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Prevalence and Correlates of Psychotropic Medication Use in Adolescents with an Autism Spectrum Disorder with and without Caregiver-Reported Attention-Deficit/Hyperactivity Disorder

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Abstract

Background: Many youths with an autism spectrum disorder (ASD) benefit from psychotropic medication treatment of co-morbid symptom patterns consistent with attention-deficit/hyperactivity disorder (ADHD). The lack of clear indications and algorithms to direct clinical practice has led to a very poor understanding of overall medication use for these youths. The present study examined the prevalence of psychotropic medication use compared across individuals with an ASD without a caregiver-reported ADHD diagnosis (ASD-only), ADHD without ASD (ADHD-only), and an ASD with co-morbid ADHD (ASD + ADHD). Correlates of medication use were also examined.

Methods: Data on psychotropic medication from the first wave of the National Longitudinal Transition Study 2, a nationally representative study of adolescents ages 13–17 in special education, were used to compare the prevalence of medication use across the three groups, overall and by class. Separate logistic regression models were constructed for each group to examine the correlates of psychotropic medication use. Poisson regression models were used to examine correlates of the number of medications.

Results: Youths with ASD + ADHD had the highest rates of use (58.2%), followed by youths with ADHD-only (49.0%) and youths with ASD-only (34.3%). Youths with an ASD, both ASD-only and ASD + ADHD, used medications across a variety of medication classes, whereas stimulants were dominant among youths with ADHD-only. African American youths with ASD-only and with ASD + ADHD were less likely to receive medication than white youths, whereas race was not associated with medication use in the ADHD-only group.

Conclusions: Clearer practice parameters for ADHD have likely contributed to more consistency in treatment, whereas treatment for ASD reflects a trial and error approach based on associated symptom patterns. Additional studies examining the treatment of core and associated ASD symptoms are needed to guide pharmacologic treatment of these youths. Interventions targeting African American youths with ASD and the physicians who serve them are also warranted.

Introduction

Individuals with autism spectrum disorders (ASD) show variable impairments in social interaction, communication, and restricted/repetitive behaviors. By definition, these impairments are pervasive and affect multiple domains of health and functioning. In addition to these core symptom domains, behavioral co-morbidities are common and include symptom patterns indicative of attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, oppositional behavior, mood disorders, thought dysfunction/psychosis, severe irritability, and aggression (Lee and Ousley 2006; Zafeiriou et al. 2007; LoVullo and Matson 2009; MacNeil et al. 2009; Matson and Neal 2009; Souders et al. 2009). A growing body of efficacy and effectiveness studies have demonstrated that many individuals with ASD benefit from medication treatment of associated symptoms and co-morbidities (Huffman et al. 2011), either as a first-line

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treatment (McCracken et al. 2002; Shea et al. 2004; Marcus et al. 2009; Owen et al. 2009) or combined with behavior therapy (Aman et al. 2009; Frazier et al. 2010).

In spite of the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, Text Revision (DSM-IV-TR) (American Psychiatric Association 2000) prohibition against a comorbid ADHD diagnosis, ADHD is one of the most common ASD-associated co-morbidities, with upper bound estimates approaching 78% of ASD cases (Fein et al. 2005; Lee and Ousley 2006). Medication treatment, particularly stimulant medication, has long been recommended for treatment of ADHD symptoms in individuals without ASD. However, stimulant treatment is less established in individuals with ASD (Aman 1982; Santosh et al. 2006; Nickels et al. 2008). In fact, the only FDA-approved medications for ASD, risperidone and aripiprazole, are indicated specifically for the treatment of irritability or aggression (McCracken et al. 2002; Shea et al. 2004; Marcus et al. 2009; Owen et al. 2009). Yet many other medications are used to treat ASD with ADHD or other co-morbidities (Aman et al. 2005; Rosenberg et al. 2009). Further complicating matters, some data suggest decreased efficacy or increased side effects of psychiatric medications in individuals with ASD (Campbell et al. 1996; Aman et al. 1997; McDougle 2002), creating uncertainty regarding the appropriateness of medications historically used to treat other conditions.

The clinical result is often a trial-and-error approach to medication treatment in individuals with ASD, with medication selection based on physician preference and familiarity, guided by identified co-morbidities (Tsai 1999; McDougle 2002). The lack of clear indications and algorithms to direct clinical practice leads to a very poor understanding of overall psychiatric medication use in individuals with ASD, including individuals with co-morbid ASD and ADHD (Wisniewski et al. 2007).

An important first step in advancing our understanding of medication treatment of ASD with and without co-morbid ADHD is to identify current trends in overall and class-specific medication use. Previous studies of medication use in ASD suggest variable, but generally substantial overall prevalence, with estimates ranging from 30% to 70% of people with an ASD taking at least one medication (Martin et al. 1999; Aman et al. 2005; Witwer and Lecavalier 2005; Green et al. 2006; Goin-Kochel et al. 2007; Oswald and Sonenklar 2007; Mandell et al. 2008; Rosenberg et al. 2009) and as many as 30% taking two or more psychotropics (Martin et al. 1999). Antipsychotics, antidepressants, alpha agonists, and stimulants have been identified as the most frequently used medication types (Martin et al. 1999; Myers and Johnson 2007; Rosenberg et al. 2009).

However, previous estimates of medication use and factors influencing medication use were derived from convenience or community samples. Convenience sampling decreases the generalizability of estimates of medication use in the ASD population. Also, previous studies tended to focus only on ASD and have not systematically compared medication use to other common neurodevelopmental conditions, such as ADHD, to benchmark overall use and identify specific patterns of use across medication types (Aman et al. 2005; Rosenberg et al. 2009).

The first aim of the present study was to examine the prevalence of medication use, both overall and across specific medication classes, in a nationally representative sample of adolescents. Psychotropic medication prevalence was compared across individuals with ASD without a caregiver-reported ADHD diagnosis (ASD-only), ADHD without ASD (ADHD-only), and ASD with co-morbidADHD (ASD + ADHD). We anticipated that the co-morbid group would show a higher prevalence of medication use relative to individuals with ASD-only. Youths with ADHD-only were expected to show lower rates of medication use, with stimulants being predominant.

