THE CARLAT REPORT CHILD PSYCHIATRY A CME Publication

UNBIASED INFORMATION FOR CHILD PSYCHIATRISTS

Daniel Carlat, MD Editor-in-Chief

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Learning objectives for this issue: 1. Describe how the new FDAapproved EEG test to help diagnose ADHD in children works and whether it is clinically useful. 2. Summarize the appropriate use of antipsychotic medications in children. 3. Detail the antipsychotic medications that can be used to treat various disorders in children, as well as the side effects of these drugs. 4. Evaluate some of the current findings in the literature regarding psychiatric treatment.

The New FDA-Approved EEG Test for ADHD: Should You Order It?

Daniel Carlat, MD Associate Clinical Professor of Psychiatry, Tufts University School of Medicine, Boston, MA

Dr. Carlat has disclosed that he has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

ver the decades, finding a truly useful objective diagnostic test in psychiatry has proven both elusive and frustrating.

The latest candidate is a device called the NEBA system, which was approved by the US Food and Drug Administration (FDA) in July of 2013. NEBA stands for Neuropsychiatric EEG-Based Assessment Aid for ADHD, and the FDA has allowed it to be marketed as a "confirmatory" test for the diagnosis of ADHD in children ages 6 to 17. It is a 20-minute proce-

In Summary

- The FDA approved the NEBA system in 2013 as a "confirmatory" test for diagnosing ADHD in children
- Its manufacturer says the system helps clinicians diagnose ADHD by using the theta/beta ratio, which in most studies is higher in children with the disorder
- No study has been conducted to test whether the system improves clinical decision-making

——— Continued on page 2



Using Antipsychotics Judiciously in Children Glen R. Elliott, MD, PhD

Chief Psychiatrist and Medical Director Children's Health Council, Palo Alto, CA Clinical Professor (Affiliated), Stanford University School of Medicine, Division of Child and Adolescent Psychiatry

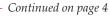
Dr. Elliott has disclosed that he has no relevant relationships or financial interests in any commercial company pertaining to this educational activity.

CCPR: Dr. Elliott, in your view, when is it is most appropriate to use antipsychotics in children?

Dr. Elliott: In adolescents, sometimes a clear psychotic thought process appears, and in such cases the use of antipsychotics is unambiguously appropriate. The symptoms may involve hallucinations or delusions, and the diagnosis may be schizophrenia or some other disorder; regardless of the diagnosis, antipsychotics work well in such cases. As you move to younger children, frank psychosis becomes less common, but it can still occur. In my own clinical experience, the youngest, clearly psychotic individual I've worked with was 4½-years-old. When I

first saw him I thought he had a brain tumor, because he was so dysfunctional. He had clang associations, he was rocking back and forth and drooling, and there appeared to have been a fairly abrupt onset. But a medical work up showed no neurologic explanation and his psychosis cleared with haloperidol (Haldol).





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The New FDA-Approved EEG Test for ADHD: Should You Order It? Continued from page 1

dure that can be done in the office and the out-of-pocket cost to patients is a maximum of \$425, according to NEBA Health's website.

In this article, as in so many articles about the usefulness of diagnostic tests, you will encounter terms such as sensitivity and specificity—statistics that are meant to show how accurate a test is. But before we discuss the numbers, let's be clear about what such numbers *can* and *cannot* show you—by using the analogy of an apple.

If you pick up an apple, you would label it as an "apple" because you've seen so many of them in your life and you have high confidence in your abil-

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This CME/CE activity is intended for psychiatrists, psychiatric nurses, psychologists and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

ity to recognize them. Let's imagine that there's a new apple-recognizing device on the market called the "Apple Rec," which uses various technologies to measure the wavelength of light reflected by an object, its mathematical curvature, etc. The manufacturer provides impressive data showing that the Apple Rec has 100% sensitivity and 100% specificity for diagnosing (recognizing) an object as being an apple. Given these dazzling statistics, would you buy the Apple Rec? No, because even though it's exquisitely accurate, it provides you with no useful diagnostic information beyond what you can obtain by looking at the apple yourself. However, if the Apple Rec provided you with added value, you might consider it a good investment. For example, if, in addition to correctly recognizing it as an apple, it also calculated its sweetness and crispness, the Apple Rec suddenly becomes a useful tool, because these are qualities that you would otherwise struggle to ascertain.

