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Predictors of Treatment Response in Adolescents with Comorbid Substance Use Disorder and Attention-Deficit/Hyperactivity Disorder

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Abstract

Attention-Deficit/Hyperactivity Disorder (ADHD) frequently co-occurs with substance use disorder (SUD) and is associated with poor substance-use treatment outcomes. A trial evaluating osmotic-release oral system methylphenidate (OROS-MPH) for adolescents with ADHD and SUD, concurrently receiving behavioral therapy, revealed inconsistent medication effects on ADHD or SUD. Clinical care for this population would be advanced by knowledge of treatment outcome predictors. Data from the randomized placebo-controlled trial (n=299) were analyzed. Significant treatment predictors included: 1) Substance use severity, associated with poorer ADHD and SUD outcomes, 2) ADHD severity, associated with better ADHD and SUD outcomes, 3) comorbid conduct disorder, associated with poorer ADHD outcomes, and 4) court-mandated status, associated with better SUD outcomes but poorer treatment completion. An interaction effect showed that OROS-MPH improved SUD outcomes in adolescents with comorbid conduct

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disorder compared to placebo. While severe SUD may require more intensive psychosocial treatment, OROS-MPH may improve substance treatment outcomes in adolescents with co-morbid attention and conduct problems.

Keywords

Attention-Deficit/Hyperactivity Disorder; Substance Use Disorder; OROS-MPH; conduct disorder; Predictors of treatment response

1.0 Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common disorders of childhood (Tamm, 2009). The disorder persists into adolescence/adulthood in about half of diagnosed cases, and is associated with significant negative outcomes including substance use, abuse, and dependence (Mannuzza & Klein, 2000; Upadhyaya, et al., 2005). Studies have shown that up to 50% of individuals with continuing ADHD symptoms have a substance-use disorder (SUD) (Sullivan & Rudnik-Levin, 2001). Further, up to one fifth of individuals with an SUD have comorbid ADHD (Wilens, 2007). The presence of ADHD may affect the course of adolescent substance abuse in several ways including predicting an earlier age of onset (Ernst, et al., 2006), longer duration of substance-use disorder, and progression from alcohol abuse to another drug-use disorder (Kousha, Shahrivar, & Alaghband-Rad, 2011; Sullivan & Rudnik-Levin, 2001). Research suggests that individuals with ADHD have a shorter interval between the onsets of drug abuse and drug dependence (Kousha, et al., 2011; Riggs, Mikulich, Whitmore, & Crowley, 1999; Wilens, 2007). Such individuals are also at greater risk for treatment failure, as their disruptive behaviors may interfere with treatment adherence and compliance (Whitmore & Riggs, 2006; Wise, Cuffe, & Fischer, 2001). Adolescents who have co-morbid ADHD and SUD are at greater risk for negative outcomes (Barkley, Murphy, & Fischer, 2008) and may be more difficult to treat than adolescents with only one of the diagnoses.

While there is a need for effective treatments for ADHD in adolescents with co-occurring SUD, little is known about the safety and efficacy of pharmacotherapy for this population. This is partly due to the fact that individuals with comorbid SUD are often excluded from ADHD pharmacotherapy trials due to concerns about potential adverse interactions between medication and drugs/alcohol and concern about potential use and diversion (Whitmore & Riggs, 2006; Winhusen, et al., 2011). A National Institute on Drug Abuse (NIDA) Clinical Trials Network (CTN) study of osmotic-release oral system methylphenidate (OROS-MPH) or placebo, both combined with cognitive behavioral therapy for SUD, addressed this gap as the first clinical trial to evaluate outcomes in adolescents when both ADHD and SUD are treated. This trial, which included adolescents (13–18 years old) meeting diagnostic criteria for ADHD and at least one non-nicotine SUD, revealed that participants in both treatment arms evidenced significant reductions in their ADHD symptoms and past 28-day substance use with no significant difference between treatment groups on the primary outcomes (adolescent self-report of ADHD symptoms and frequency of substance use) but an advantage for OROS-MPH over placebo on secondary outcomes (parent report of ADHD symptoms and negative urine drug screens) (Riggs, et al., 2011). As noted in the research priorities for the National Institutes of Mental Health, identifying predictors of treatment response can advance care for clinical populations (National Institutes of Mental Health, 2010). For the present paper, secondary analyses of the adolescent OROS-MPH dataset were conducted to evaluate baseline characteristics that have been shown to be predictive of OROS-MPH treatment response and of general treatment outcomes. We selected the

following relevant baseline characteristics for predictor analyses: substance use severity, ADHD severity, conduct disorder, and court-mandated status.