Correlates of medication use

In addition to understanding the rates of medication use in people with ASD, it is important to examine whether medication use is primarily driven by need and clinical characteristics (e.g., symptom severity) or is partly a function of access to services and other socio-demographic factors. Andersen's (1995, 2007) model of health care utilization posits three broad factors associated with accessing health services: predisposing (e.g., age, gender, education level, and race/ethnicity), enabling (e.g., income, SES, and insurance status), and need (e.g., symptom severity, level of dysfunction, and co-morbidity) factors. In this model, need is defined as both the perceived view of one's own health and evaluated need or professional judgment regarding health or diagnosis. The enabling factors primarily refer to individual-level characteristics facilitating the ability to obtain health care (e.g., financial and insurance status). Predisposing characteristics refer to aspects of the person that influence the likelihood of seeking medical care, such as race/ethnicity, which can be a proxy for variability in beliefs about medical treatments.

Prior research suggests that predisposing and enabling factors influence service usage in individuals with medical and psychiatric conditions (Cohen and Hesselbart 1993; Pumariega et al. 1998; Naar-King et al. 2006; Williams et al. 2006; Ellis et al. 2007). Less information is available for identifying factors altering medication use in youths with specific disorders (Rizzo et al. 2007; Mendenhall et al. 2011). A recent internet registry study of medication use in ASD (Rosenberg et al. 2009) reported significant associations between several predisposing and enabling factors, including decreased medication use in youths with Hispanic ethnicity; individuals from urban areas; youths with co-morbidities, more severe symptoms, or intellectual disability; and youths whose caregivers did not report insurance coverage (Rosenberg et al. 2009). Similarly, in a study of Medicaid-enrolled patients, older and male patients, and youths with co-morbidities were more likely to have used psychotropic medications (Mandell et al. 2008). However, studies have differed as to the role of race/ethnicity and other predisposing factors (Aman et al. 2005; Mandell et al. 2008; Rosenberg et al. 2009).

The second aim of our study was to examine correlates of medication use in each of the three groups. Factors beyond need, including both predisposing and enabling factors, were expected to be significantly associated with medication usage in youths with ASD with and without ADHD. The ASD groups were expected to show greater associations between predisposing and enabling factors relative to the ADHD-only group based on the lack of specific algorithms and practice parameters in ASD medication treatment, the paucity of data concerning medication efficacy and safety, the fact that approved medications do not treat core ASD symptoms, and the lack of widespread insurance coverage for ASD diagnoses. The present study builds on prior findings by using a large nationally representative sample, examining a wide range of socio-demographic correlates, organizing analyses based on Andersen's conceptual framework, and examining both the presence/absence of medication use and the number of medications reported.

Discovering answers to these questions is important for clinical researchers because it may identify medications and medication

classes in greatest need of additional efficacy and effectiveness studies in ASD with and without ADHD. Examining factors associated with medication usage will also be useful to clinicians, caregivers, advocates, and policy makers in order to identify individuals who are under-served and may benefit from interventions to improve access to psychiatric care.

Methods

Study sample

The data for the current study come from the National Longitudinal Transition Study-2 (NLTS2), a 10-year prospective study with data collected from 2000 to 2009 by SRI International for the U.S. Department of Education. At the study's outset, the NLTS2 sampled more than 11,000 students who were receiving special education services in 7th through 12th grades or in ungraded programs and who were ages 13 through 16 on December 1, 2000. The two-stage NLTS2 sampling procedure first drew a stratified random sample of school districts that served students in the eligible age range and then randomly selected students from each district within each of the 12 special education disability categories, including the category of autism (SRI International 2000). The overall response rate for the study was 81%. The NLTS2 sampling plan was designed to produce weighted population estimates that are nationally representative of all students receiving special education services in the targeted age range and of students in each disability category. Full details of the weighting strategy for NLTS2 were previously published (Wagner et al. 2005). The study reported here was approved by the University's Institutional Review Board. In accordance with the U.S. Department of Education data use agreement, all unweighted sample size numbers are rounded to the nearest 10 for reporting.

Each student's eligibility for special education services was determined by the school district that provided rosters from which the students were sampled, resulting in an unknown amount of district-to-district variation in eligibility criteria. Cases for this study were drawn from two special education disability categories—Autism and Other Health Impairment (OHI). Analyses for this article relied on interview/survey data supplied by caregivers in the first wave of data collection (2001); 920 sample members with Autism and 920 sample members with OHI had wave 1 caregiver interview/survey data.

Youths were classified as having an ASD in our study based on their assignment to the special education category of autism. School eligibility criteria for this category do not necessarily conform to *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, DSM-IV (American Psychiatric Association 1994) criteria (McFarlane and Kanaya 2009). Recent U.S. epidemiological surveillance data indicate that 99% of adolescents served under the autism educational designation also meet DSM-IV criteria for an ASD (Bertrand et al. 2001; Yeargin-Allsopp et al. 2003). Some adolescents, however, who meet the DSM-IV criteria for ASD could be served under another category such as mental retardation or emotional disturbance and would not be included in this analysis.

Students who qualify for special education services primarily due to an ADHD diagnosis are typically classified in the OHI category (U.S. Department of Special Education OSEP 2007). Thus, the sample of ADHD-only was drawn from students enrolled in this category who had a caregiver report of an ADHD diagnosis ($n = 520$). Excluded from the ADHD-only group were students with other parent-reported comorbidities that had a strong likelihood of influencing the rate of psychotropic medication use (e.g., emotional disturbance, epilepsy). The ADHD sample for the current study includes 56% of the total number classified into the OHI category.