The apple principle applies to diagnostic tests in psychiatry. Before you refer your patients to an expensive test that diagnoses ADHD, you need to make sure that it does something that you can't easily do yourself. Keep that in mind as we look at the evidence for NEBA.

How EEGs Work

First, let's review some of the basics of EEGs. First developed in the 1920s, the electroencephalograph involves applying electrodes to the scalp's surface in order to visually examine brain waves. Brain waves are labeled according to their frequency. The faster frequency bands are associated with wakefulness, the lower frequency bands with relaxation or sleep. A good way to memorize the confusing names is to use the mnemonic BAT-D (progressing from most alert to most asleep):

- Beta (16 hz, or waves per second): Alert, intellectual activity
- Alpha (8–11 hz): Relaxed, daydreaming
- Theta (4–8 hz): Deep relaxation, meditation
- Delta (1–3 hz): Deep sleep

Researchers have been studying EEG for the diagnosis and treatment of ADHD for a surprisingly long time-over 40 years. Using a refinement of EEG called Quantitative EEG, or QEEG, a fairly consistent finding has been that ADHD is associated with more activity of theta waves and less activity of beta waves. This makes intuitive sense, if you think of ADHD as a disorder in which dreaminess (theta) takes precedence over focused mental activity (beta). In most studies, the so-called TBR-theta/beta ratio-is found to be higher in ADHD kids, but that's not always true. A recent study, in fact, compared 32 children and 22 adults with ADHD to matched healthy controls and found no evidence of increased theta activity (Liechti MD et al, Brain Topogr 2013;26(1):135-151). Nor is higher theta activity necessarily specific to ADHD, since studies have shown an association with bipolar disorder, polysubstance abuse, and epilepsy.

Regardless of these inconsistencies, NEBA claims that they have developed a system that helps clinicians diagnose ADHD by using the TBR. The study has not yet been published in a peerreviewed journal, but the FDA reviewed it and was impressed enough with the data to allow the test to be marketed. You can find all this data on the FDA website at http://1.usa.gov/1A5g05d.

The Study the FDA Looked At

NEBA Health, the Georgia-based company that won approval for the NEBA system, divided its study into two phases, called Study 1 and Study 2. First, in Study 1, they recruited 275 children and teenagers who presented with "attention and/ or behavioral concerns" to various mental health clinics throughout the US. All the patients were evaluated by clinicians via a comprehensive evaluation including an interview, various symptom scales, physical exams, and other testing as deemed necessary by the individual practitioners. In addition to the clinical evaluations, the subjects were given QEEGs via the NEBA system by separate investigators who were blinded to the clinical diagnosis. The original clinicians were blinded to the results of the EEG.



The New FDA-Approved EEG Test for ADHD: Should You Order It? Continued from page 2

of a well-conducted comparison of a clinical diagnosis with an objective test. But here's where the study design got a little too complicated. Instead of using a real world diagnosis as the gold standard by which to judge the accuracy of the EEG, the researchers used a multidisciplinary team diagnosis as the gold standard. The team consisted of a clinical psychologist, a neurodevelopmental pediatrician, and a child psychiatrist, and they reviewed all the patient files created by the clinician. However, unlike the clinician, the team didn't actually see or talk to the patients.

Nonetheless, this once-removed team diagnosis was considered by researchers to be the gold standard by which the NEBA system would be judged, and was termed the "Best Estimate Diagnosis" or BED.

To summarize, the study's comparison is between the following two diagnostic methods for ADHD:

- 1. Best estimate diagnosis: A multidisciplinary team that never saw the patient and is basing the diagnosis on retrospectively reading chart notes and psychological testing results.
- 2. The NEBA interpretation: The EEG theta/beta ratio, combined in some way with the clinician's diagnosis.

The Study Results

Here are the basic results for the NEBA as compared to their gold standard diagnosis, separated out by age group.

