Published in final edited form as:

Am J Drug Alcohol Abuse. 2012 January ; 38(1): 93–100. doi:10.3109/00952990.2011.600395.

Attention-Deficit/Hyperactivity Disorder Subtypes in Adolescents with Comorbid Substance-Use Disorder

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Abstract

Background—Little is known about the relationship between attention-deficit/hyperactivity disorder (ADHD) subtypes and substance-use disorder (SUD). As there is literature suggesting different subtype phenotypes, there may be subtype differences in regard to the risk for developing SUD and substance treatment response.

Objectives—To characterize the sample in a Clinical Trials Network (CTN) study according to ADHD subtypes and baseline psychosocial and substance-use characteristics and to compare subtypes on response to treatment.

Methods—Secondary analyses on data collected from adolescents ($n = 276$) diagnosed with ADHD and SUD (non-nicotine) and treated with stimulant medication or placebo and cognitive behavioral therapy (CBT) for substance use. Participants were characterized as inattentive or combined ADHD subtype and compared on baseline characteristics and treatment outcome.

Results—The combined subtype presented with more severe SUDs and higher rates of conduct disorder. There were a greater proportion of boys with inattentive subtype. The inattentive subtype appeared less ready for treatment (greater University of Rhode Island Change Assessment precontemplation scores) with poorer coping skills (poorer problem-solving and abstinence focused coping) at baseline. However, the two subtypes responded equally to treatment even after controlling for baseline differences.

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Declaration of Interest

Drs. Tamm and Nakonezny report no biomedical financial interests or potential conflicts of interest. *Financial disclosure*: McNeil provided active medication and matching placebo for the CTN 0028 study.

Conclusions—Findings from this large community sample indicate that there were no subtype differences in treatment response, although there were differences in terms of substance use, antisocial behavior, readiness for treatment, and gender prior to treatment.

Scientific Significance—This study is the first to report on subtype differences for treatment response for non-nicotine SUD in a comorbid ADHD-SUD population. Despite some baseline differences, both subtypes responded equally to treatment, suggesting limited relevance for subtype designation on treatment planning.

Keywords

ADHD inattentive subtype; ADHD combined subtype; substance-use disorder

INTRODUCTION

Studies have shown that the comorbidity of attention-deficit/hyperactivity disorder (ADHD) and substance-use disorder (SUD) in adolescents ranges from 16% (population studies) to 25–40% (clinical populations) (1). The presence of ADHD may affect the course of adolescent substance abuse in several ways, including increased likelihood of an earlier age of onset, longer duration of SUD, and progression from alcohol abuse to another drug-use disorder. Individuals with ADHD are also at greater risk for treatment failure as their disruptive behaviors interfere with treatment access, compliance, and response.

While there is a strong relationship between ADHD and SUD, less is known about the relationship of ADHD subtypes (i.e., inattentive, combined, and hyperactive-impulsive) and SUD. The inattentive subtype is characterized by inattention, distractibility, disorganization, forgetfulness, and lethargy, while the hyperactive-impulsive subtype is characterized by hyperactivity and/or impulsiveness (e.g., interrupting, difficulty waiting turn, fidgetiness). The combined subtype, most commonly represented in studies of ADHD, includes both inattentive and hyperactive-impulsive symptoms. There are few studies investigating the hyperactive-impulsive subtype, which is much less prevalent, and there are significant concerns regarding its validity (2). However, there is a burgeoning literature suggesting different phenotypic profiles for the ADHD inattentive and combined subtypes including different patterns of psychiatric comorbidity (e.g., (3)), gender ratios (e.g., (4)), and response to medication (e.g., (5)). For example, the inattentive subtype has been shown to respond to lower doses of stimulant medication than the combined subtype (5). These two subtypes have also been characterized by different neuropsychological profiles (e.g., (2)), with the combined subtype showing a disinhibited/impulsive response style, and the inattentive subtype showing a sluggish cognitive tempo. Recent literature suggests a relationship between cognitive functioning and SUD treatment outcomes (6). Impaired executive functioning was found to be more predictive of tobacco use than behavioral activity (7), while better cognitive functioning has been associated with greater treatment gains (8). Therefore, there may be a different pattern of substance use and/or response to treatment between the inattentive and combined subtypes.

