Pharmacotherapeutics of Tourette Syndrome and Stereotypies in Autism

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Tourette syndrome (TS) and stereotypy in autism spectrum disorders (ASDs) are 2 common movement disorders in childhood. The objective of this review was to summarize randomized controlled trials published over the past 5 years as an update of the current pharmacotherapeutic options for the treatment of tics, TS, and motor stereotypies in children with ASD. We searched MEDLINE (2005-May 2010) for randomized controlled trials of medications used for the treatment of these disorders. For the treatment of tics in TS, 2 trials suggest that levetiracetam is not effective, whereas 1 trial found that topiramate was effective. Single clinical trials of metoclopramide, atomoxetine, and ondansetron were of limited quality, preventing conclusions to be made regarding the usefulness of these treatments for tic disorders. For the treatment of stereotypy in children with ASD, risperidone has been shown in both a Cochrane review in 2006 and 2 subsequent randomized control trials to be effective. The addition of pentoxifylline to risperidone may have added benefit. Haloperidol did not improve stereotypy and was poorly tolerated. There is good evidence that aripiprazole is effective in the treatment of sterotypies in children with ASD. A large randomized trial of citalopram did not show any improvement in stereotypy. Single trials of levetiracetam, guanfacine, and atomoxetine suggest they are not useful in the reduction of stereotypy in children with ASD.

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autism spectrum disorders (ASD). Motor stereotypies are repetitive and rhythmic movements that have a predictable pattern and location, seem purposeful but serve no obvious function, tend to be prolonged, and can be suppressed. Common examples include movements such as arm flapping, hand waving, head nodding, and body rocking.

The underlying pathophysiology of stereotypies is unknown, and hypotheses range from psychological to neurobiological mechanisms. A similar stereotyped behavior known as punding can be seen in patients with Parkinson disease receiving excessive dopaminergic replacement therapy. In punding, it has been suggested that combined activation of both dopamine and N-methyl-D-aspartic acid receptors is required. Antipsychotic medications have been efficacious in reducing the frequency of stereotypy in autistic children, suggesting similar mechanisms.

The purpose of this review was to summarize RCTs published over the past 5 years as an update of the current pharmacotherapeutic options for the treatment of tics, TS, and motor stereotypies in children with ASD. We chose to focus on tic disorders and motor stereotypies because these are the most common movement disorders encountered in clinical practice in child neurology.

Search Methods and Criteria

We searched MEDLINE (2005-May 2010) for clinical trials of medications used for the treatment of tics, TS, and motor stereotypy in children with ASD. Randomized, double-blind, controlled trials of any pharmacologic treatment for these disorders were included. Only trials that included children were examined. Trials for symptoms of autism that did not assess the effect on motor stereotypies were excluded. Both parallel group and crossover study designs were included.

Data Collection and Analysis

Articles meeting the search criteria were discussed between the 2 authors before dismissal or consideration for this review based on fulfillment of inclusion criteria. Data were abstracted independently by 1 author onto standardized forms. Levels of quality were assigned to RCTs using criteria (Table 1) based on guidelines from the US Preventive Services Task Force.

<table>
<thead>
<tr>
<th>Levels of Quality</th>
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<td>Good</td>
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<td>Comparable groups assembled</td>
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<td>Follow-up at least 80% (80% contribute at least one postbaseline efficacy measurement)</td>
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<td>Interventions are clearly stated</td>
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<td>All important outcomes are considered</td>
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<td>Measurement instruments acceptable and applied equally</td>
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<td>Outcome assessment is blinded</td>
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<td>Appropriate attention to confounders in analysis</td>
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<td>Intention to treat is used</td>
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<td></td>
<td>Concealment: adequate measures to conceal allocation to study groups from those responsible for assessing patients for entry in the trial</td>
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<td>Fair</td>
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<td>Generally comparable groups or some minor problems with follow-up</td>
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<td>Some but not all important confounders are accounted for</td>
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<td>Poor</td>
<td>Studies are graded poor if any of the following fatal flaws exist:</td>
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<td>Unreliable or invalid measurements are used or are not applied equally</td>
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<td>Key confounders are not addressed</td>
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<td>Intention-to-treat analysis is lacking</td>
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<td>Inadequate power of study</td>
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*Based on the current methods of the US Preventive Services Task Force.