Youths were classified into subgroups for analysis based on caregiver-reported ADHD clinical diagnosis. Caregivers were asked, ''With what physical, sensory, learning, or other disabilities or problems has [YOUTH] been diagnosed?'' Those that did not explicitly state that the youth had ADHD were then asked, ''Has [YOUTH] been diagnosed with attention deficit disorder or attention deficit/hyperactivity disorder?'' These questions were used to create an indicator for whether youth had ADHD. Youths in the autism special education category were divided into those with caregiver-reported co-morbid ADHD (ASD + ADHD) ($n = 290$) and those with autism but without ADHD (ASD-only) ($n = 600$). Thirty youths were excluded from analysis because they were missing a response about their ADHD status. Because of the DSM-IV prohibition against a co-morbid ADHD diagnosis in individuals with ASD, the caregiver-reported ADHD diagnosis should be viewed as a proxy for significant co-occurring ADHD-like behavior in individuals with ASD.

Data collection procedures

This study draws on data from two sources. First, structured telephone interviews were conducted with the adult who was best able to respond about the sampled youths; 91% of respondents were parents. An abbreviated mail questionnaire was sent to families who could not be reached by telephone. In the Autism and OHI subgroups, 97% of respondents completed the telephone interview and 3% responded via the mail questionnaire. These instruments were the source of data on students' medication use, disability and demographic characteristics, household income, health insurance status, functional ability, and indicators of behavior.

Second, for each school attended by an NLTS2 sample member, a school staff person knowledgeable about the characteristics and policies of those schools was surveyed by mail. Broad information about the school (e.g., grade levels served), as well as information about the student body (e.g., demographic characteristics), was collected. School policies that affected students with disabilities (e.g., inclusion in mandated standardized testing) also were addressed. School-level information was linked to each NLTS2 sample member enrolled at a given school. Survey data were supplemented from the U.S. Department of Education's Common Core of Data to in-fill data on student enrollment, grade levels served, the racial/ethnic distribution of the student body, and the percentage of students eligible for the federal free/reduced price lunch program.

Measures

Psychiatric medication use was assessed with the question: ''Is [youth] taking any prescription medicine that controls [his/her] attention, behavior, or activity level, or changes [his/her] mood, such as Ritalin or an antidepressant?'' Respondents who answered yes to this question were asked: ''What is the name of the prescription medicine [youth] takes to control [his/her] behavior, or change [his/her] mood?'' The interviewer then probed for the names of additional medications until the respondent said there were no other medications; respondents were not directly asked to report whether youth took specific, named medications. Medications were grouped into medication classes for the purpose of this analysis using a standardized approach we have used in previous work (Findling et al. 2010; Frazier et al. 2010). A count variable of number of medications was also constructed by summing the number of medications the caregiver named.

Gender, race, and ethnicity were used as predisposing factors. Enabling resources included the urbanicity of the youth's school as assessed through the school survey, the education level of the parent/guardian respondent, whether the household was non-English-speaking, the level of income, and the type of health insurance (i.e., whether private, government assisted, or other; whether health maintenance organization (HMO) or not).

Need indicators for core symptoms of ASD and ADHD were also included. Conversational ability was assessed with the question: ''How well does [youth] carry on a conversation?'' A dichotomous indicator for significant conversational impairment was created for those who responded that the youth has a lot of trouble conversing or does not converse at all. Functional mental skills were assessed with a four-item scale that assessed the youth's ability to look up telephone numbers and use them, tell time on an analog clock, read and understand common signs, and count change. The items were summed into an overall scale (range 4–16) with higher scores indicating higher ability ($\alpha = 0.88$). Pro-social behaviors were measured using four items that asked caregivers to rate how often the youth joins groups without being told, makes friends easily, seems confident in social situations, and starts conversations. These items were summed into a scale with a range from 0 to 8 ($\alpha = 0.80$), with higher scale scores indicating greater pro-social skills. Externalizing behaviors were measured with a 3-item scale that asked caregivers to rate how often the youth gets into situations that are likely to results in trouble, controls temper when arguing, and behaves at home in a way that causes problems for the family. The items were summed into a scale with a range from 0 to 6 ($\alpha = 0.54$). A dichotomous indicator was created for poor organizational skills if the caregiver reported that the youth is ''not very good'' or ''not at all good'' at being organized. Other co-morbid conditions such as intellectual disability were not queried in the survey.

Statistical analysis

Univariate statistics were computed for each group in the sample (Table 1). We tested for the significance of pairwise differences among group characteristics and medication use rates using a series of logistic regression models with dummy coding for each group. Separate multivariate logistic regression models estimated the correlates of any medication usage for each group of youths. A Poisson model was used to estimate the correlates of medication count. All reported estimates were weighted and variances adjusted to account for the complex sampling using the ''mi svy'' procedures available in Stata v11 (StataCorp 2009). Fifty multiply imputed data sets were created using sequential regression in IVEware to handle missing data in the independent variables (Raghanuthan et al. 2001).

Results

The sample characteristics for the three groups are presented in Table 1. Mean ages were similar across groups (ASD-only = 15.04, ASD + ADHD = 14.94, and ADHD-only = 15.15). Significant differences were noted across the groups in several areas. Although less than a quarter of youths were female in all groups, the percentage of females was lowest in the group with co-morbid ASD + ADHD (11.7%). Both the ASD-only and the ASD + ADHD groups had significantly higher percentages of African American youths than the ADHD-only group. Youths in the ASD groups were also significantly more likely to live in a large city or suburb, whereas the ADHD-only group had the highest percentage of youths living in rural regions. Youths in both ASD groups had higher levels of public insurance than those in the ADHD category. ASD-only and ASD + ADHD groups were significantly more likely to have a conversational impairment, weaker social skills, and poorer functional abilities relative to youths with ADHD-only.

Table 2 presents medication usage rates for the entire sample. Although 34.3% of youths with ASD-only were taking a medication, these rates were significantly lower than rates for the ADHD only (49.0%) and the ASD + ADHD groups (58.2%). Across medication types, rates of use were substantial for all three groups. For the antipsychotic, antidepressant/anxiety, serotonin-selective reuptake inhibitor (SSRI), and mood stabilizer drug classes as well as risperidone individually, medication usage for youths with ASD-only consistently fell between the co-morbid ASD + ADHD group (highest usage) and the ADHD only group (lowest usage).