- 1. Adolescents (12-18):
 - a. Sensitivity: 89% (Sensitivity= the proportion of people with the disease who test positive)
 - b. Specificity: 79% (Specificity= the proportion of patients without the disease who test negative)
 - c. Positive predictive value: 81% (PPV= the proportion of patients with a positive test who actually have the disease)
 - d. Negative predictive value:
 93% (NPV= the proportion of patients with negative tests who do not have the disease)

- 2. Children (6-12):
 - a. Sensitivity: 79%
 - b. Specificity: 97%
 - c. PPV: 96%
 - d. NPV: 82%

These numbers are pretty good. For example, a 96% PPV for children means that 96% of kids with a positive NEBA had ADHD. The PPV for adolescents is less impressive—81%, meaning that 19% of adolescents with a positive NEBA did not have ADHD. Nonetheless, these are all robust numbers—as long as the information that we get is actually clinically useful.

Is it Clinically Useful?

A positive NEBA provides "confirmatory support" that your patient has a cluster of symptoms that we commonly label "ADHD." But wait—isn't this what we already do? We ask a series of questions and we make observations in order to ascertain whether there is a particular cluster of symptoms labeled ADHD. What the NEBA does for us is it says, "Yes, I confirm that you recognized that your patient has an attention issue, labeled ADHD by *DSM-5*." How does this help me? I'm not sure. It's telling me that an apple is, indeed, an apple.

Recognizing that there is an attention problem is the easy part—we often know this before the child even enters the room, and we definitely know after talking to the parents for 30 seconds. We don't need an EEG to tell us this. And NEBA can't provide information to help us with any of the following crucial questions:

• What comorbidities does the patient have that will affect our choice of treatment? A positive NEBA result may be specific for differentiating some problem from no problem, but it cannot distinguish ADHD from a host of conditions that often accompany the disorder—or can be mistaken for ADHD. At least two-thirds of kids with ADHD have a comorbid diagnosis, such as anxiety disorders, oppositional defiant disorder, learning disorders, or mood disorders (http://bit.ly/1Bla0EL).

- How severe are the symptoms? Are they mild enough so that the child can stay in the same school or so severe that a change might be needed?
- Should I start a stimulant?
- Should I refer to a behavioral therapist?

NEBA provides no information on any of the issues that affect treatment which is just another way of saying that NEBA has little, if any, clinical utility. All NEBA can do is tell us that an attentional issue is an attentional issue. Full stop. How much is that worth to you—or, more relevantly, to your patients?

Lest it appear that we are trashing NEBA, we are not—we're simply pointing out that it's a promising technology with no proven clinical benefit. The next step for the company would be to demonstrate that benefit. A good way to do this would be to conduct a randomized trial—recruit 200 kids arriving at clinics for evaluations and then randomly assign 100 to standard evaluation and 100 to standard evaluation plus NEBA. Re-evaluate three to six months later, comparing the two groups. Here are some questions I'd be interested in:

- Does NEBA improve diagnostic certainty, as measured by a scale given to clinicians?
- Can it result in more rapid initiation of treatment?
- Does it lead to more rapid symptoms improvement?
- Will it improve parental satisfaction?

There are many other questions. These could be answered by appropriate research, and we hope to see such studies in the future.

Not ready for prime time. We recommend avoiding NEBA and instead focusing your energy on the less technologically exciting basics—figuring out the individualized treatment plans needed to help kids succeed despite their ADHD.

Expert Interview Continued from page 1

CCPR: This makes sense, and I think most of us would agree that frank psychosis in a child is an indication for a trial of antipsychotics. But there are other situations where the picture is murkier.

Dr. Elliott: Yes there are, and this is partly because the atypical antipsychotics (APs) have been relabeled and used as mood stabilizers in adults. With children, unfortunately, mood instability is often quite difficult to diagnose with precision. The whole idea of bipolar disorder in children has broadened over the years, especially in the US, to cover a wide range of behaviors. At its broadest, any child with recurrent meltdowns who can't handle transitions may be at risk of receiving a diagnosis of bipolar disorder. If that happens, the likelihood is high that APs will be recommended. This is partly

These children have a sort of internal picture of how the world is supposed to be; and, when that changes, there is a behavioral deterioration

Glen R. Elliott, MD, PhD

because we are really treating their behavior, and partly because APs are easier than mood stabilizers to use, as it may be difficult to get the frequent blood samples in these children that are required for medications such as lithium or valproic acid (Depakote) or other non-AP mood stabilizers.

