Abstract

**Background:** Medications are often recommended for patients to control unwanted behaviors. Treatment with prescription drugs for autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and acquired brain injury (ABI) has benefits and side effects. Gains may be made in attention and mental focus while accommodation and eye tracking may be compromised. Benefits versus side effects must be considered when managing these conditions with drugs.

**Case Summary:** A five-year-old girl presented for preschool evaluation. She destroyed the tape in the audio tape player in the waiting room, broke several legos, tore pages from the children’s books and magazines and spilled a soda before being called back for her exam. History was positive for Rett's syndrome. No medications were taken. All examination parameters were within normal limits.

The following year she returned complaining of difficulty reading and focusing at near. She managed to sit quietly in the waiting area and play with a puzzle before her eye exam began. The history revealed that she had started taking Prozac orally during the school year. Her mother reported that she read constantly. Reading material was constantly held close. She became aggressive when challenged to move it away. Exam findings showed distance visual acuities at 20/20 and near acuities reduced to 20/50. Accommodative testing showed reduced amplitude. A near prescription of +1.00 OU was recommended to assist in her reading focus.

**Conclusion:** Behavior modifying medications were used to help this child and manage behavior in the classroom. Reduced accommodation is a known side effect of many commonly used drugs in the treatment of disorders such as ASD, ADHD, and ABI. Awareness of these medications and their side effects is warranted by eye care providers.

**Key Words**
acquired brain injury, attention deficit hyperactivity disorder, autism spectrum disorder, behavior management medications, traumatic brain injury

Background

Unwanted behaviors secondary to Autism Spectrum Disorders (ASD), Attention Deficit Hyperactivity Disorder (ADHD), and Acquired/Traumatic Brain Injury (ABI, TBI) are often treated with pharmaceutical agents. These conditions are prevalent in both adult and pediatric populations.

ASD occurs in all racial, ethnic, and socioeconomic groups, but is four times more likely to occur in males than females. The United States Center for Disease Control (CDC) estimates that between 1 in 80 and 1 in 240, with an average of 1 in 110 children, have an ASD.\(^1\)

ADHD is estimated to affect 3% to 7% of school aged children. As of 2007, approximately 9.5% or 5.4 million children four to 17 years of age have been diagnosed with ADHD. Boys (13.2%) were more likely than girls (5.6%) to have been diagnosed with ADHD. Prevalence of ADHD has increased at a greater rate among older teens as compared to younger children. The highest rates of parent-reported ADHD diagnosis were noted among children covered by Medicaid and multiracial children. Prevalence of parent-reported ADHD diagnosis varies by state. Nevada has the lowest rate at 5.6% and North Carolina has the highest rate of 15.6%.\(^2,3\)

Each year, an estimated 1.7 million people sustain a TBI. Children aged zero to four years, older adolescents aged 15 to 19 years, and adults aged 65 years and older are most likely to sustain a TBI. Almost half a million (473,947) emergency department visits related to TBI are made annually by children aged zero to 14 years. Adults aged 75 years and older have the highest rates of TBI-related hospitalization and death.\(^4\)

Medications may be added to the treatment plan for long or short term management of undesired behaviors. A survey of over 3,000 families in North Carolina found that 46% of respondents reported that their family member with ASD was prescribed psychotropic medication for behavioral symptoms.\(^5,6\) Another recent study documented that 13.5% of children in the welfare system were using psychotropic medications. This is two to three times the rate of other children in the community.\(^7\) Pharmaceutical agents may allow time for patients and their families to learn behavioral and discipline strategies to keep negative actions and emotional outbursts to a minimum. As verbal communication skills improve, management with prescription medications may be minimized or eliminated.
Pharmaceutical treatment for ASD, ADHD, and ABI/TBI has benefits and side effects. Managing excessive activity may allow some success in academic and social settings, but can cause unwanted side effects. Increased focus of attention may be undermined by distress to the accommodative/convergence system. This case illustrates the beneficial and detrimental effects of medication to manage behavioral issues.