Table 3 presents the proportion of youth taking one, two, or three or more medications as well as class-specific medication rates for those who were taking at least one psychotropic medication. Among these individuals, the overwhelming majority of ADHD-only youths took only one medication (72.6%). In contrast, the majority of ASD-affected youths who were using at least one medication were taking two or more medications (ASD-only 52.1%; ASD + ADHD 58.2%). For youths taking three or more medications, the co-morbid ASD + ADHD group had the highest prevalence (29.5%). Youths with ASD-only or ASD + ADHD had very high and comparable rates across all medication classes except stimulants and mood stabilizers. Rates for stimulants and mood stabilizers were lower but non-trivial (> 18%) in these groups. As expected, rates of stimulant use were significantly higher in the ADHD-only group and the magnitude of this rate (90.4%) indicates that the vast majority of ADHD-only youths were taking a stimulant and no other medicine.

To examine the effects of predisposing, enabling, and need factors on medication usage, logistic regression models were computed separately for each of the three groups (Table 4). Within the ASD only and the ASD + ADHD groups, African American youths were significantly less likely to take medications than white youths. None of the identified enabling factors was significant with two exceptions. Youths from non-English-speaking households in the ASD-only group were significantly less likely to use medications than youths from households where English was the primary language. In the ADHD-only group, youths whose parents had 4-year college degrees were more likely than those with less than a high school education to use medications. Across all three groups, youths who had higher scores on the externalizing behaviors scale were more likely to use medication.

Similar patterns of significant correlates emerged when Poisson regression models were used to examine medication counts (not reported). Once again, African American youths in the ASD-only and the ASD + ADHD groups took significantly fewer medications compared with white youths and this pattern remained consistent for youths with ASD-only from non-English-speaking households.

Discussion

As predicted, individuals with ASD and ADHD had a higher prevalence of any medication use and a greater proportion of individuals taking multiple medications relative to youths with ASD or ADHD alone. Almost 6 in 10 youths in this group were taking at least one medication, and the majority of youths were taking more than one medication. Also striking are the high rates of antipsychotic, antidepressant/antianxiety, and stimulant medication use in

Table 1. Sample Characteristics for Predisposing, Enabling, and Need Factors Across Three Comparison Groups: Autism Spectrum Disorder Only, Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder, and Attention-Deficit/Hyperactivity Disorder Only

	ASD	*ASD and ADHD*	*ADHD*	*Comparison test*
Predisposing factors				
Female	17.5%	11.7%	24.3%	a*, b*, c***
Age	15.04	14.94	15.15	n.s.
Race				
White	64.3%	68.4%	81.2%	b***, c**
African American	24.0%	19.1%	10.5%	b***, c*
Other/Biracial	11.7%	12.5%	8.3%	n.s.
Ethnicity				
Hispanic	12.8%	8.3%	8.7%	n.s.
Enabling				
Rural or small town	19.4%	31.1%	53.1%	a*, b***, c***
Medium city, suburb	19.0%	12.4%	16.0%	n.s.
Large city, suburb	30.2%	28.2%	16.5%	b***, c*
Very large city, suburb	31.4%	28.3%	14.5%	b**, c**
Respondent education				
Less than high school	8.7%	7.9%	11.4%	n.s.
High school	22.8%	27.3%	30.3%	b**
Some post high school training or associate degree	34.0%	32.1%	34.0%	n.s.
4 year degree	17.8%	20.7%	14.6%	c*
Graduate education	16.7%	12.0%	9.7%	b**
Income				
<25,000	21.3%	21.2%	18.0%	n.s.
25,000–50,000	32.2%	30.0%	37.2%	n.s.
50,001–75,000	23.7%	24.8%	25.0%	n.s.
>75,000	22.9%	23.9%	19.9%	n.s.
Insurance				
Private	72.4%	68.7%	78.8%	c*
Public/Other	23.2%	28.3%	14.8%	b**, c***
None	4.3%	3.1%	6.5%	n.s.
Non-English-speaking household	15.3%	13.7%	7.2%	b**, c*
Need				
Significant conversational impairment	58.4%	48.9%	3.8%	a*, b***, c***
Pro-social behaviors scale mean	2.8	3.0	5.4	b***, c***
Externalizing behavior scale mean	3.9	3.6	3.5	a*, b***
Functional abilities scale mean	10.7	11.2	14.2	b***, c***
% good at being organized	55.1%	39.4%	31.4%	a***, b***

Source: National Longitudinal Transition Study 2.

Notes: Number of multiply imputed data sets = 50. Weighted to population levels. Variances adjusted for sampling method.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

a = ASD only versus ASD and ADHD; b = ASD only versus ADHD only; c = ASD and ADHD versus ADHD only; ASD = autism spectrum disorder; ADHD = attention-deficit/hyperactivity disorder; n.s. = not significant.

these youths. Observations from the present study reinforce the complexity of pharmacologic treatment of challenging behavior in youths with ASD and ADHD and underscore the need to identify efficacious medication algorithms for this population.

Individuals with ASD-only were least likely to take any medication, but when they did use a medication, they often used more than one. Individuals with ASD-only showed a diverse medication profile, with large proportions taking an antipsychotic or antidepressant/antianxiety medication. In contrast, adolescents with ADHD-only were more likely to use only a single medication, often a stimulant medication as would be expected per current practice parameters. The high prevalence of any medication use in youths with ADHD-only (49.0%) underscores the effectiveness of stimulant medication and the existence of clear practice parameters guiding ADHD medication treatment (American Academy of Child and Adolescent Psychiatry 2002). It is likely that the diverse array of observed medication usage and the substantial prevalence of poly-pharmacy in individuals with ASD are at least partly due to the current trial-and-error treatment approach focusing on associated behavioral disturbances. Clearly, additional efficacy and effectiveness studies examining the treatment of core and associated ASD symptoms are needed to guide pharmacologic treatment of these youths. This is particularly important given the added side effect burden often present with poly-pharmacy and the possibility that individuals with ASD may not be fully able to communicate about side effects.