The literature investigating the association between ADHD subtypes and SUDs is mixed. Some studies do not report a significant relationship (e.g., (3)), while others have suggested that hyperactive/impulsive symptoms are more associated with risk for SUDs (e.g., (9)) than inattentive symptoms (10). A prospective study showed that hyperactivity/impulsivity predicted initiation of all types of substance use and that relationships between inattention and substance outcomes disappeared when hyperactivity/impulsivity and conduct disorder were controlled (except nicotine dependence) (9). Furthermore, a study in adults with ADHD reported that the combined subtype had a higher incidence of lifetime SUDs than the inattentive subtype (11), suggesting greater contribution of hyperactive/impulsive

symptoms. Other studies report differences between the subtypes and types of SUDs. For example, hyperactivity/impulsivity has been associated with earlier smoking and illicit drug use (12), alcohol use (13), dependence (14), and cocaine dependence (15). In contrast, inattention has been associated with early illicit drug use, frequency and recency of alcohol and marijuana use, and heavier cigarette use (12), tobacco (13) and marijuana use, and nicotine dependence (16). Thus, the findings are inconclusive.

There is a dearth of research investigating the relationship between ADHD and SUD in regard to treatment outcomes, with even less known about the relationship of ADHD subtype and substance treatment outcomes. Arguably, individuals with the combined or hyperactive-impulsive types, types characterized by poor judgment and impulsivity, may be more vulnerable to treatment drop-out and relapse. One study reported that the inattentive subtype was more amenable to treatment for nicotine addiction while the hyperactive-impulsive subtype had lower abstinence rates (14). No other literature was found investigating whether ADHD subtypes and SUD are associated with differential treatment response for ADHD or substance-use outcomes and/or describing demographic/clinical characteristics of adolescents with co-occurring ADHD-SUD. Thus, the relevance of ADHD subtypes as predictors of SUD or ADHD treatment outcomes remains unexplored.

A study performed in the Clinical Trials Network (CTN) funded by the National Institute on Drug Abuse entitled Osmotic-Release Methylphenidate (OROS-MPH) for ADHD in Adolescents with SUD (CTN0028) evaluated the efficacy of OROS-MPH, relative to placebo, in treating ADHD and decreasing substance use in adolescents with ADHD-SUD. All participants received weekly cognitive behavioral therapy (CBT) focusing on SUD. CBT consisted of approximately one 60-minute session per week during study weeks 1–16 and focused on the treatment of the adolescent's SUD. The CBT manual utilized was based a manual that was developmentally adapted for adolescents from a standard, published, empirically supported adult CBT manual (17). It was not adapted for ADHD. Motivational enhancement techniques were used in conjunction with behavioral and cognitive behavioral techniques to help adolescents reduce their drug use by improving coping strategies and problem-solving and decision-making skills. Results of the primary study showed that both medication and placebo groups had significant reductions in ADHD and substance-use outcomes and will be reported elsewhere (18). The study provides an excellent opportunity to investigate the ADHD subtypes in a comorbid ADHD-SUD population.

The current report is designed to answer questions from CTN0028 data: (1) Are there baseline differences in the demographic and clinical characteristics, as well as patterns of substance use, between the inattentive and combined ADHD subtypes? (2) Are the subtypes associated with differential treatment response (medication response, substance-use outcomes)? Given the inconclusive findings regarding the subtypes and SUD and the scant previous literature on treatment response as a function of subtype, we did not have specific hypotheses regarding the direction of findings.

METHODS

Participants for CTN0028 were 303 adolescents (ages 13–19) recruited by substance abuse treatment programs affiliated with the CTN. Study protocols and consent forms were approved by the Institutional Review Board of the academic center with which each community treatment program was affiliated. Inclusion criteria included meeting diagnostic criteria for ADHD and at least one non-tobacco SUD. Substance abuse/dependence diagnoses were assessed using the Composite International Diagnostic Interview which utilizes DSM-IV criteria to define Abuse and Dependence. Exclusion criteria were current or past psychotic disorder, bipolar disorder, suicide risk, opiate dependence, methamphetamine

abuse/dependence, cardiac or serious medical illness, pregnancy, past month use of psychotropic medications or participation in other substance or mental health treatment. Diagnoses of ADHD, Conduct Disorder, and Major Depression were determined by the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiological Version (K-SADS-E).