Baseline substance use severity is of interest since research with adults has shown that greater substance use severity predicts poorer substance use outcomes in adults (Adamson, Sellman, & Frampton, 2009; Ahmadi, et al., 2009; Timko & Moos, 2002) but research in adolescents has produced mixed results (Crowley, Mikulich, MacDonald, Young, & Zerbe, 1998; Latimer, Newcomb, Winters, & Stinchfield, 2000). ADHD severity as a predictor of treatment outcome also is not clear. In non-SUD samples, ADHD severity has been found to predict worse treatment response for ADHD symptoms. In the multimodal treatment study of ADHD (MTA) study, children (without SUD) with the most severe levels of ADHD before treatment showed under 50% chance of an excellent response with medications, while those with less severe ADHD had a greater than 70% chance of response (Hinshaw, 2007). However, little is known about the impact of ADHD severity on ADHD and substance treatment outcomes in comorbid adolescents. One study suggested that substance use severity at intake did predict severity of substance involvement at follow up but the study was complicated by all participants also having comorbid conduct disorder (Crowley, et al., 1998), precluding examination of the independent effects of substance use severity without conduct disorder..

Court-mandated treatment in adolescents with SUD is proportionally higher than in adults with SUD (Indig, Copeland, & Conigrave, 2008) but most of the literature focuses on mandated treatment in adults. There has been substantial debate over the benefits and shortcomings of mandating individuals to drug treatment. Opponents of this approach argue that motivation is essential for treatment to be effective and that individuals who are forced into treatment are less motivated and show more resistance to being in treatment compared to those who volunteer (Klag, O'Callaghan, & Creed, 2005). Being court ordered to treatment can also be argued as important in motivating participants to start treatment and court-mandated adults have been shown to have better treatment outcomes (Clark & Young, 2009; Goldkamp, White, & Robinson, 2001; Klag, et al., 2005) and to be more likely to remain in treatment (N. S. Miller & Flaherty, 2000).

Finally, conduct disorder is of interest given that ADHD and conduct disorder co-occur in 30% to 50% of cases in both epidemiologic and clinical samples with ADHD (Biederman, Newcorn, & Sprich, 1991). In terms of predicting ADHD treatment response, there is increasing evidence that children with ADHD and conduct disorder tend to have a more impulsive and particularly severe form of ADHD (Newcorn, et al., 2001) and some argue that these children make up a subgroup with a more serious prognosis (Biederman, et al., 1991; Moffitt, 1990; Thompson, Riggs, Mikulich, & Crowley, 1996). Individuals with ADHD and comorbid CD have higher rates of substance use than those with ADHD alone (Harty, Ivanov, Newcorn, & Halperin, 2011). However, children with and without conduct disorder (and ADHD) have shown similar patterns of improvement in response to stimulants with regard to ADHD symptoms (Biederman, et al., 1991; Buitelaar, Van der Gaag, Swaab-Barneveld, & Kuiper, 1995; Loney, Prinz, Mishalow, & Joad, 1978). In the MTA study, 54% of adolescents in the sample showed comorbidity with oppositional defiant disorder and conduct disorder, but this was not a significant moderator of findings for ADHD symptomatology (Hinshaw, 2007; Jensen, et al., 2001). The added comorbidity of SUD in adolescents with conduct disorder has not generally been shown to affect the response to stimulants in regard to ADHD (Thompson, et al., 1996). However, the literature on the impact of conduct disorder on SUD suggests that conduct disorder can be associated with worse SUD outcomes. Follow up studies of children and adolescents with the diagnosis of conduct disorder show a strong predictive pattern of conduct disorder for cigarette smoking, alcoholism, marijuana and hard drug use (Biederman, et al., 1991; Ohannessian, Stabenau,