FDA approval of antipsychotic medications for the treatment of irritability or aggression in youths with ASD has likely increased use of these medicines in adolescents with and without ADHD symptoms. To date, we are not aware of any studies that have specifically examined the efficacy of these medications separately in individuals with and without ADHD. Given the recognized heterogeneity of ASD (Hus et al. 2007), this will be an important next step. Additionally, few studies have moved beyond efficacy to

Table 2. Population-Based Prevalence of Prescription Psychotropic Medication Use in Percentages, Compared Across Three Groups

	ASD Only	*ASD and ADHD*	*ADHD*	*Comparison test*
Overall				
Any medication	34.3%	58.2%	49.0%	a***, b**
Class specific				
Antipsychotic	14.8%	23.0%	2.8%	a*, b**, c***
Risperidone	10.6%	17.3%	1.4%	a*, b***, c***
Antidepressant or antianxiety	20.9%	29.9%	11.2%	a*, b**, c***
SSRI	15.6%	19.4%	5.3%	b***, c***
Mood stabilizer or antiseizure	7.7%	10.8%	2.9%	b**, c***
Stimulant	6.3%	33.0%	44.3%	a***, b***, c*

Source: National Longitudinal Transition Study 2.

Notes: Number of multiply imputed data sets = 50. Weighted to population levels. Variances adjusted for sampling method. Antidepressant or antianxiety includes SSRIs and other medication classes such as tricyclics and benzodiazepines. Because the majority of usage in this heterogeneous category was from SSRIs we also include this more specific group.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

a = ASD only versus ASD and ADHD; b = ASD only versus ADHD only; c = ASD and ADHD versus ADHD only; SSRI = serotonin-selective reuptake inhibitor.

examine the effectiveness of antipsychotic medications in individuals with ASD with or without ADHD. The potential for significant weight gain and metabolic syndrome further reinforces the need for longer-term effectiveness studies that also evaluate long-term side effect profiles in ASD groups. These effectiveness studies may initially focus on populations examined in the efficacy studies, but this may allow secondary analyses to examine whether these medications are also effective for treating ADHD-like behaviors in ASD-affected youths. Recently, our group identified that antipsychotic medications augment the effectiveness of intensive behavior management in youths who showed only minimal response to medication alone (Aman et al. 2009; Frazier et al. 2010). Combination effectiveness studies, analogous to those done in youths with ADHD, will be crucial for identifying the most effective treatment regimens for sub-groups of individuals with ASD.

Table 3. Class-Specific Prevalence of Psychotropic Medications and Medication Count, Among Those Who Took At Least One Medication

	ASD Only	*ASD and ADHD*	*ADHD*	*Comparison test*
Medication count				
1	48.0%	41.8%	72.6%	b***, c***
2	31.9%	28.7%	20.5%	b*
3+	20.2%	29.5%	7.0%	b***, c***
Antipsychotic	43.1%	39.5%	5.7%	b***, c***
Risperidone	31.0%	29.7%	2.8%	b***, c***
Antidepressant or antianxiety	60.9%	51.4%	22.9%	b***, c***
SSRI	45.4%	33.4%	10.8%	b***, c***
Mood stabilizer or antiseizure	22.4%	18.6%	5.8%	b***, c**
Stimulant	18.4%	56.8%	90.4%	a***, b***, c***

Source: National Longitudinal Transition Study 2.

Notes: Number of multiply imputed data sets = 50. Weighted to population levels. Variances adjusted for sampling method.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

a = ASD only versus ASD and ADHD; b = ASD only versus ADHD only; c = ASD and ADHD versus ADHD only.

The present estimates of medication use are similar to estimates from other medication surveys of individuals with ASD (Martin et al. 1999; Aman et al. 2005; Mandell et al. 2008; Rosenberg et al. 2009). The use of a nationally representative sample of adolescents with ASD-only and ASD + ADHD confirms the high rates of medication use in these youths. Consistent with previous studies, we identified nontrivial rates of mood stabilizer and stimulant use in individuals with ASD (Aman et al. 2005; Hellings et al. 2005; Research Units on Pediatric Psychopharmacology Autism Network 2005; Rosenberg et al. 2009). Careful studies of the efficacy and effectiveness of these medication classes, which have been less well studied than antipsychotics and SSRIs, are needed. In particular, the present results suggest that future studies examining these medication classes may consider focusing on individuals with both ASD and ADHD, as these youths appear to represent a sub-group with distinct and intense psychopharmacologic needs.

Two need factors, greater externalizing behavior and lower functional ability, significantly predicted medication use in the ASD-only group and approached significance in the ASD + ADHD group. Contrary to expectation, predisposing and enabling factors were generally unrelated to medication use across all groups. The most notable exception to this pattern was lower medication use in African American (both ASD groups) youths. This finding is consistent with previous results (Mandell et al. 2008) and suggests that race may be an important moderator of access to psychiatric services. Interestingly, adolescents with ADHD-only did not show this pattern. There are several possibilities for this difference, including greater historical awareness of the ADHD diagnosis relative to the recent recognition of ASD, heavy reliance on teacher report in identifying ADHD (Vaughn et al. 1997; Wolraich et al. 2003), and the widespread availability of effective ADHD medication treatments. Regardless, lower medication use in African American youths suggests that they are currently underserved, and interventions targeting these populations and the physicians who serve them are warranted.

The primary limitations of this study were the reliance on caregiver report and special education designations in obtaining diagnostic classifications, caregiver report of medication use, lack of information concerning other ASD-associated co-morbidities, and the cross-sectional nature of the design. Caregiver report of a clinical ADHD diagnosis is sub-optimal because this combination is not actually permitted by DSM-IV, although it is often used in clinical practice to increase the likelihood of appropriate treatment. Thus, the ADHD diagnosis should be viewed as a proxy for the clinical observation of co-occurring ADHD symptoms in individuals with ASD. Use of caregiver report and special education classifications for obtaining ASD diagnosis is also clearly inferior to using direct assessment or semi-structured psychiatric interviews to derive clinical diagnoses. Fortunately, this design weakness is likely to under-estimate rather than over-estimate group differences in medication use. This is because caregiver-reported ADHD and ASD education classifications may result in misclassifications that reduce the purity of these groups. Thus, it is likely that significant group differences are an accurate reflection of medication use across these conditions, but that nonsignificant results may be due to classification error or reflect true equivalency.