The average age was 16.5 years ($SD = 1.3$) and ethnic distribution was Caucasian (62%), African-American (22%), Hispanic (15%), or Mixed/Other (16%); 33% of the participants were court-ordered to treatment, and 13% met criteria for comorbid Major Depression. The average dose prescribed at the end of treatment was 68 mg ($SD = 15$ mg). Additional information regarding sample characteristics is provided in Table 1.

Consistent with DSM-IV (19) criteria, participants were characterized as inattentive subtype if they met criteria for 6 inattentive symptoms and did not have 6 hyperactive-impulsive symptoms (13 subjects were excluded because they did not meet for a subtype). Too few subjects met criteria for the hyperactive-impulsive subtype and were excluded from further analysis ($n = 14$). The sample for the present secondary analyses included 103 participants with the inattentive subtype and 173 with the combined subtype. However, there are concerns that the literature regarding ADHD subtypes is confounded by variation in the definition of predominantly inattentive type, which might include individuals with clinically significant inattentive symptoms but no hyperactive/impulsive behaviors and individuals with similar inattentive symptoms and substantial but subthreshold hyperactive/impulsive behaviors (2,20). Therefore, in addition to subtyping according to DSM-IV criteria, we conducted additional analyses on more strictly defined subtypes (i.e., strict inattentive subtype with 6 inattention symptoms and 3 hyperactive-impulsive symptoms; strict combined type with 6 inattention symptoms and 8 hyperactive-impulsive symptoms) to address potential concerns regarding overlap in the samples (20). There were 52 individuals meeting stricter definition of inattentive subtype and 97 individuals meeting the stricter definition of combined subtype.

Measures

ADHD treatment response was assessed with the adolescent-completed DSM-IV ADHD Rating Scale (ADHD-RS) (21) and the Clinical Global Impression-Improvement (CGI-I) rating scale. The ADHD-RS was completed weekly, referencing symptoms in the past week. The CGI-I was completed monthly by blinded study clinicians. ADHD treatment response was defined a priori as a final CGI-I score of very much improved or much improved in comparison to baseline ADHD severity. Measures of substance use included self-report of substance use and urine toxicology results. The number of substance-use days was assessed using standardized timeline follow-back (TLFB) procedures. A rapid urine screen for amphetamine, barbiturates, benzodiazepines, cocaine, methamphetamine, opiates, and THC was collected weekly, with the outcome of interest being the mean number of negative urine drug screens weekly (avoiding problems associated with imputing positive urine drug screen results for missed visits).

The University of Rhode Island Change Assessment (URICA) (22) was used to assess motivation to change substance-use behaviors. Four scales are derived: Pre-contemplation, Contemplation, Action, and Maintenance; a Readiness score which combines these scales was also used. The Adolescent Relapse Coping Questionnaire (ARCQ) (23) was used to assess skills for coping with temptations to use substances and provides a cognitive appraisal of relapse risk situations including motivation and confidence for abstinence.

Analytic Approach

To investigate subtype differences at baseline, we used independent sample *t*-tests, with the Satterthwaite method for unequal variances and χ^2 statistic or, when appropriate, Fisher's exact test. The likelihood ratio χ^2 test, in a negative binomial regression model (a generalization of the Poisson model for overdispersed count data), was used to test for differences between the subtypes on each count variable (e.g., days of substance use). Odds ratios were estimated for each baseline SUD by ADHD subtype using simple logistic regression. The likelihood ratio χ^2 statistic was used to test for a significant association between each SUD and ADHD subtype. We utilized the same analytic strategies for the analyses with the stricter subtype definitions.

To investigate subtype differences for treatment outcome, 2 (Group: inattentive, combined) $\times$ 2 (Treatment: OROS, placebo) linear model analysis of covariance (ANCOVA) was used to examine the ADHD-RS scores at week 16, while controlling for the baseline score. We also conducted exploratory analyses to investigate whether subtype differences at baseline contributed to treatment outcome. Specifically, separate 2 (Group: inattentive, combined) $\times$ 2 (Treatment: OROS, placebo) ANCOVA models (ADHD-RS) or negative binomial regression models (days substance use, cigarettes per day) were carried out for the outcome variables with covariates in the model: respective baseline score and (1) gender, (2) conduct disorder, (3) number of dependence diagnoses, (4) problem solving, and (5) precontemplation. We utilized the same analytic strategies for the analyses with the stricter subtype definitions.