& Hesselbrock, 1995; Riggs, et al., 1999) and it is suggested that children with comorbid ADHD and conduct disorder or other externalizing disorders have a greater risk for substance abuse than children with ADHD only (August, et al., 2006; Biederman, et al., 1991; Elkins, McGue, & Iacono, 2007; Flory & Lynam, 2003; Thompson, et al., 1996). Earlier conduct disorder onset, more severe conduct disorder and more drug dependence predicted worse outcomes (progression to more severe /chronic addiction and persistence of antisocial behavior) in participants with comorbid conduct disorder and SUD (Crowley, et al., 1998). Conduct disorder does not appear to be a moderator for ADHD outcomes but does appear to worsen substance use outcomes.

For the present analyses, we hypothesized that greater substance use severity at baseline would be associated with poorer treatment outcomes (Adamson, et al., 2009; Ahmadi, et al., 2009; Crowley, et al., 1998) and greater ADHD severity would be associated with poorer treatment outcomes (Buitelaar, et al., 1995; Owens, et al., 2003; Taylor, et al., 1987). We did not have a specific hypothesis for the direction of findings for being court-mandated to treatment as that has been associated with both worse (Lincour, Kuettel, & Bombardier, 2002) and better treatment outcomes (Burke & Gregoire, 2007; Ondersma, Winhusen, & Lewis, 2010). We anticipated poorer SUD outcomes for individuals with comorbid conduct disorder (Crowley, et al., 1998).

2.0 Materials and Methods

2.1 Participants

The participants for the ADHD and SUD study were 303 adolescents (aged 13–18 years) recruited by 11 participating substance abuse treatment programs affiliated with the NIDA CTN. Criteria for study participation included meeting DSM-IV diagnostic criteria for current ADHD and at least one non-tobacco SUD. Exclusion criteria were current or past psychotic disorder, bipolar disorder, suicide risk, opiate dependence, methamphetamine abuse or dependence, cardiac illness or serious medical illness, pregnancy, past month use of psychotropic medications or participation in other substance or mental health treatment. Study protocols and consent forms were approved by the Institutional Review Board of the academic center with which each community treatment program was affiliated. For this paper, we included data from 299 participants (4 children were excluded; 2 did not have a non-tobacco SUD and 2 because they did not meet inclusion criteria for ADHD).

2.2 Procedures

A full description of procedures for the CTN adolescent OROS-MPH trial is described elsewhere (Riggs, et al., 2011). In brief, participants were randomized to OROS-MPH or matching placebo in a 1:1 ratio, stratified by site, and completed by computer at a centralized location. For OROS-MPH, the starting dose of 18 mg/day was escalated during the first two study weeks to a maximum of 72 mg/day or to the highest dose tolerated. The study included a 16 week active treatment phase. All participants were enrolled in concurrent outpatient substance treatment consisting of weekly individual cognitive behavioral therapy. Medication compliance was assessed by pill counts in conjunction with weekly review of subjects' medication diaries and self-reported medication compliance.

2.3 Measures

2.3a Substance use measures—The primary substance use measure was number of days of non-nicotine substance use, including drugs and alcohol, collected for the past 28 days at baseline and weekly throughout the 16 week trial using standardized Timeline Follow-Back (TLFB) procedures (W. R. Miller & Del Boca, 1994; Sobell & Sobell, 1992). Urine drug screens (UDS) were also collected at screening/baseline and weekly throughout

the trial and analyzed based on the number of UDS negative results for drugs of abuse. This approach avoids imputation of a “positive” UDS result if an expected sample is missing (Ling, et al., 1997).

2.3b ADHD measure—The primary outcome measure for ADHD was the DSM IV ADHD-RS symptom checklist (DuPaul, Power, Anastopoulos, & Reid, 1998) administered by blinded medical clinicians with the adolescent at baseline for the prior 28 days, and weekly throughout the study. The scale is medication sensitive and correlated with ADHD in children and adolescents (Bostic, et al., 2000; Prince, et al., 2000).