Table 4. Logistic Regression Modeling Use of Any Prescription Psychotropicmedication in Each Group, Odds Ratios and 95% Confidence Intervals

	ASD	*ASD and ADHD*	*ADHD*
Predisposing factors			
Female	0.8 (0.4, 1.4)	0.8 (0.4, 1.9)	0.9 (0.5, 1.5)
Race			
White	1.0	1.0	1.0
African American	0.3** (0.2, 0.6)	0.4* (0.2, 0.8)	0.7 (0.3, 1.5)
Other	0.8 (0.4, 1.8)	0.8 (0.3, 2.2)	1.3 (0.6, 2.7)
Ethnicity			
Hispanic	0.6 (0.3, 1.2)	1.8 (0.5, 5.8)	0.6 (0.2, 1.6)
Enabling			
Urbanicity			
Rural or small town	1.0	1.0	1.0
Medium city, suburb	1.6 (0.7, 3.7)	0.6 (0.2, 2.0)	0.7 (0.3, 1.5)
Large city, suburb	1.9 (0.9, 4.0)	0.8 (0.3, 2.1)	1.1 (0.6, 2.0)
Very large city, suburb	1.3 (0.6, 2.7)	0.6 (0.2, 1.5)	0.9 (0.4, 1.8)
Respondent education:			
Less than high school	1.0	1.0	1.0
High school	0.8 (0.3, 2.0)	1.2 (0.3, 4.8)	1 (0.5, 2.0)
Post high school training/associate degree	0.6 (0.2, 1.4)	0.8 (0.2, 2.9)	1.5 (0.7, 3.2)
4 year degree	0.8 (0.3, 2.2)	0.9 (0.2, 3.5)	2.7* (1.1, 6.8)
Post BA/BS education	0.8 (0.3, 2.5)	2.3 (0.5, 10.2)	2 (0.7, 5.8)
Income			
<25,000	1.0	1.0	1.0
25,000–50,000	1.4 (0.7, 2.9)	1.3 (0.5, 3.2)	1 (0.5, 2.1)
50,001–75,000	1.3 (0.6, 2.6)	3.2 (0.9, 11.9)	1.5 (0.7, 3.4)
>75,000	1.3 (0.6, 2.7)	2.1 (0.7, 6.1)	2 (0.8, 4.8)
Insurance			
Private	1.0	1.0	1.0
Public/Other	1.7 (0.9, 3.2)	1.4 (0.5, 3.9)	1.6 (0.8, 3.3)
None	0.6 (0.2, 2.0)	0.9 (0.2, 4.8)	1 (0.4, 2.3)
Non-English-speaking household	0.5* (0.3, 1.0)	0.5 (0.2, 1.2)	1.2 (0.5, 2.6)
Need			
Significant conversational impairment	1.4 (0.8, 2.5)	0.5 (0.3, 1.0)	1.4 (0.4, 5.0)
Prosocial behaviors scale	0.9 (0.8, 1.1)	1 (0.8, 1.2)	0.9* (0.8, 1.0)
Externalizing behaviors scale	0.7** (0.5, 0.8)	0.7* (0.6, 1.0)	0.8* (0.7, 1.0)
Functional Abilities scale	1 (0.9, 1.1)	1 (0.9, 1.1)	1 (0.9, 1.1)
Poorly organized	0.7 (0.4, 1.1)	0.7 (0.4, 1.3)	0.9 (0.6, 1.6)

Source: National Longitudinal Transition Study 2.
Notes: Number of multiply imputed data sets = 50. Weighted to population levels. Variances adjusted for sampling method.
*$p < 0.05$, **$p < 0.001$.

Caregiver report of medication use, while less ideal than direct monitoring of medication, permitted national sampling of ASD-affected youths—a primary strength of this study. The cross-sectional nature of the design limits conclusions regarding the use of medication over time. Some studies have suggested increases over time in the rates of psychotropic medication use in ASD, particularly for antidepressants and antipsychotics (Aman et al. 2005; Esbensen et al. 2009). Additional waves of data from this study will be helpful for examining factors influencing the onset of new psychotropic medication use. These studies will substantially add to existing knowledge of medication use in ASD because most previous studies, including the present study, have only focused on any current medication use.

Importantly, analysis of demographic differences across study groups suggested a misclassification bias affecting the identification of ASD. This bias indicates that some individuals who likely have ASD were misclassified as having ADHD-only or other conditions. Specifically, youths from rural regions, with less educated caregivers, and who had public/nonprivate insurance were less likely to receive an ASD diagnosis relative to an ADHD diagnosis. Fortunately, this misclassification bias should serve to reduce group differences, resulting in an under-estimate of effects. The implications of this bias are that nonsignificant findings may simply be due to misclassification of ASD and ADHD groups rather than truly non-significant results. Coupling this bias with reduced classification precision (resulting from the use of caregiver reports of ADHD and educational classifications of ASD instead of clinical psychiatric diagnoses) suggests that significant results are likely to be of even greater magnitude than estimated by the present study.

Conclusion

In summary, the present study adds to the existing literature by providing and comparing estimates of medication use in youths with ASD and/or ADHD using a nationally-representative sample of adolescents ages 13 through 17. Results highlight the high prevalence of medication use in ASD-affected youths, particularly those with co-morbid ADHD, the need for additional efficacy and

effectiveness studies of existing pharmacological classes, and the need to reduce medication use disparities in African American youths with ASD.