Case Summary
A five-year-old girl presented to the clinic for preschool evaluation. She destroyed the tape in the audio tape player in the waiting room, broke several legos, tore pages from the children’s books and magazines in the waiting room, and spilled a soda before she was called back for her exam. She threatened to kill the doctor and staff, saying, “All doctors are evil, and you should die!” History was positive for Rett’s syndrome (a form of autism spectrum disorder).8 No medications were taken. The mother shared that the child did not sleep at night and was difficult everywhere she went. Visual acuities were 20/20 in each eye at distance and near. Retinoscopy was +1.50 in each eye with bright clear reflexes. Cover test showed low exophoria at distance and near. Ocular health was normal. No prescription for glasses was recommended and follow up was set up for one year.

The following year she returned for vision evaluation. She was complaining of difficulty reading and focusing at near. She managed to sit quietly in the waiting area and played with a puzzle before her eye exam began. The history revealed that she had started taking Prozac orally during the last school year. Her mother reported that she had learned to read and read constantly. Reading material was constantly held close, and she became aggressive when challenged to move it away. Examination findings showed distance visual acuities at 20/20 and near acuities reduced to 20/50. Accommodative testing showed reduced amplitude of accommodation, with PRA at -1.00 and NRA at +2.00. She was diagnosed with accommodative insufficiency. A near prescription of +1.00 OU (single vision), was recommended to assist her when reading. The parents were educated about this condition and were supportive of the treatment plan. The importance of regular follow up visits was stressed, especially if the medication was changed or if dosage was increased.

Discussion
Behavior modifying medications were used to help this child attend school and manage behavior in a classroom setting. Reduced accommodation is a known side effect of many commonly used drugs to treat disorders such as ADHD. Problems with accommodation are noted with tricyclic antidepressants and low potency antipsychotics.9, 10 Behavior management medications are frequently used to manage ADHD. A customized treatment plan must be formed with careful observation of behavior by parents and physicians.11 As of 2007, 2.7 million youths aged 4-17 years (66.3% of those with a current diagnosis) were receiving treatment in the form of medications for the disorders.1 Many different categories of medication have been used in Federal Drug Administration (FDA) approved treatments and “off label” treatments.12 Off label treatments involve the use of an approved medication to treat a non-approved condition, or the use of the medication for treatment of a child younger than that for which FDA approval has been granted.

Behavior modification along with medication has shown to have more positive results than medication alone for ASD.13 Behavioral treatment combined with antipsychotic medication was the most effective approach to reducing aggressive behaviors in youths with ASD.14 Commonly used classes of medications include anti-psychotics, neuroleptics, anti-depressants, anti-anxiety agents, stimulants, anti-hypertensives, anti-convulsants, mood stabilizers, and noradrenaline re-uptake inhibitors. Optometrists should be familiar with the desired effects and negative side effects of these pharmaceutical agents Table 1.

Wide arrays of transmitter systems that may contribute to ASD include serotonin, dopamine, acetylcholine, and brain-derived neurotropic factor.15 Serotonin, dopamine, acetylcholine, oxytocin, and amino acid neurotransmitters are among the neurochemicals being investigated with regard to the development and expression of ASD. Evidence that acute depletion of the dietary precursor of serotonin (tryptophan) increases the symptoms of ASD is stimulating further research on serotonin.15

Selective serotonin reuptake inhibitors (SSRIs) including Prozac (fluoxetine), Paxil (paroxetine), and Celexa (citalopram), have been reported to be the most prescribed psychotropic medications for those with autism. They are effective in managing behaviors such as compulsions, stereotypes, and self-injury.3 Dopamine is a catecholamine that is synthesized from the dietary amino acid tyrosine. Dopamine function in the brain involves systems that contribute to movement control, emotion, stimuli reinforcement, memory, and higher-order functioning.16 Dopamine blockers, such as antipsychotics, have been observed to alleviate symptoms of ASD, including hyperactivity, various stereotypical behaviors, aggression, and self-injury.17,18 Dopamine antagonists were found in one study to decrease accommodative ability and the rate of accommodative recovery after discontinuing medication use.19