CCPR: Yes, the overdiagnosis of bipolar disorder in kids is a problem. How do you go about clarifying the diagnostic picture to prevent this?

Dr. Elliott: Part of what I'm looking for is where and when the problem began. Can we identify any precipitating factors? The differential diagnosis is fairly broad—the most common competing diagnoses are anxiety, attachment problems, behavioral rigidity, and ADHD. Often, these children have problems from very early on, starting in preschool with a pattern of getting kicked out of class, having meltdowns, and getting aggressive if confronted about not following rules. But, a cardinal feature is inability to handle unexpected situations and responding with a meltdown. For example, a child's school schedule changes—he expects math at 11 a.m. and instead has to attend a school assembly. Telling him to go to the auditorium may send him into a rage, or he might start crying inconsolably. Or, the mother might say, "Instead of going home, we have to stop at the grocery store," and he may jump out of his seat belt and threaten to jump out of creal. The real difficulty is it is unpredictable: one day he is fine, and another day the whole world collapses when the family runs out of creal. These children have a sort of internal picture of how the world is supposed to be; and, when that changes, there is a behavioral deterioration.

CCPR: How do we approach helping kids respond differently?

Dr. Elliott: Every case is different. There are a variety of established techniques, such as parent management training and evidencebased treatments for disruptive behaviors. One technique is to teach children to tolerate changes in routine or create a structure to minimize the impact of the changes. For example, imagine the child will have to go to a doctor's appointment, which is not part of his usual routine. His parents may need to warn him three weeks in advance, put it on the calendar, talk about it every other day, and that may work great. But a different child may spend the three weeks obsessing about it, getting so anxious that he cannot go to school. In these cases, you're better off waiting until the morning of the appointment and just say, "Hey, we are going to do something different today." Usually, parents learn this about their particular child, and there is no single recipe.

CCPR: At what point do you move to medications with these children?

Dr. Elliott: The most common scenario is when the behavior therapists throw up their hands and say, "Nothing is working." The parents have been trying hard—they've read some of the books such as *The New Strong-Willed Child*, they've tried various techniques at home, but the child is still irritable and having meltdowns and the parents want to try medications (Dobson JC. *The New Strong-Willed Child*. Carol Stream, Illinois: Tyndale House Publishers; 2014). An interesting example of this was in the research studies leading to the approval of risperidone for irritability in autism. The original research plan was that risperidone would be used sparingly, in a way that would calm down the child enough to maximize benefits from behavioral and parenting techniques parents learned as part of the study. The design was to start with risperidone, train parents with more effective parenting approaches, and then discontinue the risperidone, with parents using just behavioral techniques. But it turned out that a lot of parents found, when they stopped the risperidone, the difficult behaviors returned. Many of them dropped out of the study because they preferred to continue the risperidone, finding it to be more helpful in allowing the children to do normal activities. So generally, I broach the possibility of medications when other techniques have been tried and were not helpful enough. The threshold varies: some clinicians insist that failure go on for a long time. I have a lower threshold because we have evidence that a combination of medications and non-medication approaches work better than either one alone, and the success rate of behavior therapy is higher if the child is less volatile, which APs help to achieve. Ultimately though, this is a family decision; usually, they are coming to me and asking me to start meds.

CCPR: What do you start with?

Dr. Elliott: I generally don't start with APs—more often with an antidepressant or an alpha-adrenergic blockade agent. They often work and, from a side-effect perspective, tend to be less worrisome.

CCPR: Why do these medications work for behavioral issues?