Results

2005 to 2010

Pharmaceutical Treatment of Tics

Six RCTs for the treatment of tics were published during the search period of this review. One trial each evaluated levetiracetam, clonidine versus levetiracetam, metoclopramide, atomoxetine, topiramate, and ondansetron. The primary outcomes used in most trials were tic severity as measured using the Yale Global Tic Severity Scale (YGTSS) or the Clinical Global Impression Scales. The YGTSS has a total tic score (TTS) of 50 possible points, which is divided equally into motor and vocal tics. The YGTSS also has an impairment score of 50 points. The impairment and TTS are added together to give a total possible score of 100. The Clinical Global Impression Scales (CGI) for severity (CGI-S) and improvement (CGI-I) are used to assess both the severity of illness and clinical improvement by comparing the conditions of the person standardized against other people with the same diagnosis or in the same individuals before and after therapy.

Levetiracetam

Smith-Hicks et al studied the effectiveness of levetiracetam for the treatment of moderate to severe tics. They designed a fair-quality double-blind, randomized, placebo-controlled, crossover trial involving 22 patients. Subjects were randomized to 28 days of levetiracetam or placebo given twice daily and crossed over to the alternate treatment after a tapering and washout period of 15 days. Standardized outcome scales used included the YGTSS and CGI-I.

Twenty of 22 subjects completed the study at an average daily dose of levetiracetam of 1563 mg/d. None of the pri-
mary outcomes showed a significant treatment effect. No evidence of a carryover effect was observed. Side effects reported with levetiracetam included irritability, hypokinesias, insomnia, tiredness, sadness, verbal aggression, anxiety, reduced school participation, and headache. Placebo complaints included headache, irritability, aggression, low frustration tolerance, insomnia, tiredness, sadness, worry, hypokinesias, anxiety, and dry mouth.

This study suggests that levetiracetam is not more beneficial than placebo in suppressing tics. Limitations of the study include a short treatment protocol of 4 weeks that may have missed some responders as well as a very brief washout period between treatment arms.

Hedderick et al\textsuperscript{10} compared the efficacy of clonidine and levetiracetam in the treatment of tics. Twelve subjects with moderate to severe tics were enrolled in a 15-week randomized, double-blind, flexible-dose crossover protocol. After a baseline visit, there was a 1-week placebo “run-in” treatment period to exclude high placebo responders. Levetiracetam dosing was increased by 5 to 10 mg/kg/d weekly to a maximum of 50 mg/kg/d (or 2500 mg/d) as needed for tic suppression. A 2-week washout period was implemented between each of the 6-week treatment phases. Ten subjects completed the study.

The baseline to posttreatment change in TTS of the YGTSS did not improve significantly in the levetiracetam group versus the clonidine group (22.7 vs 23.6, \( P = .655 \)). There was no significant difference in the TTS related to drug order or carryover. Secondary outcomes measuring neuropsychiatric comorbidities at baseline and posttreatment showed no improvement with levetiracetam. Side effects most commonly reported with levetiracetam were irritability and anxiety.

Initial clonidine dosing was 0.05 mg twice daily and increased as needed for tic suppression by 0.05 to 0.1 mg/wk to a maximum dose of 0.4 mg/d. With clonidine, the mean TTS improved 3.4 points from baseline to posttreatment (\( P = .013 \)) with an effect size of 0.57. The secondary outcomes (mean YGTSS score and CGI scale) did not show significant improvement with clonidine. The most commonly reported side effect for clonidine was sedation.

This crossover study was of poor quality because an intention-to-treat analysis was lacking. Nevertheless, the study results suggest that treatment with clonidine but not levetiracetam resulted in a small reduction in TTS, with an effect size of 0.57. As with any crossover study, it remains unclear whether the lasting effects of previously dosed medications, if any, may have long-term consequences that can affect study results. In summary, 2 RCTs of fair and poor quality do not support the use of levetiracetam for the treatment of tics.