All statistical analyses used SAS, version 9.2 (SAS Institute Inc., Cary, NC, USA). Cohen's *d* was interpreted as an effect size estimator. The level of significance was set at $\alpha = .05$ (two-tailed) and, because this article is an exploratory one, we did not correct for multiple testing.

RESULTS

Baseline Comparisons

The subtypes did not differ with regard to age [$t(274) = .35$] or ethnicity [$\chi^2(1) = 1.71$]. The combined subtype had higher rates of conduct disorder. The inattentive type had a higher proportion of males (Table 1). The combined subtype had significantly more inattentive [$M = 8.2$, $SD = 1.0$; $t(274) = -2.7$, $p = .008$] and hyperactive-impulsive [$M = 7.6$, $SD = 1.1$; $t(274) = -27.6$, $p = .000$] symptoms than the inattentive subtype (inattentive symptoms $M = 7.9$, $SD = 1.1$, hyperactive-impulsive symptoms $M = 3.3$, $SD = 1.5$). No differences were observed for days of substance use, cigarettes per day, or urinalyses (Table 1). The combined type had higher URICA maintenance scores while the inattentive subtype had significantly higher precontemplation scores. Further, the inattentive subtype had significantly lower problem-solving and abstinence-focused coping scores on the ARCQ. The combined subtype had more dependence diagnoses, including higher rates of alcohol and cocaine dependence, whereas the inattentive subtype had higher rates of alcohol abuse (Table 2).

For the analyses utilizing stricter subtype definitions, the pattern of results did not markedly differ (see Tables 1 and 2). While some findings became less significant, this was likely due to the decrease in power. Two findings which became significant (that were not significant in the DSM-IV subtype analyses) were that the strictly defined combined type had higher ARCQ self-critical and URICA contemplation scores than the strictly defined inattentive type.

Outcome Comparisons

At the end of treatment, the subtypes did not differ on ADHD ratings, number of negative urine samples, number of substance-use days (of last 28 rated at week 16), number of cigarettes per day, ratings of improvement (CGI-I), or number of counseling sessions attended (Table 3). Exploratory ANCOVAs and negative binomial regressions for count variables investigating the association of baseline differences (gender, comorbid conduct disorder, number of substance abuse diagnoses, URICA precontemplation, and ARCQ problem-solving and abstinence-focused coping scores) with ADHD symptoms, number of substance-use days, and cigarettes per day were all nonsignificant. For the analyses utilizing stricter subtype definitions, the pattern of results was the same (see Table 3).

DISCUSSION

In this sample of adolescents diagnosed with comorbid ADHD and nonnicotine SUD, both ADHD subtypes (inattentive and combined) showed a similar response to treatment. The combined subtype had more severe substance dependence disorder and higher rates of conduct disorder relative to the inattentive subtype. There was also evidence that they were more ready for treatment than the inattentive type. Exploratory analyses showed that baseline differences were not associated with ADHD or substance-use outcomes. Furthermore, the pattern of results did not differ when stricter subtype definitions (controlling for the number of hyperactive-impulsive symptoms) were utilized. Thus, based upon our sample referred by community treatment programs for substance use, it appears the subtypes have little apparent clinical relevance for treatment. However, it may be important for clinicians to anticipate higher rates of substance dependence diagnoses, particularly alcohol and cocaine, in the combined subtype of adolescents seeking substance-use treatment.

The most clinically significant result of this study is the finding that the two subtypes did not differ in response to treatment. No subtype differences in treatment outcome emerged for ADHD symptoms, CGI-I, days of substance use, number of negative urine samples, or treatment compliance, even after controlling for baseline subtype differences. This was unexpected given reports that the inattentive subtype requires lower doses and responds better to OROS-MPH than the combined subtype in samples without SUD (5). The lack of subtype differences may have been partly due to higher coping skills (ARCQ) and being further along in the treatment process in the combined subtype (e.g., reports of more behaviors related to promoting abstinence and avoiding relapse on the URICA maintenance scale) and less readiness for treatment in the inattentive subtype at baseline. For example, studies have shown that being in the URICA precontemplation stage is related to attrition from substance abuse treatment (24) while being in the URICA maintenance stage is related to treatment retention and negative drug screens (25). Less research has been done with the ARCQ, although positive coping strategies have been associated with less substance use following inpatient hospitalization for SUD treatment and poorer coping strategies with risk for relapse (26). However, the URICA and ARCQ variables did not emerge as significant covariates. Alternatively, the lack of differences may have resulted from our treatment approach which involved ramping all participants up to the maximum FDA-approved dose and providing all participants high-quality CBT which is known to improve ADHD (27) and SUD (28) outcomes. The high-quality treatment might have overcome the potential differential treatment response based on subtype. Regardless, the current findings indicate the two subtypes respond equally to treatment for both ADHD and SUD outcomes. This was surprising given that we would anticipate worse outcomes for individuals with more severe SUDs particularly in conjunction with higher rates of antisocial behaviors.

