JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 24, Number 2, 2014

Pp. 78–82
DOI: 10.1089/cap.2013.0099

Body Mass Index Change in Autism Spectrum Disorders: Comparison of Treatment with Risperidone and Aripiprazole

Logan K. Wink, MD,[1] Maureen Early, BS,[2] Tori Schaefer, PhD,[1] Amy Pottenger, BS,[2] Paul Horn, PhD,[1,3] Christopher J. McDougle, MD,[4] and Craig A. Erickson, MD[1]

Abstract

Objective: The purpose of this study was to assess change in body mass index (BMI) and age- and gender-adjusted BMI *Z*-score in subjects ages 2–20 years with autism spectrum disorders (ASD), who were treated longitudinally with risperidone or aripiprazole at a tertiary care ASD clinic.

Method: As part of a larger project involving longitudinal drug treatment data in ASD, detailed demographic and treatment data were collected for 142 subjects ages 2–20 years who had been started on risperidone or aripiprazole for treatment of irritability. Mean age at start of treatment, treatment duration, final Clinical Global Impressions-Improvement Scale score, BMI change per year of treatment, and BMI *Z*-score change per year of treatment (primary outcome measure) were calculated for each drug treatment group. Group means were compared using *t* tests and Wilcoxon rank sum tests.

Results: There was a statistically significant BMI and BMI *Z*-score increase in the risperidone and aripiprazole treatment groups individually. No statistically significant difference between the two treatment groups was noted in mean BMI change per year of treatment or BMI *Z*-score change per year of treatment.

Conclusions: In our review of long-term naturalistic treatment of irritability using risperidone versus aripiprazole in persons with ASD, a significant increase in both BMI and age- and gender-adjusted BMI *Z*-score was noted for each treatment group. No significant difference in BMI or BMI *Z*-score change was noted when the two treatment groups were compared. We conclude that in our patient population at a tertiary care ASD clinic, the effects of risperidone and aripiprazole on body weight gain in naturalistic long-term treatment are no different.

Introduction

Since Kanner's original description of autistic disorder in 1943 (Kanner 1943), interfering behavioral symptoms associated with autism spectrum disorders (ASD) have been a major focus of pharmacotherapy research. Irritability (aggression, self-injury, and severe tantrums) is a frequent and disruptive behavioral symptom cluster in persons with ASD, often limiting access to educational and community programming and causing significant parent and caregiver stress (McDougle et al. 2008). To date, treatment of ASD-associated irritability with atypical antipsychotics has proven successful (Wink et al. 2010). However, use of risperidone or aripiprazole, the two United States Food and Drug Administration (FDA)-approved atypical antipsychotics for treatment of irritability in youth with autistic disorder, is at times limited by significant adverse effects such as weight gain. Extensive research has been conducted on the efficacy, safety, and tolerability of risperidone and aripiprazole both in short- and longer-term use in ASD. Despite the frequency of weight gain noted with use of each drug for treating irritability in persons with ASD, comparison of body mass index (BMI) and age- and gender-adjusted BMI *Z*-score change associated with risperidone versus aripiprazole has not been undertaken (Maayan and Correll 2011).

The efficacy of risperidone, a dopamine type 2 (D2) and serotonin type 2A (5-HT2A) receptor antagonist, for the treatment of irritability in youth with autism is supported by multiple placebo-controlled studies (McCracken et al. 2002; Erickson et al. 2007). In an 8-week double-blind, placebo-controlled trial of 101 children and adolescents with autism (ages 5–17 years), the Research Units on Pediatric Psychopharmacology (RUPP) Autism Network demonstrated a significant risperidone effect marked by a 69% drug treatment response versus a 12% response in those receiving placebo (McCracken et al. 2002). In this report, mean weight gain was 2.7 kg for the treatment group compared with 0.8 kg for the placebo group ($p < 0.001$) (McCracken et al. 2002). The work of the RUPP Autism Network was replicated when Shea et al. (2004)

[1]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.
[2]Indiana University School of Medicine, Indianapolis, Indiana.
[3]University of Cincinnati, Cincinnati, Ohio. Dr. McDougle is affiliated with
[4]Harvard Medical School and the Lurie Center for Autism, Lexington, Massachusetts.