Dr. Elliott: Because, at least for non-autistic children, often anxiety is the underlying cause of the meltdowns. Antidepressants can raise the threshold and allow the child to tolerate a little more frustration, avoiding an episode. A classic example is a child with a lot of obsessive behaviors whose meltdowns occur almost always when they are involved in a behavior that gets interrupted such as



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Antipsychotic Medications Used for Children				
Medication	Indication(s)	Age group (years)		
FDA-approved for children				
First-generation antipsychotics				
Chlorpromazine (Thorazine)	Schizophrenia Bipolar disorder	1–12		
Perphenazine (Trilafon)	Schizophrenia	>12		
Pimozide (Orap)	Tourette's syndrome	>12		
Prochlorperazine (Compazine)	Schizophrenia	>2		
Trifluoperazine (Stelazine)	Schizophrenia	>6		
Second-generation antipsychotics				
Aripiprazole (Abilify)	Schizophrenia Bipolar disorder monotherapy or with lithium/valproate Irritability associated with autism	13–17 10–17 6–17		
Olanzapine (Zyprexa)	Schizophrenia Bipolar disorder	13–17		
Quetiapine (Seroquel)	Schizophrenia Bipolar disorder (acute mania)	13–17 10–17		
Risperidone (Risperdal)	Schizophrenia Bipolar disorder Irritability associated with autism	13–17 10–17 5–16		
Paliperidone (Invega)	Schizophrenia	12–17		
Not FDA-approved for children, but sometimes used off-label				
Asenapine (Saphris)				
Iloperidone (Fanapt)				
Lurasidone (Latuda)				
Amisulpride (Amipride)				
Ziprasidone (Geodon)				
Clozapine				
Paliperidone (Invega)				

Source: Hari Nair, MD, Department of Child and Adolescent Psychiatry, Mount Sinai-St. Lukes's/Roosevelt Health System, New York, NY. References: Agency for Healthcare Research and Quality. Future Research Needs for First- and Second-Generation Antipsychotics for Children and Young Adults. http://www.ncbi.nlm.nih.gov/books/NBK84660. Published February, 2012. Accessed December 9, 2012; Kumar A et al, *Cocbrane Database Syst Rev* 2013;10:CD009582; Haddad PM & Sharma SG, *CNS Drugs*, 2007;21(11):911–936.

Possible Side Effects of Antipsychotic Medications		
Classification	Side effects to watch for	
First-generation antipsychotics	Extra pyramidal symptoms, Dry mouth Sedation, Neuroleptic malignant syndrome Tardive dyskinesia, Sialorrhea* Agranulocytosis* Leukopenia* Neutropenia*	
Second-generation antipsychotics	Dry mouth, Sedation Significant weight gain** Hyperlipidemia** Hyperprolactinemia** QTC prolongation***	

* Clozapine-specific adverse side effects ** Clozapine and Olanzapine with the highest risk; Aripiprazole, Lurasidone, and Ziprasidone with the lowest risk *** Ziprasidone, Quetiapine, Iloperidone with the highest risk

Source: Hari Nair, MD, Department of Child and Adolescent Psychiatry, Mount Sinai-St. Lukes's/Roosevelt Health System, New York, NY.





SUBSTANCE ABUSE

Prescribing Anxiety Meds for Teens May Trigger Later Drug Abuse

Adolescents are commonly prescribed anti-anxiety or sleep medications, which is often reasonable, given the efficacy of these agents. We often worry about abuse potential, but we've had little data to tell how much we should worry, until now. It turns out that we may be prodding some of these teens down the road toward addiction.

University of Michigan researchers conducted a longitudinal study that looked at more than 2,700 adolescents attending five Detroit area secondary schools between 2009 and 2012.

The adolescents were divided into three groups: Those who were never prescribed anxiety or sleep medication; those prescribed those medications but not during the study period; and those prescribed the medications during the study period.

Almost 9% of the teens had received a prescription for anxiety or sleep medications during their lifetime and 3.4% had received at least one prescription during that three-year period. Compared with adolescents never prescribed either type of medication, adolescents prescribed these medications during the study period were 10 times more likely to use them for "sensation-seeking motivations," such as to get high or to experiment. They were also three times more likely to use someone else's prescription to self-treat anxiety or to help them sleep.