The higher rate of comorbid conduct disorder in the combined subtype is consistent with literature reporting more externalizing behavior in the combined subtype in the non-substance using ADHD population (29). Somewhat surprisingly, our sample included a larger proportion of males with the inattentive subtype given reports that females are more likely to present with the inattentive subtype (30). However, not all studies report gender differences in the ADHD subtypes (31), and subtype gender differences do not appear to affect treatment outcome (32).

The greater rate of cocaine and alcohol dependence in the combined subtype is consistent with the literature reporting subtype differences (11,13–15). The almost equal rates of cannabis abuse/dependence and nicotine use were somewhat unexpected given findings that the inattentive group had higher rates of cannabis abuse/dependence (13) and nicotine use (12,13). This may be because there were more males in the inattentive group, since females have been reported to have higher rates of cannabis dependence (33). Alternatively, the fact that the subtypes in our sample differed in rates of inattention symptoms (combined subtype had more) may account for not finding greater nicotine/cannabis use in the inattentive subtype. The higher numbers of alcohol abuse cases in the inattentive subtype, relative to higher rates of alcohol dependence in the combined subtype, suggest less severe alcohol use in the inattentive subtype.

Our sample is one of the largest to date to investigate subtype differences in a comorbid ADHD-SUD community sample and included individuals with a broad range of SUDs. A potential limitation was the use of unadjusted *p*-values reflecting the exploratory nature of the study. In addition, our ability to assess treatment efficacy is limited by the fact that there was no “no treatment” or “stimulant medication only” treatment groups in the primary study; all participants received CBT. The combined subtype includes both symptoms of inattention and hyperactivity-impulsivity precluding the ability to investigate the independent contribution of hyperactive-impulsive symptoms. However, the predominantly hyperactive-impulsive subtype is increasingly coming under scrutiny as to its validity, and much of the literature reporting ADHD subtype differences is comparing the inattentive to combined type. It might be argued that the criteria used to define the subtypes (<6 hyperactive-impulsive symptoms for inattentive type and >5 hyperactive-impulsive symptoms for the combined type) may have separated out individuals who may have differed very little from one another. The fact that the pattern of results remained consistent even when utilizing stricter subtyping procedures suggests that this concern is not as relevant, at least for this sample.

CONCLUSION

These data suggest that there were important differences at baseline between the ADHD subtypes, with the combined subtype presenting with more severe substance dependence disorder, higher rates of antisocial behavior, and less readiness for treatment than the inattentive type. Both inattentive and combined subtypes of ADHD with comorbid SUD responded equally to treatment. Consequently, subtype designation may not be as relevant when assessing treatment needs for an adolescent with comorbid ADHD-SUD.

Acknowledgments

Dr. Riggs is supported by grants U10 DA012732 and NIDA K12 DA 000357; Dr. Adinoff by grants U10 DA012732 and CTN U10DA020024; and Dr. Winhusen by grant U10-DA013732.

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TABLE 1

Subtype comparisons at baseline.