demonstrated in an 8 week double-blind, placebo-controlled trial of 79 children (ages 5–12 years) with ASD that risperidone treatment was associated with significant improvement compared with placebo on several outcome measures (Shea et al. 2004). Significant weight gain was again seen in this study, with mean weight gain of 2.7 kg for the risperidone group and 1.0 kg for the placebo group ($p \leq 0.001$) (Shea et al. 2004). Additionally, nearly every placebo controlled trial of risperidone for treatment of pediatric behavior, mood, and psychotic disorders has demonstrated significant weight gain over placebo, suggesting that weight effects of risperidone are not associated solely with ASD diagnosis (Maayan and Correll 2011).

Aripiprazole, a D2 and 5-HT1A receptor partial agonist and 5-HT2A receptor antagonist (Potkin et al. 2003), has been shown to be effective in two double-blind, placebo-controlled studies, as well as in several open-label studies in the treatment of irritability in youth with autistic disorder (Marcus et al. 2009; Owen et al. 2009). In an 8 week double-blind, placebo-controlled study involving 98 youth with autistic disorder (ages 6–17 years), Owen et al. (2009) reported a significant effect of aripiprazole on irritability, marked by a 52.2% drug treatment response rate compared with a 14.3% placebo response rate (Owen et al. 2009). At 8 weeks, the increase in mean BMI was 0.7 kg/m^2 for the aripiprazole group and 0.1 kg/m^2 for the placebo group ($p < 0.05$) (Owen et al. 2009). Also in 2009, Marcus et al. reported on a fixed dose (15 mg/day; 10 mg/day; 5 mg/day vs. placebo) four arm 8 week double-blind, placebo-controlled study of aripiprazole targeting irritability in 218 children and adolescents with autism (ages 6–17 years). Treatment response was seen in all three treatment arms compared with placebo ($p < 0.05$ for the 15 mg/day group compared with placebo). Mean weight gain in this study was 1.5 kg with the 15 mg/day dose, 1.3 kg with the 10 mg/day or 5 mg/day dose, and 0.3 kg with placebo ($p < 0.05$ for each dose of aripiprazole compared to placebo) (Marcus et al. 2009). In a recent systematic review of placebo-controlled antipsychotic studies in youth regardless of diagnosis, De Hert et al. demonstrated that aripiprazole was associated with average weight gain of 0.79 kg (CI: 0.54–1.04 kg), suggesting that weight gain with aripiprazole is not solely related to ASD diagnosis (De Hert et al. 2011).

In addition to weight gain noted in controlled short-term ASD studies, longer-term studies of aripiprazole and risperidone in youth with ASD have demonstrated significant weight gain in excess of developmental norms. In a 2004 study of 63 youth with autism receiving risperidone for 6 months, excessive weight gain was shown to occur more rapidly with the initiation of treatment, although the gain continued throughout the period of risperidone use marked by a mean increase in BMI *Z*-score of 0.6 (Martin et al. 2004). In an open-label continuation study of aripiprazole in youth with autistic disorder, those receiving aripiprazole for >9 months ($n = 220$) had a mean increase in BMI *Z*-score of 0.31 (Marcus et al. 2011). Additionally, studies have also demonstrated significant increase in BMI *Z*-score in youth treated longitudinally with atypical antipsychotics compared with controls, regardless of psychiatric diagnosis(de Hoogd et al. 2012).

In this review, we hypothesized that use of either risperidone or aripiprazole would be associated with a significant mean increase in raw BMI and BMI *Z*-scores during treatment. Furthermore, based upon weight change data from other disorders in which risperidone and aripiprazole are FDA-approved (Stroup et al. 2011; Ben Amor 2012; Cohen et al. 2012), data from a large scale treatment study in atypical antipsychotic naive children and adolescents with a variety of psychiatric diagnoses (Correll et al. 2009), and short-term data from autism trials (McCracken et al. 2002; Martin et al. 2004; Shea et al. 2004; Marcus et al. 2011), we hypothesized that risperidone use would be associated with a greater increase in mean raw BMI and BMI *Z*-score per year of treatment compared with aripiprazole.