**Metoclopramide**

Nicolson et al\textsuperscript{11} studied metoclopramide for the treatment of children with tic disorders. Twenty-seven patients were enrolled in an 8-week, double-blind, randomized, placebo-controlled trial of metoclopramide after a 2-week washout period of previous medications. Metoclopramide was started at 5 mg daily and titrated every 3 days to a maximum dose of 40 mg daily as required (mean dose, 32.9 ± 5.1 mg). Tics were rated every 2 weeks along with adverse events. Assessment for comorbid neuropsychiatric disease was made at baseline and every 2 weeks via the Yale Brown Obsessive Compulsive Scale and the Conners Parent Rating Scale-Revised. Twenty-four of 27 subjects completed the study. One subject on metoclopramide withdrew because of increased crying, and 2 subjects on placebo withdrew because of increased tic severity.

After 8 weeks of treatment, subjects receiving metoclopramide showed a 39% reduction in their TTS on the YGTSS, whereas placebo subjects only experienced a 13% reduction (\( P = .001 \)). There was no significant difference on the Yale Brown Obsessive Compulsive Scale or Conners Parent Rating Scale-Revised.

The most frequently reported adverse events in the metoclopramide group were increased appetite and sedation. No subjects showed any evidence of extrapyramidal symptoms or dyskinesias. There were no significant group differences in any cardiac conduction parameters or liver function tests. One subject taking metoclopramide had a 30-fold increase in prolactin that resolved with medication discontinuation at the end of the trial.

Overall, this trial was of poor quality. The process of randomization is not stated in the methods, and an intention-to-treat analysis was not conducted. A key confounder between the groups was the number of patients who had previously received medical therapy for their tics. It is uncertain whether the 2-week washout period was adequate and if there were any lingering effects of prestudy medications that could compromise study results. As with many other studies, small sample sizes and brief duration were also limiting factors.

**Atomoxetine**

Spencer et al\textsuperscript{12} examined the changes in severity of tics and attention-deficit hyperactivity disorder (ADHD) during atomoxetine treatment in children with ADHD and TS.\textsuperscript{12} This article provided a post hoc subgroup analysis of data from an 18-week parallel group, placebo-controlled, double-blind study. Subjects met DSM-IV criteria for ADHD and concur- rent TS. Patients were randomly assigned to double-blind treatment with either placebo or atomoxetine (0.5–1.5 mg/kg/d) for 18 weeks. Subjects were evaluated using the YGTSS, CGI, and Tic Symptom Self-Report scales. A total of 148 were assigned to treatment, and 145 provided data for the primary efficacy analysis. The baseline characteristics between treatment groups were not significantly different.

On the primary measure of efficacy (ie, the YGTSS total score), the atomoxetine treatment group showed a significantly greater decrease from baseline in tic severity relative to placebo (\( P = .027 \)), and this was associated with a small to moderate effect size (ES = 0.40). This difference was reached in the atomoxetine group by week 1 and continued to become highly significant (\( P < .001 \)) at the endpoint of the study. Scores on the Tic System Self-Report showed improvement in tic severity in both groups with atomoxetine showing a larger but not significant (\( P = .134 \)) improvement relative to placebo despite a small-to-moderate effect size (ES = 0.37). On the CGI scale, improvement in the atomoxetine...
group at endpoint was significant compared with placebo and was associated with a moderate to large effect size (ES = 0.63). Adverse events reported in the atomoxetine group included headache (21.3%), vomiting (16.4%), decreased appetite, and nausea (18%). Treatment group differences were significant in the decreased appetite and nausea categories.