	DSM-IV inattentive (<i>n</i> = 103)	DSM-IV combined (<i>n</i> = 173)	Statistical test	<i>d</i>	Strict inattentive (<i>n</i> = 52)	Strict combined (<i>n</i> = 97)	Statistical test	<i>d</i>
Mean abuse diagnoses	.96 (1.18)	.88 (1.03)	$\chi^2(1) = .33, p = .56$	.07	1.09 (1.33)	.85 (1.04)	$\chi^2(1) = 1.55, p = .21$	.20
Mean dependence diagnoses	.99 (.79)	1.21 (.93)	$\chi^2(1) = 3.93, p = .04$	.24	.94 (.80)	1.20 (.94)	$\chi^2(1) = 2.17, p = .14$	.24
Mean days substance use	13.7 (8.81)	15.5 (9.89)	$\chi^2(1) = 1.60, p = .20$	.15	12.82 (8.36)	15.64 (9.85)	$\chi^2(1) = 2.32, p = .12$	.25
Mean cigarettes per day	6.1 (7.7)	5.9 (7.8)	$\chi^2(1) = .02, p = .89$	.02	5.29 (6.80)	4.73 (6.09)	$\chi^2(1) = .17, p = .67$	.06
Positive urinalysis	<i>n</i> = 74 (72%)	<i>n</i> = 127 (73%)	$\chi^2(1) = .02, p = .87$	.02	<i>n</i> = 38 (73%)	<i>n</i> = 72 (74%)	$\chi^2(1) = .02, p = .87$	.02
Gender								
Male	<i>n</i> = 89 (86%)	<i>n</i> = 128 (74%)	$\chi^2(1) = 5.92, p = .01$	.30	<i>n</i> = 45 (86.5%)	<i>n</i> = 64 (66%)	$\chi^2(1) = 7.28, p = .007$	.45
Female	<i>n</i> = 14 (14%)	<i>n</i> = 45 (26%)			<i>n</i> = .07 (13.5%)	<i>n</i> = 33 (34%)		
ADHD score	34.6 (8.0)	42.2 (8.1)	$t(274) = -7.57, p = .0001$	.94	32.2 (7.5)	44.7 (7.2)	$t(147) = -9.92, p < .0001$	1.7
Comorbid conduct disorder	<i>n</i> = 26 (25%)	<i>n</i> = 64 (37%)	$\chi^2(1) = 4.06, p = .04$	.24	<i>n</i> = 16 (31%)	<i>n</i> = 42 (43%)	$\chi^2(1) = 2.23, p = .13$	.24
ARCQ								
Problem solving	45.6 (17.2)	50.8 (17.0)	$t(274) = -2.46, p = .01$	.30	44.2 (17.3)	50.8 (17.3)	$t(147) = -2.24, p = .02$	.38
Self-critical	23.3 (10.4)	25.4 (9.4)	$t(274) = -1.71, p = .08$	.21	22.2 (9.5)	26.7 (8.7)	$t(147) = -2.91, p = .004$	.50
Abstinence-focused coping	29.8 (12.4)	34.0 (12.6)	$t(274) = -2.74, p = .006$	.34	29.8 (12.7)	33.8 (12.3)	$t(147) = -1.86, p = .06$	.32
URICA								
Precontemplation	2.7 (.7)	2.5 (.6)	$t(174) = 1.92, p = .05$	.24	2.7 (.8)	2.5 (.5)	$t(73.2) = 1.96, p = .05$	.33
Contemplation	3.6 (.7)	3.7 (.6)	$t(184) = -1.03, p = .30$	.12	3.5 (.8)	3.8 (.6)	$t(77.7) = -2.27, p = .03$	.39
Action	3.6 (.7)	3.6 (.6)	$t(274) = -.54, p = .59$	.06	3.5 (.7)	3.7 (.7)	$t(147) = -1.44, p = .15$	.24
Maintenance	3.0 (.7)	3.2 (.7)	$t(274) = -2.00, p = .05$	.24	3.0 (.7)	3.3 (.7)	$t(147) = -2.39, p = .02$	.41
Readiness for change	7.5 (2.3)	8.0 (1.9)	$t(185) = -1.72, p = .08$	.21	7.3 (2.6)	8.3 (1.9)	$t(80.51) = -2.47, p = .01$	.42

Notes: DSM-IV, Diagnostic and Statistical Manual, 4th Edition; ARCQ = Adolescent Relapse Coping Questionnaire, URICA, University of Rhode Island Change Assessment. Sample means (SD) are reported for the ADHD, ARCQ, and URICA variables. The geometric means (SD) – exponentiation of the LS means on the log scale – are reported for the count-substance-use variables.

¹Likelihood ratio χ^2 test in a negative binomial regression model. *d* = Cohen's *d* was calculated and interpreted as the effect size estimator.

²Two independent sample *t*-test, with Satterthwaite method for unequal variances.

TABLE 2

Odds ratios for baseline SUD and ADHD subtype.

