historical Society—the Yorkers. We dug up our town of Williamsville and put artifacts in our new museum on the site of a defunct Nike ICBM missile base, including the rusted chassis of a Model T and, digging deeper, the bones of our town founder Jonas Williams. At Carlat we also dig deeper: Last fall it was the possibility of suicidality with antidepressants when we see the real data; this winter, it was the lack of clinical relevance of CYP enzyme testing when we use medications carefully; and this spring, beneath the apparent weight of thousands of studies that turn out to be flawed, we found an absence of a definable effect size for the massive $17 billion applied behavioral analysis industry.

We didn't believe it. We had the statistical methodology verified and then sent our interview out for peer review. Our usually spirited group of colleagues uniformly concurred with the findings of the article.

How to respond to this seismic shift? With better informed consent: We've supplemented with an article on the three main kinds of autism treatment so that you'll be prepared to help families know that they have choices.

Also in this issue are research reviews on the efficacy of ECT and on the best timing for gender-affirming care for children and adolescents. As always, let us know what you think.