Method

As part of a larger ongoing comprehensive assessment of medication management in ASD, we analyzed data drawn from individuals with ASD evaluated and treated at the Christian Sarkine Autism Treatment Center (CSATC) from July 2004 through April 2012. From our RedCap medication management database, we identified subjects ages 2–20 years newly started on risperidone or aripiprazole for treatment of irritability. For each subject, data were collected including age, race, gender, ASD diagnostic subtype, presence of intellectual disability, concomitant medication use, duration of risperidone or aripiprazole treatment, end dose of respective medication, Clinical Global Impressions-Improvement (CGI-I) rating at last recorded visit (rating anchored to change in irritability), BMI prior to initiation of treatment with risperidone or aripiprazole, and BMI at last recorded treatment visit. BMI values were transformed into BMI *Z*-scores based on Center for Disease Control growth charts to account for BMI variation in children caused by age, gender, height, and weight relative to a reference distribution (Flegal and Ogden 2011).

ASD diagnosis (autistic disorder, pervasive developmental disorder not otherwise specified [PDD-NOS], or Asperger's disorder) was made by clinicians with expertise in ASD diagnosis (C.A.E., C.J.M.) using diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders,* 4th ed., Text Revision (DSM IV-TR) (American Psychiatric Association 2000). Intellectual disability data collected were based on review of neuropsychological testing and school reports when available, combined with elements of the clinical interview focused on adaptive functioning and cognition. Because of inconsistency in whether degree of intellectual disability (mild, moderate, severe, profound) was specified in the evaluation notes, we limited our intellectual disability data analysis to whether intellectual disability was present or absent. Subjects were excluded from this study if risperidone or aripiprazole use was initiated prior to evaluation at the CSATC, if an individual received multiple antipsychotics at any time during treatment, or if <2 BMI data points were available.

For each treatment group, the mean age at baseline, treatment duration, final CGI-I, BMI change, BMI change per year of treatment, and age- and gender-adjusted BMI *Z*-score change and change per year of treatment was determined. We chose BMI *Z*-score per year of treatment as our primary outcome measure, given that this measure controls for age- and gender-associated BMI differences while also accounting for differences in treatment duration in a naturalistic treatment setting. Group means for all variables were compared using independent sample two tailed *t* tests, as well as Wilcoxon rank sum tests. Potential group differences in race, gender, ASD subtype, presence of intellectual disability, and concomitant drug use (by drug class), were evaluated using Fisher's exact tests. This project was approved by our local institutional review board.

Results

Seventy-two subjects treated with risperidone and 70 treated with aripiprazole met study inclusion criteria. On average, subjects started on aripiprazole were older at baseline (Table 1). Baseline mean BMI *Z*-scores were 0.67 ± 1.44 and 0.64 ± 1.94 for

Table 1. Baseline Subject Characteristics

	Risperidone	*Aripiprazole*	*Comparison*
Male	$n=60$ (83.3%)	$n=56$ (80%)	$p=0.67$[a]
Female	$n=12$ (16.7%)	$n=14$ (20%)	$p=0.67$[a]
Caucasian	$n=56$ (77.8%)	$n=53$ (75.7%)	$p=0.84$[a]
African American	$n=6$ (8.3%)	$n=5$ (7.1%)	$p=1.00$[a]
Hispanic	$n=1$ (1.4%)	$n=1$ (1.4%)	$p=1.00$[a]
Other race/ethnicity	$n=1$ (1.4%)	$n=1$ (1.4%)	$p=1.00$[a]
Autistic disorder	$n=40$ (55.6%)	$n=44$ (62.9%)	$p=0.40$[a]
PDD-NOS	$n=29$ (40.3%)	$n=19$ (27.1%)	$p=0.12$[a]
Asperger's disorder	$n=3$ (4.1%)	$n=7$ (10%)	$p=0.21$[a]
Presence of intellectual disability	$n=34$ (49%)	$n=30$ (44%)	$p=0.61$[a]
Age at initiation	8.41 ± 3.59 years	9.74 ± 3.46 years	$p=0.03$[b]
Baseline BMI	19.05 ± 4.90	20.41 ± 5.53	$p=0.12$[b]
Baseline *Z*-score	0.67 ± 1.44	0.64 ± 1.94	$p=0.93$[b]