Baseline SUD	DSM-IV subtype results				Strict subtype results			
	Odds ratio	95% CI	χ^2	p	Odds ratio	95% CI	χ^2	p
Alcohol abuse	.56	.33-.96	4.44	.03	.49	.24-1.01	3.66	.05
Alcohol dependence	1.97	1.12-3.55	5.63	.02	1.97	.90-4.62	2.85	.09
Opioid abuse	1.84	.85-4.33	2.42	.12	1.32	.44-3.99	.26	.61
Cannabis abuse	.93	.53-1.64	.06	.80	.84	.39-1.85	.18	.66
Cannabis dependence	1.10	.65-1.85	.14	.70	1.18	.57-2.41	.20	.64
Sedative abuse	.88	.35-2.33	.06	.79	.50	.16-1.54	1.48	.22
Sedative dependence	1.19	.31-5.77	.06	.80	1.62	.20-33.35	.18	.66
Cocaine abuse	.34	.08-1.48	2.13	.14	.52	.06-4.49	.39	.53
Cocaine dependence	6.23	1.75-39.62	9.05	.002	6.52	1.21-52.01	4.98	.02
Amphetamine abuse	.73	.19-3.03	.19	.65	.26	.01-2.78	1.27	.25
Amphetamine dependence	1.80	.22-36.63	.28	.59	Poor fit		Poor fit	
Hallucinogen abuse	1.64	.65-4.72	1.07	.29	1.87	.54-8.66	.93	.33
Hallucinogen dependence	.58	.17-1.90	.83	.36	.34	.04-2.14	1.35	.24

Note: 95% CI = Profile Likelihood Confidence Interval for Odds Ratios; χ^2 = Likelihood Ratio Chi-Square Statistic. Odds ratio >1.0 reflects Combined > Inattentive and Strict Combined > Strict Inattentive.

TABLE 3

Subject characteristics at week 16.

	DSM-IV inattentive (<i>n</i> = 102)	DSM-IV combined (<i>n</i> = 169)	Statistical test	Strict inattentive (<i>n</i> = 52)	Strict combined (<i>n</i> = 97)	Statistical test
ADHD Rating Scale						
OROS-MPH	16.8 (1.7)	18.9 (1.3)	Treatment: $F(1,199) = 0, p = .96$	19.9 (2.6)	18.4 (2.1)	Treatment: $F(1,105) = .07, p = .79$
Placebo	19.1 (1.8)	16.5 (1.6)	Group: $F(1,199) = .02, p = .90$ G $\times$ T: $F(1,199) = 2.1, p = .14$	22.8 (3.1)	16.8 (2.1)	Group: $F(1,105) = 1.57, p = .21$ G $\times$ T: $F(1,105) = .93, p = .34$
Responder (CGI-I <3)						
No	<i>n</i> = 59 (75%)	<i>n</i> = 96 (77%)	$\chi^2(1) = .12, p = .73$	<i>n</i> = 30 (77%)	<i>n</i> = 52 (75%)	$\chi^2(1) = .03, p = .85$
Yes	<i>n</i> = 20 (25%)	<i>n</i> = 29 (23%)		<i>n</i> = 09 (23%)	<i>n</i> = 17 (25%)	
Mean number days substance use	8.02 (8.3)	8.43 (9.2)	$\chi^2(1) = .08, p = .78$	7.5 (7.6)	8.1 (9.3)	$\chi^2(1) = .09, p = .76$
Mean number negative urine samples	3.11 (4.3)	3.39 (4.7)	$\chi^2(1) = .14, p = .70$	3.03 (4.3)	3.20 (4.5)	$\chi^2(1) = .03, p = .86$
Mean number cigarettes per day	4.7 (6.6)	3.8 (5.5)	$\chi^2(1) = .82, p = .36$	3.6 (6.0)	3.3 (5.3)	$\chi^2(1) = .04, p = .83$
Mean number counseling sessions attended	10.5 (3.6)	9.8 (4.0)	$\chi^2(1) = 1.95, p = .16$	10.2 (3.4)	9.6 (3.9)	$\chi^2(1) = .50, p = .47$

Notes: DSM-IV = Diagnostic and Statistical Manual – 4th Edition; CGI, Clinical Global Impression, G, group; T, treatment.

Least squares means (SE), adjusted for baseline ADHD score, are reported for ADHD outcome at week 16. The geometric means (SD) – exponentiation of the LS means on the log scale – are reported for the count-outcome substance-use variables.

^LLikelihood ratio χ^2 test in a negative binomial regression model.