The parent study was initially designed as a noninferiority analysis with the hypothesis that atomoxetine causes no greater worsening of tic symptoms than placebo. The most noteworthy limitation in this study is the post hoc subgroup analysis with the hypothesis that atomoxetine causes no significant in the decreased appetite and nausea categories. There is a potential for type I errors (false-positives) because of multiple subgroup analyses, and the authors do not discuss how this issue was addressed. In addition, power calculations for the study were made based on the overall subject sample and not for the subsample analyzed. Finally, bias may have been introduced with the measurement of ADHD symptom improvement. A clear improvement in ADHD symptoms would likely have been appreciable to parents and investigators and may have led to potential unblinding of the randomization. Overall, however, this is a randomized control trial of fair quality.

**Topiramate**

Jankovic et al\(^1\) investigated the effects of topiramate on tics. They designed a multicenter, randomized, double-blind, placebo-controlled parallel group study. Twenty-nine subjects with TS ranging from ages 7 to 65 years (mean age, 16.5 years) were enrolled. Topiramate was increased from a minimum of 50 mg/d over a 6-week period up to 200 mg/d as needed followed by a 4-week maintenance phase, with a subsequent 12-day tapering phase. Efficacy analyses were based on an intention-to-treat analysis that included all subjects who had taken at least 1 dose of study medication and had at least 1 postbaseline efficacy evaluation. The last observation carried forward method was used to analyze data in the case of those subjects with early withdrawal. Twenty out of the 29 patients completed the double-blind phase of the study. The primary outcome was the TTS, which improved by 14.29 points from baseline to visit 5 (day 70) with topiramate (mean dose, 118 mg) compared with a 5-point change in the placebo group (\(P = .0259\)).

There were no differences in adverse events observed between the 2 treatment groups. Most commonly reported adverse effects included headache, abdominal pain and diarrhea, and drowsiness. One child in the topiramate group reported cognitive slowing, and one had a kidney stone. There was also a mean weight loss of 2.1 kg from baseline to endpoint in the topiramate group.

Overall, this was a fair quality trial with promising data on the use of topiramate in the treatment of TS. This may be an especially useful treatment option in children in whom weight gain may pose a significant health problem. Limitations include the inclusion of adults in this study, which challenges the applicability to children alone. Some of the commonly observed side-effects of topiramate such as somnolence, cognitive slowing, and weight loss may not have been evident because of the short trial duration of 70 days.

Further evidence in the form of RCTs is required to increase support for the efficacy of topiramate for the treatment of tics.

**Ondansetron**

Toren et al\(^1\) evaluated the efficacy of ondansetron in alleviating tics in a placebo-controlled trial of 30 subjects (mean age, 22 years; 15 subjects younger than 18 years). In this poor quality trial, patients who had previously failed treatment with haloperidol were randomized to ondansetron (up to 24 mg/d) or placebo for a period of 3 weeks. At baseline, patients randomized to ondansetron had significantly lower tic severity scores than those randomized to placebo as measured using the YGTSS and the Tourette Syndrome Global Scale. Analysis controlling for baseline differences in severity found a significant improvement in tics in the ondansetron-treated subjects on the Tourette Syndrome Global Scale but not the YGTSS. Overall, because of the poor quality of the study, it is difficult to draw any conclusions about the efficacy of ondansetron as a treatment for tics.

**2005 to 2010 Pharmaceutical Treatment of Stereotypy in Autism**

There were 10 trials and 1 systematic review published during the search period of this review that assessed motor stereotypies in children with autism. These publications included evaluations of risperidone, aripiprazole, haloperidol, pentoxyfilline, omega-3 fatty acids, citalopram, atomoxetine, levetiracetam, and guanfacine.

**Rating Scales**

Various rating scales were used in the 13 studies to describe the severity of motor stereotypies. The following scales were used:

1. The Nisonger-Child Behaviour Rating Form consists of 60 items subdivided among 6 scales: conduct problem, insecure/anxious, hyperactive, self injury/stereotypic, self isolated/antisocial, and overly sensitive.

2. The Ritvo-Freeman Real Life Rating Scale (RF-RLRS) is an in vivo observational measure for a variety of symptoms of autism. It is comprised of 5 subscales. For the purposes of this review on stereotypy, we report statistically significant changes in “subscale I—sensory motor (rocking, flapping).”