[a]Fisher's exact test.
[b]Two tailed *t* test.
Race/ethnicity data missing in risperidone group ($n=7$) and aripiprazole group ($n=10$).
PDD-NOS, pervasive developmental disorder – not otherwise specified; BMI, body mass index.

risperidone and aripiprazole, respectively, indicating a relatively overweight population at treatment initiation. No statistically significant difference in gender, race, ASD diagnostic subtype, or presence of intellectual disability was identified between treatment groups. Concomitant medication use rates defined by drug class were also similar between groups (Table 2). Subjects in the risperidone group had a longer average treatment duration (2.37 ± 2.55 years for risperidone vs. 1.47 ± 1.21 years for aripiprazole [$p=0.01$]) (Table 3). Final drug doses were well within the approved dose range for use in ASD targeting irritability (2.23 ± 1.30 mg/day for risperidone and 11.85 ± 7.23 mg/day for aripiprazole). Final CGI-I scores between groups were similar. As expected, mean raw BMI and calculated BMI *Z*-scores increased with use of both risperidone and aripiprazole (Table 4). No statistically significant difference between the two treatment groups was noted in raw BMI change per year or in our primary outcome measure BMI *Z*-score change per year of treatment (Table 3).

Table 2. Concomitant Medication Use

Concomitant drug/drug class	*Risperidone group (total* n = *72)*	*Aripiprazole group (total* n = *70)*	*Fisher's exact test result (2 by 2 contingency table)*
Selective serotonin reuptake inhibitor	$n=20$ (28%)	$n=21$ (30%)	$p=0.85$
Antiepileptic	$n=5$ (7%)	$n=4$ (6%)	$p=1.00$
Stimulant	$n=15$ (21%)	$n=10$ (14%)	$p=0.38$
Metformin	$n=4$ (6%)	$n=2$ (3%)	$p=0.68$
α 2-agonist	$n=27$ (37%)	$n=22$ (31%)	$p=0.48$
Benzodiazepine	$n=0$ (0%)	$n=2$ (3%)	$p=0.24$
Other medication use not specified above	$n=26$ (36%)	$n=24$ (34%)	$p=0.86$
Free of concomitant medication	$n=19$ (26%)	$n=20$ (29%)	$p=0.85$

Table 3. Treatment Results: Group Comparisons

	Risperidone	*Aripiprazole*	*Two tailed* t *test*
Treatment duration	2.37 ± 2.55 years	1.47 ± 1.21 years	$p=0.01$
Final dose	2.23 ± 1.30 mg/day	11.85 ± 7.23 mg/day	NA
Final CGI-I[a]	3.2 ± 1.2	2.9 ± 1.2	$p=0.32$
BMI change per year of treatment	2.36 ± 3.80	2.05 ± 5.02	$p=0.68$
BMI *Z*-score change per year of treatment	0.53 ± 1.21	0.56 ± 2.21	$p=0.91$

[a]Clinical Global Impressions – Improvement (CGI-I) scale ranges from1 to 7 with 1 = very much improved and 7 = very much worse.
BMI, body mass index.

Further, Wilcoxon rank sum tests were conducted to look for treatment differences for the variables in Tables 3 and 4. These results are not reported because they concur with those of the *t* test provided in the tables.

Based upon our data, we additionally completed a post-hoc analysis to determine how many patients per group would be necessary to detect, with 80% power (actual $\alpha=0.05$), a statistically significant difference in BMI *Z*-score change per year of treatment using a two-sample *t* test, assuming that the variances of the two populations were not equal. Given our results, we would need to conduct a study with 46,308 subjects per treatment group to detect a difference in BMI *Z*-score change per year of treatment when comparing risperidone and aripiprazole use in this population. (The Power and Sample Size module, PASS, from SAS ® Version 9.3 was used for this calculation.)