Clinical Significance

Results underscore the need for clear practice parameters for the pharmacologic treatment of associated symptoms in ASD. The development of widely disseminated guidelines may help reduce poly-pharmacy or provide empirical rationale for the use of multiple medicines. Decreasing medication burden is particularly important for severely ASD-affected individuals who may be unable to consistently describe side effects. Additional data will be crucial for developing an empirical base to guide future practice parameters. Given the lower rates of medication use among African American youths with ASD, clinicians should ensure that their practice reflects cultural competency, make efforts to provide education, and facilitate discussions of patient concerns regarding medication use.

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References

Aman MG: Stimulant drug effects in developmental disorders and hyperactivity—toward a resolution of disparate findings. J Autism Dev Disord 12:385–398, 1982.

Aman MG, Lam KS, Van Bourgondien ME: Medication patterns in patients with autism: Temporal, regional, and demographic influences. J Child Adolesc Psychopharmacol 15:116–126, 2005.

Aman MG, McDougle CJ, Scahill L, Handen B, Arnold LE, Johnson C, Stigler KA, Bearss K, Butter E, Swiezy NB, Sukhodolsky DD, Ramadan Y, Pozdol SL, Nikolov R, Lecavalier L, Kohn AE, Koenig K, Hollway JA, Korzekwa P, Gavaletz A, Mulick JA, Hall KL, Dziura J, Ritz L, Trollinger S, Yu S, Vitiello B, Wagner A: Medication and parent training in children with pervasive developmental disorders and serious behavior problems: Results from a randomized clinical trial. J Am Acad Child Adolesc Psychiatry 48:1143–1154, 2009.

Aman MG, Van Bourgondien ME, Osborne PW, Sarphare G: Side effects associated with psychoactive medication in individuals with autism. J Autism Dev Disord 27:342–344, 1997.

American Academy of Child and Adolescent Psychiatry: Practice parameter for the use of stimulant medications in children, adolescents, and adults. J Am Acad Child Adolesc Psychiatry 41:4s–25s, 2002.

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV). Washington, DC: American Psychiatric Association; 1994.

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Text Revision (DSM-IV-TR). Washington, DC: American Psychiatric Association; 2000.

Andersen RM: Revisiting the behavioral model and access to medical care: Does it matter? J Health Soc Behav 36:1–10, 1995.

Andersen RM, Davidson PL: Improving access to care in America: Individual and contextual indicators. In: Changing the US Healthcare System: Key Issues in Health Services Policy and Management, edited by R.M. Andersen, T.H. Rice, G.F. Kominsky. San Francisco, CA: John Wiley & Sons, Inc., 3–31, 2007.

Campbell M, Schopler E, Cueva JE, Hallin A: Treatment of autistic disorder. J Am Acad Child Adolesc Psychiatry 35:134–143, 1996.

Cohen P, Hesselbart CS: Demographic factors in the use of children's mental health services. Am J Public Health 83:49–52, 1993.

Ellis DA, Yopp J, Templin T, Naar-King S, Frey MA, Cunningham PB, Idalski A, Niec LN: Family mediators and moderators of treatment outcomes among youths with poorly controlled type 1 diabetes: Results from a randomized controlled trial. J Pediatr Psychol 32:194–205, 2007.

Esbensen AJ, Greenberg JS, Seltzer MM, Aman MG: A longitudinal investigation of psychotropic and non-psychotropic medication use among adolescents and adults with autism spectrum disorders. J Autism Dev Disord 39:1339–1349, 2009.

Fein D, Dixon P, Paul J, Levin H: Brief report: Pervasive developmental disorder can evolve into ADHD: Case illustrations. J Autism Dev Disord 35:525–534, 2005.

Findling RL, Youngstrom EA, Fristad MA, Birmaher B, Kowatch RA, Arnold LE, Frazier TW, Axelson D, Ryan N, Demeter CA, Gill MK, Fields B, Depew J, Kennedy SM, Marsh L, Rowles BM, Horwitz SM: Characteristics of children with elevated symptoms of mania: The Longitudinal Assessment of Manic Symptoms (LAMS) study. J Clin Psychiatry 71:1664–1672, 2010.

Frazier TW, Youngstrom EA, Haycook T, Sinoff A, Dimitriou F, Knapp J, Sinclair L: The effectiveness of medication combined with intensive behavioral intervention for reducing aggression in youth with autism spectrum disorder. J Child Adolesc Psychopharmacol 20:167–177, 2010.

Goin-Kochel R, Myers B, MacKintosh V. Parental reports on the use of treatments and therapies for children with autism spectrum disorders. Res Autism Spectrum Disord 1:195–209, 2007.

Green VA, Pituch KA, Itchon J, Choi A, O'Reilly M, Sigafoos J: Internet survey of treatments used by parents of children with autism. Res Dev Disabil 27:70–84, 2006.

Hellings JA, Weckbaugh M, Nickel EJ, Cain SE, Zarcone JR, Reese RM, Hall S, Ermer DJ, Tsai LY, Schroeder SR, Cook EH: A double-blind, placebo-controlled study of valproate for aggression in youth with pervasive developmental disorders. J Child Adolesc Psychopharmacol 15:682–692, 2005.

Huffman LC, Sutcliffe TL, Tanner IS, Feldman HM: Management of symptoms in children with autism spectrum disorders: A comprehensive review of pharmacologic and complementary-alternative medicine treatments. J Dev Behav Pediatr 32:56–68, 2011.

Hus V, Pickles A, Cook EH, Risi S, Lord C: Using the autism diagnostic interview-revised to increase phenotypic homogeneity in genetic studies of autism. Biol Psychiatry 61:438–448, 2007.

Lee DO, Ousley OY: Attention-deficit hyperactivity disorder symptoms in a clinic sample of children and adolescents with pervasive developmental disorders. J Child Adolesc Psychopharmacol 16: 737–746, 2006.

LoVullo SV, Matson JL: Comorbid psychopathology in adults with autism spectrum disorders and intellectual disabilities. Res Dev Disabil 30:1288–1296, 2009.

MacNeil B, Lopes V, Minnes P: Anxiety in children and adolescents with autism spectrum disorders. Res Autism Spectrum Disord 3:1–21, 2009.