3. Aberrant behavior checklist (ABC) consists of 58 items subdivided among 5 scales: irritability, lethargy and social withdrawal, stereotypic behavior, hyperactivity, and inappropriate speech.


5. Repetitive behavior scale-revised (RBS-R) is a parent-rated scale comprising 43 items across 6 subscales assessing repetitive behaviors.

**Risperidone**

A systematic review of risperidone for ASD was published in the Cochrane Database of Systematic Reviews in 2006. Three RCTs were included in this review. The ABC subscale
on stereotypic behavior was examined in 2 of the studies, including 178 subjects. Meta-analysis of these studies found that subjects treated with risperidone had lower stereotypy subscale scores than those treated with placebo, with a mean difference of −1.71 points (95% confidence interval, −2.97 to −0.45).

Pandina et al\textsuperscript{17} performed a subgroup analysis of 55 children enrolled in an 8-week, randomized, double-blind, placebo-controlled trial of risperidone for pervasive developmental disorders (PDD). Subjects were randomized to risperidone (n = 27) or placebo (n = 28). The ABC subscale for stereotypic behavior and the Nisonger-Child Behaviour Rating Form Self-Injury/Stereotypic Subscale showed no significant change from baseline to endpoint (P = .053 and P = .183) although the ABC subscale result very closely approached statistical significance. Adverse effects were reported in 100% of the risperidone group and 71% of the placebo group. The most common adverse effect in the risperidone group was somnolence. Although 2 patients on risperidone gained weight, this was not deemed statistically significant. The mean ESRS scores with respect to extrapyramidal side effects were low throughout the trial. This trial was of fair quality and that data suggested that risperidone may be effective in reducing stereotypy in children with autistic disorder; the result was very close (P = .053) but not statistically significant. Also of concern was the high percentage of candidates with reports of somnolence. Limitations of this study include the small sample size and brief study duration. Also, data were analyzed as a subgroup analysis of a larger study initially aimed at testing the hypothesis that risperidone would significantly reduce disruptive behavior in children with PDD.

Miral et al\textsuperscript{18} conducted a study on the safety, efficacy, and tolerability of risperidone compared with haloperidol in the treatment of autistic disorder. The 12-week trial enrolled 30 subjects. Twenty-eight of the 30 subjects completed the study. The mean daily dosages of both haloperidol and risperidone were 2.6 mg. Results indicated that the risperidone group, but not the haloperidol group, had a statistically significant change from baseline to endpoint in the sensory motor subscale for stereotypy of the RF-RLRS. There was no significant change from baseline to endpoint in the ESRS scores in the risperidone group; however, the haloperidol group showed a significant increase on this measure, indicating an increased incidence of extrapyramidal symptom complaints in this group. There were no significant weight gain differences between the 2 groups at baseline or the 12-week endpoint of the study. Both groups had significant increases in weight and prolactin at endpoint compared with baseline measurements. However, there was a larger increase in prolactin in the risperidone group compared with the haloperidol group (P = .0128).

Overall, the Miral et al study\textsuperscript{18} is a randomized, double-blind, placebo-controlled trial of fair quality. This study found that risperidone was superior to haloperidol on the RF-RLRS sensory motor subscale in significantly reducing stereotypic behaviors in the population studied. Risperidone also had a more tolerable side effect profile and notably fewer reports of extrapyramidal symptoms.

**Pentoxifylline**

Pentoxifylline is a methylated xanthine derivative that increases red blood cell deformability, reduces blood viscosity, and decreases the potential for platelet aggregation and thrombus formation. This medication is indicated for the treatment of intermittent claudication on the basis of chronic occlusive arterial disease of the limbs. Akhondzadeh et al\textsuperscript{19} investigated the effects of the immune-modifying agent pentoxifylline as an adjunctive treatment with risperidone in the management of autism in children. This study was a 10-week, parallel group, randomized, placebo-controlled trial. Forty patients with the DSM-IV-TR diagnosis of autistic disorder were randomized to pentoxifylline + risperidone or placebo + risperidone, and all patients completed the trial. The dose of risperidone was increased up to 2 mg/d for children weighing 10 to 40 kg and 3 mg/d for children weighing above 40 kg. The dose of pentoxifylline was titrated up to 400 mg/d for children between 10 and 40 kg and up to 600 mg for children weighing over 40 kg.