We also completed a post-hoc robust analysis-of-covariance, ANCOVA, analysis (ROBUSTREG procedure in SAS) to assess the impact of potential covariates on our primary outcome measure of change in BMI *Z* score per year of treatment. A robust approach was used in order to minimize the impact of potential outliers in the data. No potentially significant covariates (age at baseline, race, gender, diagnosis of intellectual disability, concomitant drug use, duration of treatment, baseline BMI/*Z*-score) were identified when analyzing both drug treatment populations combined. When assessing the risperidone and aripiprazole groups individually, no potentially significant covariates were identified for risperidone use. For aripiprazole, a minor finding ($R^2=0.03$) was noted for an interaction between presence of intellectual disability and age where a positive association (slope) was found in persons with intellectual disability and a slightly negative association with

Table 4. Treatment Results: Within-Group BMI Change

Risperidone	*Baseline*	*End-point*	*Two tailed* t *test*
BMI	19.05 ± 4.90	21.37 ± 5.28	$p<0.0001$
BMI *Z*-score	0.67 ± 1.44	0.96 ± 1.30	$p=0.05$
Aripiprazole			
BMI	20.41 ± 5.53	22.51 ± 5.59	$p<0.0001$
BMI *Z*-score	0.64 ± 1.94	1.12 ± 1.07	$p=0.01$

BMI, body mass index.

Z score per year of treatment was noted in persons without intellectual disability. However overall, we conclude that no significant factors gathered in our analysis contributed significantly to BMI *Z*-score change per year of risperidone or aripiprazole treatment.

Discussion

Both short- and longer-term studies of risperidone and aripiprazole use for treatment of irritability in youth with ASD have demonstrated weight gain as a significant adverse effect. However, to date there has been no comparison of the impact on body weight of risperidone versus aripiprazole use in ASD in a long-term naturalistic setting. Our study begins to provide some answers to this question with unanticipated results. The similarity in BMI *Z*-score change with both treatment groups is unexpected, given data from other disorders suggesting that less weight gain is associated with aripiprazole use than with other atypical antipsychotics in both youth and adults (Correll et al. 2009; Stroup et al. 2011; Ben Amor 2012; Cohen et al. 2012; Doey 2012). Weight gain is a primary adverse effect of concern with atypical antipsychotics in ASD. It must be balanced with the degree of interference from behavioral symptoms. We believe this comparison of the two first-line treatments for irritability in children and adolescents with ASD, which occurred in a naturalistic treatment setting, may be useful for clinical decision making.

The findings of this report must be taken in the context of the limitations of the analysis. The results are based on review of longitudinal clinical data, which limits our ability to control for baseline differences such as ASD diagnostic subtype, presence of intellectual disability, and concomitant medication use. Fortunately, these factors may not have impacted the study results, given the lack of group differences, with the exception of age, at baseline (Table 1). The naturalistic design of this study also limits our ability to control for medication starting dose, dosage range, and rapidity of dosage change. The dosages of risperidone and aripiprazole prescribed to the individuals in this project were well within FDA-approved dosage guidelines, but were slightly higher than mean dosages reported in the studies leading to FDA-approval of both medications (risperidone: 2.23 ± 1.30 mg/day in this review vs. 1.8 ± 0.7 mg/day in RUPP 2002 study; aripiprazole: 11.85 ± 7.23 mg/day in this review vs. 8.9 mg/day in Owen 2009 flexible dose trial). It is unclear what impact this may have had on BMI change in our population.

This study is limited to the age range for which *Z* scores are available. In ASD, the weight effects of atypical antipsychotics may differ in youth and adults, particularly given report of no significant risperidone-associated weight gain in placebo-controlled study in adults with ASD (McDougle et al. 1998). Individuals in this study were also above average weight at the time of treatment initiation, which may have impacted their BMI change with treatment. We did not have access to information regarding family metabolic history or the diet and exercise habits of study participants, which may have influenced BMI change with treatment. We also cannot account for factors such as parental obesity, which may have influenced clinician medication choice.

Additional limitations include lack of standardized diagnostic and intellectual functioning testing for the individuals included in this review. Diagnosis of ASD was made solely based upon DSM-IV-TR criteria without use of gold standard diagnostic measures such as the Autism Diagnostic Interview-Revised (ADI-R) or the Autism Diagnostic Observation Schedule (ADOS). Intellectual functioning was estimated based on clinician report and supporting chart documents rather than direct standardized assessment. Furthermore, the sample is biased toward individuals with potentially more severe pathology and previous treatment failures, therefore requiring referral to a tertiary care treatment center with expertise in ASD. The retrospective nature of this study limited our ability to control for variation in treatment duration between treatment groups. Subjects in the risperidone treatment group received the drug for a significantly longer period of time than did those taking aripiprazole. Our primary outcome measure of BMI *Z*-score change per year of treatment limits some of the impact of this difference. However, considering data from Martin et al. (2004) indicating that risperidone treatment is associated with early weight gain which slows over time, the longer risperidone treatment duration may have lowered the mean BMI *Z*-score change with risperidone, per year of treatment.