Social impairment is a primary symptom of ASD. Researchers have begun to investigate whether or not the hormone oxytocin is produced or processed in a dysfunctional manner in individuals with ASD. Recent studies suggest oxytocin deregulation may play a role in ASD.20,21 Oxytocin is associated with lactating mothers and is thought to be involved with the mother-child bonding process. Disruption of the body’s oxytocin may be at the root of issues with empathy, eye contact, and ability to form and maintain social relationships.22

Brain derived neurotropic factor (BDNF) is a protein found in the brain that plays a significant role in long-term neuronal development and survival. BDNF is commercially available as a dietary supplement without a prescription. The levels of BDNF have been found to be significantly decreased in individuals with ASD when compared to age matched controls.23

Neuroleptic medications are used in patients with ASD and ABI/TBI. Commonly used epileptic medications are Carbechol (carbamazepine), Zaronit (ethosuximide), Felbatol (felbamate), Gabitril (tiagabine), Keppera (levetiracetam), Lamictal (lamotrigine), Lyrica (pregabalin), Neurontin (gabapentin), Dilantin (phenytoin), Topamax (topiramate), Trileptal (oxy carbazepine), Depakene (valproate), Depakote (valproic acid), Zonegran (zonisamide), and
### Table 1. Common Behavior Medications

<table>
<thead>
<tr>
<th>CLASS</th>
<th>DRUGS</th>
<th>BENEFIT</th>
<th>SIDE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-psychotics or Neuroleptics</td>
<td>Haldol, Mellaril, Stelazine, Thorazine</td>
<td>Reduce agitation, anxiety, aggression, hyperactivity, stereotypic and self-stimulatory behaviors, and temper outbursts</td>
<td>Addiction, <strong>Blurred vision</strong>, Dyskinesia, Psychosis, Sedation, Tremors</td>
</tr>
<tr>
<td>Typical Neuroleptics</td>
<td>Abilify, Clozaril, Geodon, Risperdal, Seroquel, Zyprexa</td>
<td>Reduce aggression, agitation, self-injurious behavior</td>
<td>Agitation, Increased appetite, Lowers white blood cell count, Tardive dyskinesia</td>
</tr>
<tr>
<td>Anti-depressants</td>
<td>Anafranil, Celexa, Elavil, Lexapro, Luvox, Paxil, Prozac, Tofranil, Wellbutrin, Zoloft</td>
<td>Raise serotonin levels, Reduce anxiety, Reduce obsessive-compulsive &amp; ritualistic behaviors</td>
<td><strong>Arhythmias</strong>, <strong>Blurred vision</strong>, Constipation, Dry mouth, Dizziness, Hyperactivity &amp; Impulsivity, Lowered threshold for seizures, Sleep disturbances</td>
</tr>
<tr>
<td>Anti-anxiety agents</td>
<td>Ativan, Buspar, Klonapin, Valium, Xanax</td>
<td>Reduce anxiety</td>
<td><strong>Abnormal eye movements</strong>, Crying, Disinhibition, Irritability</td>
</tr>
<tr>
<td>Stimulants</td>
<td>Adderall, Cylert, Daytrona patch, Dextedrine, Focalin, Ritalin</td>
<td>Affect dopamine, Improve focus and regulation, Monitor arousal system, Decrease impulsivity</td>
<td>Depression, Increase in perseveration &amp; repetitive behaviors, Irritability, Palpitations, Sleep disturbance</td>
</tr>
<tr>
<td>Anti-hypertensives</td>
<td>Clonidine, Tenex, Ritalin</td>
<td>Calm and improve sleep, Decrease hyperactivity &amp; impulsivity</td>
<td>Irritability, Lower blood pressure, Sedation</td>
</tr>
<tr>
<td>Anti-convulsants/Mood stabilizers</td>
<td>Depakote, Dilantin, Keppra, Phenobarbitol, Tegretol, Trileptal</td>
<td>Calm behavior, Lessen mood swings, outbursts</td>
<td>Affects kidney function, <strong>Vision impairments such as rapid eye movements</strong></td>
</tr>
<tr>
<td>Norepinephrine re-uptake inhibitor</td>
<td>Strattera</td>
<td>Reduces inattention, hyperactivity &amp; impulsivity</td>
<td>Possibly bipolar disorder</td>
</tr>
</tbody>
</table>