The data showed a significant treatment difference between pentoxifylline + risperidone versus placebo + risperidone in the ABC stereotypic behavior subscale (P ≤ .0001) by the effect of groups-by-time interaction. Commonly reported adverse events in the pentoxifylline group included drowsiness, increased appetite, and weight gain, but these results were not significantly different from the placebo group. This trial was of fair quality. The results of this study suggest that the combination of atypical antipsychotic medications, such as risperidone along with pentoxifylline, may have synergistic effects in the treatment of stereotypy in children with autism. Limitations of this study include the small sample size, short duration of the study, and the lack of immune response measurements before and after the intervention. In addition, the evaluations of the therapeutic effects of pentoxifylline without an additional neuroleptic drug were not permitted by the study country’s national ethics committee. Further RCTs with pentoxifylline in children with autism need to be performed, especially to study the safety profiles of this medication from an immune system perspective.

**Aripiprazole**

There are 2 RCTs of aripiprazole in children with autistic disorder of similar design.\textsuperscript{20,21} The Owen trial\textsuperscript{20} included 98 children and was rated “good” in quality, whereas the Marcus trial\textsuperscript{21} included 218 children and was rated “fair.” Both trials compared aripiprazole with placebo for a period of 8 weeks for the treatment of irritability as measured using the ABC. Dosages of aripiprazole ranged from 2 to 15 mg/d. The effect on aripiprazole on stereotypies was included as a secondary outcome. Meta-analysis of the results of the 2 studies for the ABC Stereotypic Behavior Subscale revealed a mean difference of −2.66 (95% confidence interval, −3.55 to −1.77, P < .00001) favoring aripiprazole over placebo. Side effects that occurred more commonly in aripiprazole-treated patients included weight gain, sedation, drooling, and tremor. The results of these 2 studies support the use of aripiprazole...
in decreasing the severity of stereotypies in children with autism.

**Omega-3 Fatty Acids**

Ammerger et al.22 conducted a 6-week pilot trial to look at the effects of 1.5 g/d of omega-3 fatty acids (0.84 g/d of eicosapentaenoic acid, 0.7 g per d of docosahexaenoic acid supplementation) in 13 children with autistic disorder. Results of the ABC subscales showed no significant difference between treatment groups in the stereotypic behavior subscale of the ABC. This trial was of fair quality. Limitations include the small number of subjects, the short intervention period, lack of laboratory testing, and side effect surveillance.

**Citalopram**

King et al.23 examined the efficacy and safety of citalopram for repetitive behavior in children with autistic disorder. This study was a randomized, double-blind, placebo-controlled study involving 149 subjects (citalopram, n = 73; placebo, n = 76) with autistic disorder. Most subjects completed the 12-week trial, and results were analyzed on an intention-to-treat principle. All participants began with 2.5 mg/d, and the maximum dosage was 20 mg/d. Results showed no significant difference in stereotypic behavior between groups in the RBS-R stereotyped behavior subscale (P = .75) or the ABC-Community Version stereotypy score (P = .57). The most commonly reported side effects in the citalopram group included increased energy level, impulsiveness, decreased concentration, hyperactivity, stereotypy, insomnia, and diarrhea. The King trial is of good quality. Its results, however, do not support the use of citalopram for the treatment of repetitive behavior in children and adolescents with ASD. In addition, the significant side effects of impulsivity and hyperactivity with decreased attention and concentration suggest that this medication should only be tried with caution in children with comorbid ADHD.