The minor finding for the aripiprazole treatment group suggesting a combined impact of age and intellectual disability in which older persons with intellectual disability may be more prone to weight gain with aripiprazole use, deserves further investigation. The significance of this finding is unclear, and would require larger study to determine the relevance of the subgroup analysis suggested by this possible association. This may be the result of multiple comparisons that arise naturally when multiple post-hoc models are examined, and is of minor significance given the associated lower R^2 value. We did not feel that this finding significantly impacted the overall results of our analysis.

Conclusions

Our results warrant further investigation using a prospective random assignment study design. Greater control of baseline characteristics, tracking detailed historical and lifestyle factors, use of methodical dosing guidelines, and limiting treatment duration may impact the results of such a study. Furthermore, including detailed metabolic analysis, such as laboratory testing for fasting glucose and lipid panels, will be important for comparison of the impact of BMI change with risperidone versus aripiprazole. Such a prospective study may be able to generate data on factors predictive of body weight gain.

Clinical Significance

Our report comparing weight change with risperidone versus aripiprazole in persons ages 2–20 years with ASD supports the idea that the weight effects of the drugs may not be clearly differentiated in a long-term naturalistic treatment setting. This finding is important for clinical decision making, given the frequent use of these drugs as the only FDA-approved agents for treating irritability in this population.

Acknowledgments

The authors thank Dr. Annemarie Loth (Saint Louis University School of Medicine, SSM DePaul and Cardinal Glennon Hospitals) for guidance during database construction, and Robert Bermingham for contributions during data collection.

Disclosures

Dr. Erickson received past research support from and was consultant to F. Hoffman-LaRoche, Novartis, and Seaside Therapeutics. He also received past research support from Bristol-Myers Squibb. Dr. Erickson is also a current equity holder in Confluence Pharmaceuticals. He receives current research support

from Autism Speaks, the Cincinnati Hospital Research Foundation, the John Merck Fund, The Roche Group, the Simons Research Foundation, SynapDx, and the United States Department of Defense. His conflicts do not overlap with the content of this manuscript. Dr. Wink and Dr. Schaefer receive current research support from the Cincinnati Children's Hospital Research Foundation the John Merck Fund, The Roche Group, the Simons Research Foundation, Synapdx, and the United States Department of Defense. Dr. Horn is a 1% owner of Shiloh Pharma, LLC. Ms. Early, Ms. Pottenger, and Dr. McDougle acknowledge no current conflicts of interest.

References

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Text Revision. Washington, DC: American Psychiatric Association; 2000.

Ben Amor L: Antipsychotics in pediatric and adolescent patients: A review of comparative safety data. J Affect Disord 138 (Suppl): S22–30, 2012.

Cohen D, Bonnot O, Bodeau N, Consoli A, Laurent C: Adverse effects of second-generation antipsychotics in children and adolescents: A Bayesian meta-analysis. J Clin Psychopharmacol 32:309–316, 2012.

Correll CU, Manu P, Olhashaneskiy V, Napolitano B, Kane JM, Malhotra AK: Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. JAMA 302:1765–1773, 2009.

De Hert M, Dobbelaere M, Sheridan E, Cohen D, Correll CU: Metabolic and endocrine adverse effects of second-generation antipsychotics in children and adolescents: A systematic review of randomized, placebo controlled trials and guidelines for clinical practice. Eur Psychiatry 26:144–158, 2011.

de Hoogd S, Overbeek WA, Heerdink ER, Correll CU, de graff ER, Staal WG: Differences in body mass index z-scores and weight status in a dutch pediatric psychiatric population with and without use of second-generation antipsychotics. J Child Adolesc Psychopharmacol 22:166–173, 2012.

Doey T: Aripiprazole in pediatric psychosis and bipolar disorder: A clinical review. J Affect Disord 138 (Suppl):S15–21, 2012.