### Table 2. Stimulant Group

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Generic Name</th>
<th>Approved Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adderall (XR)</td>
<td>amphetamine</td>
<td>3 and older</td>
</tr>
<tr>
<td>Concerta</td>
<td>methylphenidate (long acting)</td>
<td>6 and older</td>
</tr>
<tr>
<td>Daytrana</td>
<td>methylphenidate patch</td>
<td>6 and older</td>
</tr>
<tr>
<td>Desoxyn</td>
<td>methamphetamine hydrochloride</td>
<td>6 and older</td>
</tr>
<tr>
<td>Dextedrine</td>
<td>dextroamphetamine</td>
<td>3 and older</td>
</tr>
<tr>
<td>Dextrostat</td>
<td>dextroamphetamine</td>
<td>3 and older</td>
</tr>
<tr>
<td>Focalin (XR)</td>
<td>dexamethylphenidate</td>
<td>6 and older</td>
</tr>
<tr>
<td>Metadate ER</td>
<td>methylphenidate (extended release)</td>
<td>6 and older</td>
</tr>
<tr>
<td>Metadate CD</td>
<td>methylphenidate (extended release)</td>
<td>6 and older</td>
</tr>
<tr>
<td>Methylin</td>
<td>methylphenidate (oral solution and chewable tablets)</td>
<td>6 and older</td>
</tr>
<tr>
<td>Ritalin</td>
<td>methylphenidate</td>
<td>6 and older</td>
</tr>
<tr>
<td>Ritalin SR</td>
<td>methylphenidate (extended release)</td>
<td>6 and older</td>
</tr>
<tr>
<td>Ritalin LA</td>
<td>methylphenidate (long acting)</td>
<td>6 and older</td>
</tr>
<tr>
<td>Strattera</td>
<td>atomoxetine</td>
<td>6 and older</td>
</tr>
<tr>
<td>Vyvanse</td>
<td>lisdexamfetamine dimesylate</td>
<td>6 and older</td>
</tr>
</tbody>
</table>

*Adapted from http://www.nimh.nih.gov/health/publications/attention-deficit-hyperactivity-disorder/complete-index.shtml*
valium (diazepam).24 These medications are used alone or in combination to control seizures in about 70% of patients. Higher rates of epilepsy have long been reported in patients with ASD. Prevalence estimates vary from as little as 5% to as much as 46%.25,26 One of the best-known associations with central nervous system dysfunction is the high risk of epilepsy. It has been reported to occur in one third of the individuals with ASD. Autism spectrum disorder is also increased in epilepsy populations, with as high as 32% meeting diagnostic criteria.

Treatement of children with ASD and epilepsy is guided by the principles of treating childhood epilepsy. Anti-epileptic drugs (AEDs) are chosen based on seizure type, and clinicians strive for maximum seizure control with minimum side effects. The practicalities of certain treatment choices are very important in ASD. Factors such as available formulations (liquid vs. tablets vs. capsules), dosing schedules, need for blood monitoring, and, most importantly, behavioral side effects must be considered. It is important to note that treating epilepsy does not usually have a major impact on the ASD symptomatology. Some children may show improvement in cognition, communication, or behavior, but the ASD diagnosis does not change.26

Risperdal falls into the category of typical neuroleptic medication. Risperidone is used in the treatment of irritability and mood instability associated with autism, including symptoms of aggression, deliberate self-injury, and temper tantrums in children ages five to 16. Currently, risperidone is the only medication that has specific FDA approval to treat individuals with ASD.27 Other drugs prescribed for the treatment of ASD symptoms fall into the “off label” category. Although using antidepressants to treat ADHD and ASD is off label, clinically it is commonly practiced.