Along with taking a look at recent prescriptions, the study also looked at whether adolescents prescribed medications at any point in their past would be more likely to use someone else's prescription to get high. Researchers hypothesized that once exposed to these types of medications adolescents would

Research Updates IN PSYCHIATRY

be more likely to use someone else's prescription for sensation-seeking reasons.

In fact, teens prescribed the medications prior to the study period, were 12 times more likely to use someone else's anxiety medication, compared with teens never prescribed anxiolytic medications. This association was not found with sleep medications, however (Boyd CJ et al, *Pscybol Addict Bebav* 2014;epub head of print).

CCPR's Take: Be cautious when prescribing benzos to teens—once they discover the "Ativan feeling," they may well seek it out in the future, whether they are anxious or not.

EXERCISE

Exercise Not Only Good for Children's Overall Health, It's Good for their Brains

Exercise is good for the brain as well as the body—we've known for several years that this is true for adults, but a new study indicates it's true for children, too.

To test the hypothesis that exercise could improve cognitive function in kids, researchers randomly assigned 221 children, ages 8 to 9, to either a nine-month afterschool physical activity program or to a wait-list control group. The children assigned to the Fitness Improves Thinking in Kids (FITKids) program spent a total of two hours every day after school for 150 days of a school year doing a combination of moderate to vigorous exercise and less vigorous skills games. Children participated in brief, age-appropriate activities such as jumping jacks, throwing, and catching-moving to various stations targeting aerobic activities, muscular strength and endurance, or movement.

Children took both a pretest prior to starting the intervention and a post-

test when the program ended to measure changes in both mental and physical fitness. In addition to improvements in physical conditioning, such as maximal oxygen consumption, children who took part in the exercise group did much better overall on measures of attentional inhibition (the ability to restrict distractions or habits to maintain focus) and cognitive flexibility (the ability to multitask). While children in both groups improved, the children in the exercise program had greater improvement in both inhibition (3.2% more than control) and cognitive flexibility (4.8% more than control). Improvements were greater in children who attended the exercise program most often (Hillman CH et al, Pediatrics 2014;134(4):e1063-1071).

CCPR's Take: Kids and their parents should know that being fit can translate to better attention, decision-making ability, and brain function. The study should also give pause to educators about reducing physical activity during the school day, such as recess time, in an attempt to increase academic achievement.

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CME Post-Test

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Below are the questions for this month's CME post test. This page is intended as a study guide. Please complete the test online at www.TheCarlatChildReport.com. Note: Learning objectives are listed on page 1.

- 1. Which of the following is NOT true about the NEBA system (Learning Objective #1)?
 - [] a) It was approved by the US FDA in July of 2013
 [] c) It uses a blood test to determine if a person has ADHD
- [] b) It can be used in children ages 6 to 17
- DHD [] d) A positive result provides "confirmatory support" that a patient has ADHD

2. According to Glen R. Elliott, MD, PhD, antipsychotics are often recommended for bipolar disorder in children because of which of the following reasons (LO #2)?

- [] a) It may be difficult to get the frequent blood samples required for some mood stabilizers
- [] b) They have fewer side effects
- [] c) They are the only medications that can treat behavior difficulties
- [] d) Parents request them to control melt-downs
- 3. Which of the following antipsychotic medications has been approved by the FDA for treatment of Tourette's syndrome (LO #3)?

 [] a) Perphenazine (Trilafon)
 [] b) Pimozide (Orap)
 [] c) Prochlorperazine (Compazine)
 [] d) Trifluoperazine (Stelazine)
- 4. A study of more than 2,700 teens in Detroit found which of the following was true for adolescents who were prescribed anti-anxiety or sleep medications during the three-year study timeframe (LO #4)?
 - [] a) They were no more likely to use someone else's prescription for nonmedical use
 - [] b) They were more likely to use someone else's prescription for nonmedical use
 - [] c) There was no difference when compared to adolescents who were never prescribed the medications
 - [] d) They was no difference when compared to adolescents prescribed the medications at any point in their past, but prior to the study period
- 5. A study by Hillman CH et al, found that while participation in an afterschool physical education program had a positive effect on physical fitness, it had no effect on children's cognitive functioning (LO #4).
 - [] a) True [] b) False

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Expert Interview

Continued from page 4

lining things up or counting. From the school's point of view, it may simply be time to change from activity A to activity B, but the child becomes upset because they're not able to finish their routine. In these cases, antidepressants for obsessive-compulsive disorder (OCD) can make a big difference.