**Atomoxetine**

Arnold et al.24 explored the efficacy and safety of atomoxetine for ADHD symptoms in a crossover study of 16 children with ASD. Each medication was trialed over 6 weeks with a 1-week washout period between treatments. The mean atomoxetine dose was 44.2 mg/d. Study data revealed no significant change in the atomoxetine group on the ABC stereotypic behavior subscale (P = .08) or the RBS-R stereotypy subscale (P = .11). The most commonly reported adverse effects in the atomoxetine group were upset stomach, nausea/vomiting, tiredness/fatigue, and racing heart. This trial was of fair quality. A limitation of this study includes the use of a crossover design with a short washout period and a medication with known considerable pharmacodynamic properties. Other drawbacks include the small sample size and adherence of concomitant psychotropic medication.

**Levetiracetam**

Wasserman et al.25 conducted a study to determine the safety and efficacy of levetiracetam in the treatment of 20 children with autism in a 10-week trial. Levetiracetam was started at 125 mg/d and titrated to 20 to 30 mg/kg/d based on treatment response and tolerability. Seventeen patients completed the trial. There was no significant difference in the ABC stereotypic behavior subscale for the levetiracetam group as reported by parents (P = .967) or teachers (P = .688). Adverse events most commonly reported included aggression, agitation, hyperactivity, and impulsivity in the levetiracetam group. This study was of fair quality, and the data suggest that levetiracetam is not effective in treating stereotypy in children with autism. A notable limitation of the study is its small sample size.

**Guanfacine**

Handen et al.26 conducted a crossover trial of guanfacine in 11 children with autism and/or intellectual disabilities. The 6-week trial involved a maximum dose of 3 mg/d of guanfacine titrated over a 19-day period. After remaining on the highest dose for 8 days, subjects underwent a 6-day washout phase followed by an 8-day placebo phase. The alternate possible drug order began with the placebo phase followed by the guanfacine of similar durations. The study indicated no significant change within the groups with respect to the stereotypic behavior subscale of the parent ABC (P = .484) or the teacher ABC (P = .348). The most commonly reported side effects in the guanfacine group included drowsiness and lethargy. This was a trial of fair quality. Its results suggest that guanfacine is not useful in the treatment of stereotypy in children with autism and/or intellectual disabilities. Limitations of the study include the small study size, short duration of treatment, and the diversity of the patient population participating in the trial.

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**Table 2** Summary of Clinical Randomized Controlled Studies

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<th>Treatment of tics and TS</th>
<th>Levetiracetam is not effective in the treatment of tics in TS.5,10</th>
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<tr>
<td>Topiramate was effective in the treatment of tics14*</td>
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<tr>
<td>Single clinical trials of metoclopramide,11 atomoxetine,12 and ondansetron15 were of limited quality†</td>
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<tr>
<td>Treatment of stereotypy in children with ASD</td>
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<tr>
<td>Risperidone is effective in the treatment of stereotypy in children with ASD.16-18 The addition of pentoxifyline to risperidone may have added benefit.19</td>
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<td>Haloperidol, studied in comparison to risperidone, did not improve stereotypy in children with autism and was poorly tolerated.18</td>
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<tr>
<td>Aripiprazole is effective in the treatment of stereotypies in children with ASD.20,21</td>
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<tr>
<td>Citalopram in children with autism did not show any improvement in stereotypy.22</td>
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<tr>
<td>Levetiracetam,25 guanfacine,26 and atomoxetine24 each have 1 RCT, suggesting they are not useful in the reduction of stereotypy in children with autism spectrum disorder.</td>
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*The use of topiramate for the treatment of tics may be of special consideration for patients in whom weight gain associated with the use of other medications may pose a significant health risk.
†Firm conclusions could not be made regarding the usefulness of these treatments for tic disorders.
Conclusions

The last five years have produced a promising amount of literature regarding the pharmacotherapy of tics, Tourette syndrome and stereotypy in children with ASD (summarized in Table 2). While some medications hold promise in managing these conditions, further trials confirming their results would provide greater confidence in their effect estimates. In light of recent data confirming the risk of metabolic syndrome in children on atypical antipsychotic medications, it becomes essential that our efforts to treat these movement disorders in children do not result in secondary harm.

References