Erickson CA, Posey DJ, Stigler KS, McDougle CJ: Pharmacologic treatment of autism and related disorders. Pediatr Ann 36:575–585, 2007.

Flegal KM, Ogden CL: Childhood obesity: Are we all speaking the same language? Adv Nutr 2:159S–166S, 2011.

Kanner L: Autistic disturbances of affective contact. Nerv Child 2:217–250, 1943.

Maayan L, Correll CU: Weight gain and metabolic risks associated with antipsychotic medications in children and adolescents. J Child Adolesc Psychopharmacol 21: 517–535, 2011.

Marcus RN, Owen R, Kamen L, Manos G, McQuade RD, Carson WH, Aman MG: A placebo-controlled, fixed-dose study of aripiprazole in children and adolescents with irritability associated with autistic disorder. J Am Acad Child Adolesc Psychiatry 48: 1110–1119, 2009.

Marcus RN, Owen R, Manos G, Mankoski R, Kamen L, McQuade RD, Carson WH, Findling RL: Safety and tolerability of aripiprazole for irritability in pediatric patients with autistic disorder: a 52-week, open-label, multicenter study. J Clin Psychiatry 72: 1270–1276, 2011.

Martin A, Scahill L, Anderson GM, Aman M, Arnold LE, McCracken J, McDougle CJ, Tierney E, Chuang S, Vitiello B: Weight and leptin changes among risperidone-treated youths with autism: 6-month prospective data. Am J Psychiatry 161:1125–1127, 2004.

McCracken JT, McGough J, Shah B, Cronin P, Hong D, Aman MG, Arnold LE, Lindsay R, Nash P, Hollway J, McDougle CJ, Posey D, Sweizy N, Kohn A, Scahill L, Martin A, Koenig K, Volkmar F, Carroll D, Lancor A, Tierney E, Ghuman J, Gonzalez NM, Grados M, Vitiello B, Ritz L, Davies M, Robinson J, McMahon D: Risperidone in children with autism and serious behavioral problems. N Engl J Med 347:314–321, 2002.

McDougle CJ, Holmes JP, Carlson DC, Pelton GH, Cohen DJ, Price LH: A double-blind, placebo-controlled study of risperidone in adults with autistic disorder and other pervasive developmental disorders. Arch Gen Psychiatry 55:633–641, 1998.

McDougle CJ, Stigler KA, Erickson CA, Posey DJ: Atypical antipsychotics in children and adolescents with autistic and other pervasive developmental disorders. J Clin Psychiatry 69 (Suppl 4): 15–20, 2008.

Owen R, Sikich l, Marcus RN, Corey–Lisle P, Manos G, McQuade RD< Carson WH, Findling RL: Aripiprazole in the treatment of irritability in children and adolescents with autistic disorder. Pediatrics 124:1533–1540, 2009.

Potkin SG, Saha AR, Kujawa MJ, Carson WH, Ali M, Stock E, Stringfellow J, Ingenito G, Marder SR: Aripiprazole, an antipsychotic with a novel mechanism of action, and risperidone vs placebo in patients with schizophrenia and schizoaffective disorder. Arch Gen Psychiatry 60:681–690, 2003.

Shea, S., Turgay A, Carroll A, Schulz M, Orlik H, Smith I, Dunbar F: Risperidone in the treatment of disruptive behavioral symptoms in children with autistic and other pervasive developmental disorders. Pediatrics 114:e634–641, 2004.

Stroup TS, McEvoy JP, Ring KD, Hamer RH, LaVange LM, Swartz MS, Rosenheck RA, Perkins DO, Nussbaum AM, Lieberman JA: A randomized trial examining the effectiveness of switching from olanzapine, quetiapine, or risperidone to aripiprazole to reduce metabolic risk: comparison of antipsychotics for metabolic problems (CAMP). Am J Psychiatry 168:947–956, 2011.

Wink LK, Erickson CA, McDougle CJ: Pharmacologic treatment of behavioral symptoms associated with autism and other pervasive developmental disorders. Curr Treat Options Neurol 12:529–538, 2010.

Address correspondence to:
Logan K. Wink, MD
Cincinnati Children's Hospital Medical Center
3333 Burnet Ave. MLC 4002
Cincinnati, OH 45229

E-mail: Logan.Wink@cchmc.org