Most of the psychotropic medications prescribed are FDA approved for some conditions and some ages, but may not be approved specifically for ASD. Antidepressant medications include SSRIs and have been the most commonly prescribed medications in ASD. Zoloft (fluoxetine), Paxil (paroxetine), and Celsa (citalopram) are effective in managing compulsions, stereotypes, and self-injurious behavior.28 Dopamine blockers, considered atypical antipsychotics, including Clozaril (clozapine), Risperdal, Zyprexa (olanzapine), Seroquel (quetiapine), and Geodon (ziprasidone) have been observed to alleviate symptoms of hyperactivity, stereotypical behaviors, aggression, and self-injury.17

The most commonly used category of medication to treat ADHD is the stimulant group. The mechanism of action is to stimulate the central nervous system, thereby allowing concentrated focus of attention. Stimulant medications come in different forms, such as pill, capsule, liquid, or skin patch. Some medications come in short-acting, long-acting, or extended release varieties. Table 2 illustrates the medication use for ADHD by trade name and the approved age for treatment.11 Of the medications listed, Concerta, Adderall XR, Vyvanse, and Focalin XR were among the top two hundred products in the market by sales for 2009.28

Nutritional alternatives to FDA approved medication need further investigation to document their role in assisting with management of undesired behaviors. A study to compare vitamins and minerals versus standard medication management showed there were some advantages to treatment with micronutrients, including lower activity level, less social withdrawal, less anger, better spontaneity with the examiner, less irritability, lower intensity, markedly fewer adverse events, and less weight gain. Advantages of medication management were insurance coverage, fewer pills, and less frequent dosing.29

Complementary and alternative medical treatments are often used by families. The popularity of these treatments is in part attributed to the chronicity of symptoms of ASD and the absence of effective medical treatments. Popular biological based treatments include supplements, specialized diets, immune therapies, gastrointestinal treatments, chelation, and withholding immunizations. Other non-biological treatments include manipulative and body-based treatments like craniosacral manipulation, auditory integration, and mind- and body-based therapies like yoga. So far, few studies have addressed safety and effectiveness of most of these treatments. Practitioners should support families as they assess the effectiveness, risks, and costs of treatments and assist in monitoring potential side effects.30,31

Summary

Medications to control unwanted behaviors are clinically prevalent. These medicines have positive intended effects and negative unintended effects. The primary care optometrist must be aware of the interactions of these pharmaceutical agents with accommodation, convergence, refractive shifts, and diplopia. Blurred vision, asthenopia, light sensitivity, and poor depth perception may be reported as both a symptom of the disorder and a side effect of the medication. Astute clinical judgments must be made in dealing with these challenges. Communication with other members of the treatment team will maximize desired outcomes and allow concurrent progress as the management process continues.

References


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Wold SAFE Fund
2012 COVD Annual Meeting Student & Resident Travel Grants

The College of Optometrists in Vision Development Annual Meeting Travel Grant is offered to encourage and support optometry student and resident participation at the meeting. The grants are provided through the Wold SAFE Fund.

COVD members donate to this fund to support student attendance at the meeting. The number and amount of the grants given are based on monies available in the fund each year. This year, thanks to our donors and a $7,000 grant from The Vision Care Institute, LLC, up to eighty-nine $200 grants are available for students and residents.

To be eligible to receive a grant, an optometry student or resident must:

• Be a COVD member (if not already a member, join for free)
• Be enrolled in an optometry degree (OD) program at a school or college of optometry.
• Submit an application and current copy of your CV. Be sure to include any posters or papers you are presenting at the 2012 Annual Meeting.
• After your application is received, you will be given the title of an article to summarize.

Grant recipients will be selected based on a review of their CV and article summary.

The 2012 COVD Annual Meeting is October 16-20, in Fort Worth, Texas. Deadline for submission of applications is 11:59 pm on July 26, 2012. You will be given the title of an article to summarize on or before August 2, 2012. The article summary and submission of your CV is due 11:59 pm on August 23, 2012. Decisions will be made on or before September 4, 2012.

Applications are available on the COVD website or by emailing info@covd.org.