CCPR: How do you choose among the antidepressants?

Dr. Elliott: The best-studied antidepressants for children are the SSRIs, and in my opinion, there's no truly compelling evidence of one being better than another—though there is some disagreement in the field about this. Generally, my approach is that if there's a family member doing well on one, I'll choose that one. If a family just believes in one, they have a positive transference and that may enhance the likelihood they'll stick with a med. If the child is sluggish, I may use sertraline or fluoxetine, which are more activating. If they are already hyperactive or having insomnia I stay away from those, and I might go to citalopram or escitalopram.

CCPR: When you do go to antipsychotics for kids, which do you choose?

Dr. Elliott: Among the antipsychotics, we have the most experience with risperidone and aripiprazole, both of which are approved for irritability in autism, and we have a fair amount of experience with quetiapine. I personally like risperidone, which was the first one we began using in children. Risperidone is sedating, so it is good for children with insomnia. But it has a higher likelihood of side effects such as weight gain.

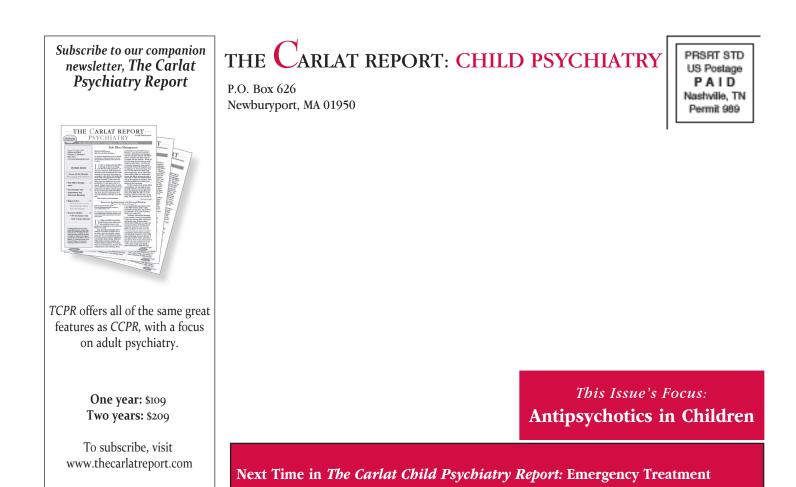
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PAGE 7

CCPR: How do you dose risperidone?

Dr. Elliott: I'll start most children on 0.25 mg or 0.5 mg once a day, but sometimes you need to dose it two or three times a





Expert Interview

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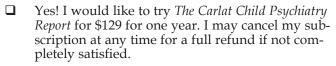
day. My personal maximum dose is 4 mg a day. In terms of increased eating, it is not always dose-related, and a patient's appetite can skyrocket. It's important to understand that while, statistically, risperidone has a higher probability than aripiprazole to cause weight gain, there are a lot of children taking risperidone who don't have increased appetite. Fortunately, if you can stop the medication, that side effect goes away. Where a conflict can arise is if the medication produces substantial improvement but also significant weight gain. Metformin sometimes works to reduce appetite and thus prevent weight gain. The pharmaceutical companies say, "Eat less and exercise more," but that's very hard advice for children—or most adults, for that matter—to follow.

CCPR: When do you choose aripiprazole?

Dr. Elliott: When a child is too sleepy and too slowed down, I use aripiprazole. I start at 2.5 mg to 5 mg once a day, and 20 mg is my maximum dose. It is less sedating than risperidone, which is sometimes good and sometimes not. Though it probably produces less of the compulsive eating, my clinical experience is that the likelihood of some weight gain is fairly high—and it tends to be the worst possible kind of weight gain, abdominal fat, so they get pot bellies. One increasingly common recommendation is to include abdominal girth as a standard measure when seeing these patients, regardless of which AP one chooses.

CCPR: Thank you, Dr. Elliott.

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