Mandell DS, Morales KH, Marcus SC, Stahmer AC, Doshi J, Polsky DE: Psychotropic medication use among Medicaid-enrolled children with autism spectrum disorders. Pediatrics 121:e441–e448, 2008.

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.

Martin A, Scahill L, Klin A, Volkmar FR: Higher-functioning pervasive developmental disorders: Rates and patterns of psychotropic drug use. J Am Acad Child Adolesc Psychiatry 38:923–931, 1999.

Matson JL, Neal D: Seizures and epilepsy and their relationship to autism spectrum disorders. Res Autism Spectrum Disord 3:999–1005, 2009.

McCracken JT, McGough J, Shah B, Cronin P, Hong D, Aman MG, Arnold LE, Lindsay R, Nash P, Hollway J, McDougle CJ, Posey D, Swiezy 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 C: Current and emerging therapeutics of autistic disorder and related pervasive developmental disorders. In: Neuropsychopharmacology: The Fifth Generation of Progress, edited by K.L. Davis, D. Charney, J.T. Coyle, and C. Nemeroff. Philadelphia: Lippincott Williams and Wilkins, 565–576, 2002.

McFarlane J, Kanaya T: What does it mean to be autistic? Inter-state variation in special education criteria for autism services. J Child Fam Stud 18:662–669, 2009.

Mendenhall AN, Demeter CA, Findling RL, Frazier TW, Fristad MA, Youngstrom EA, Arnold LE, Birmaher B, Gill MK, Axelson D, Kowatch RA, Horwitz SM: Factors Influencing Mental Health Service Utilization by Children with Serious Emotional and Behavioral Disturbance: Results from the LAMS Study. Psychiatr Serv 62:650–658, 2011.

Myers SM, Johnson CP: Management of children with autism spectrum disorders. Pediatrics 120:1162–1182, 2007.

Naar-King S, Templin T, Wright K, Frey M, Parsons JT, Lam P: Psychosocial factors and medication adherence in HIV-positive youth. Aids Patient Care STDS 20:44–47, 2006.

Nickels K, Katusic SK, Colligan RC, Weaver AL, Voigt RG, Barbaresi WJ: Stimulant medication treatment of target behaviors in children with autism: A population-based study. J Dev Behav Pediatr 29:75–81, 2008.

Oswald DP, Sonenklar NA: Medication use among children with autism spectrum disorders. J Child Adolesc Psychopharmacol 17: 348–355, 2007.

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.

Pumariega AJ, Glover S, Holzer CE 3rd, Nguyen H: Administrative update: Utilization of services. II. Utilization of mental health services in a tri-ethnic sample of adolescents. Community Ment Health J 34:145–156, 1998.

Research Units on Pediatric Psychopharmacology Autism Network: Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. Arch Gen Psychiatry 62:1266–1274, 2005.

Rizzo CJ, Esposito-Smythers C, Swenson L, Birmaher B, Ryan N, Strober M, Chiappetta L, Valeri S, Hunt J, Axelson D, Leonard H, Keller M: Factors associated with mental health service utilization among bipolar youth. Bipolar Disord 9:839–850, 2007.

Rosenberg RE, Mandell DS, Farmer JE, Law JK, Marvin AR, Law PA: Psychotropic medication use among children with autism spectrum disorders enrolled in a National Registry, 2007–2008. J Autism Dev Disord, 2009.

Santosh PJ, Baird G, Pityaratstian N, Tavare E, Gringras P: Impact of comorbid autism spectrum disorders on stimulant response in children with attention deficit hyperactivity disorder: A retrospective and prospective effectiveness study. Child Care Health Dev 32:575–583, 2006.

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–e641, 2004.

Souders MC, Mason TB, Valladares O, Bucan M, Levy SE, Mandell DS, Weaver TE, Pinto-Martin J: Sleep behaviors and sleep quality in children with autism spectrum disorders. Sleep 32:1566–1578, 2009.

SRI International: National Longitudinal Transition Study II (NLTS2) Sampling Plan. Menlo Park, CA: SRI International, 2000.

StataCorp: Stata Statistical Software: Release 11. College Station, TX: StataCorp LP, 2009.

Tsai LY: Psychopharmacology in autism. Psychosom Med 61:651–665, 1999.

U.S. Department of Special Education OSEP: Children with ADD/ADHD Topic Brief: Adding ''ADD/ADHD'' to the List of Eligible Conditions Under ''OHI.'' Washington, D.C: U.S. Department of Special Education OSEP, 2007.

Vaughn ML, Riccio CA, Hynd GW, Hall J: Diagnosing ADHD (predominantly inattentive and combined type subtypes): Discriminant validity of the behavior assessment system for children and the achenbach parent and teacher rating scales. J Clin Child Psychol 26:349–357, 1997.

Wagner M, Kutash K, Duchnowski AJ, Epstein MH: The Special Education Elementary Longitudinal Study and the National Longitudinal Transition Study: Study designs and implications for children and youth with emotional disturbance. JEmotion Behav Disord 13:25–41, 2005.

Williams PL, Storm D, Montepiedra G, Nichols S, Kammerer B, Sirois PA, Farley J, Malee K: Predictors of adherence to antiretroviral medications in children and adolescents with HIV infection. Pediatrics 118:e1745–e1757, 2006.

Wisniewski T, Brimacombe MB, Ming X: Pharmaceutical treatment studies in autism and ADHD: A design based review of study quality. J Pediatr Neurol 5:189–197, 2007.

Witwer A, Lecavalier L: Treatment incidence and patterns in children and adolescents with autism spectrum disorders. J Child Adolesc Psychopharmacol 15:671–681, 2005.

Wolraich ML, Lambert EW, Baumgaertel A, Garcia-Tornel S, Feurer ID, Bickman L, Doffing MA: Teachers' screening for attention deficit/hyperactivity disorder: Comparing multinational samples on teacher ratings of ADHD. J Abnorm Child Psychol 31:445–455, 2003.

Zafeiriou DI, Ververi A, Vargiami E: Childhood autism and associated comorbidities. Brain Dev 29:257–272, 2007.

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