2.4 Predictor Variables at Baseline

- Substance use severity was defined as number of days of substance use in the past 28 at baseline based on the TLFB. We also examined number of joints smoked per day in the past 28 at baseline and number of standard drinks drank per day in the past 28 at baseline based on the TLFB.
- ADHD severity was assessed using the baseline ADHD-RS score (adolescent self-report)
- Court-mandated to treatment was assessed based on demographic information and was operationalized as a binary indicator (yes/no, with “no” being the reference group).
- Conduct disorder comorbidity based on the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiological Version (K-SADS-E) (Orvaschel, 1994) and was operationalized as a binary indicator (yes/no, with “no” being the reference group). This measure has good reliability for conduct disorder (Chambers, et al., 1985).

2.5 Outcome Variables

- ADHD Change Score: We calculated a change score subtracting ADHD-RS score at outcome (visit 16) from the baseline ADHD-RS score. This is a common outcome variable for the ADHD-RS in pharmacotherapy trials, e.g., (Kollins, et al., 2011; Thurstone, Riggs, Salomonsen-Sautel, & Mikulich-Gilbertson, 2010).
- SUD Responder: This was defined as achieving a 50% reduction in substance use days from baseline to week 16 based on the TLFB in individuals who completed treatment. Thus, for this study, SUD responder status was a binary outcome variable operationally defined as “SUD responder” or “SUD non-responder.” This same definition of treatment response was recently utilized in another secondary analysis paper from the adolescent ADHD and SUD dataset (Gray, et al., 2011) and reflects a clinically meaningful response to treatment. In this study, we modeled the probability of “SUD Responder.”
- Treatment completer was a binary outcome variable operationally defined as completing 11 or more weeks of treatment (i.e., ~70% of treatment sessions) versus non-completer, which was defined as not completing 11 weeks of treatment. In this study, we modeled the probability of “treatment completer.”
- Number of negative urine samples.

2.6 Statistical Analysis

2.6a Demographic and Clinical Characteristics—Demographic and baseline clinical characteristics for the overall sample were described using the sample mean and standard deviation for continuous variables and the frequency and percentage for categorical variables. An independent sample *t*-test (for continuous variables) and Chi-square test (for categorical variables) were used to compare the groups on the various demographics and clinical characteristics.

2.6b Interaction-Effects Models—Multiple logistic regression was used to estimate the odds of SUD responder and treatment completer status with the main effects of Treatment (OROS-MPH vs. Placebo) and Predictor and the Predictor $\times$ Treatment interaction effect included in the model. For the predictor variable that interacts with treatment group (OROS-MPH vs. Placebo), the odds ratios (for each predictor) were estimated at each level of treatment (OROS-MPH vs. Placebo). The 95% Wald confidence intervals were calculated for each odds ratio and the Wald Chi-square statistic was used to test for a significant association between each effect and binary outcome. In addition, separate negative binomial regression models were used to estimate the number of negative urine samples at week 16 (count response variable), with the main effects of Treatment (OROS-MPH vs. Placebo) and Predictor and the Predictor $\times$ Treatment interaction effect included in the model. Further, separate two-way ANOVA models were used to examine ADHD change, with the main effect of Treatment (OROS-MPH vs. Placebo) and Predictor and the Predictor $\times$ Treatment interaction effect included in the model. A separate interaction-effects model was conducted for each predictor on each outcome measure. Models were parameterized for the binary indicators as present vs. absent (i.e., conduct disorder vs no conduct disorder, court ordered vs not court ordered) and at the treatment level of OROS-MPH.

We performed all statistical analyses using SAS software, version 9.2 (SAS Institute, Inc., Cary, NC). The level of significance for all tests was set at $\alpha=.05$ (two-tailed) and, because this is an exploratory paper, we did not correct for multiple testing.

3.0 Results

3.1 Sample Characteristics

The average age was 16.5 years ($SD=1.3$) and the sample was predominantly male (79%). The ethnic distribution was Caucasian (61%), African-American (23%), American Indian/Alaska Native (1%), Asian (1%) or Mixed/Other (14%), with 15% self-designating as Hispanic. Twenty-four percent of the participants were court-mandated to treatment and 32% met criteria for comorbid conduct disorder ($n=48$ in the OROS-MPH group and $n=49$ in the placebo group). The average ADHD-RS Score at baseline (by adolescent self-report) was 38.9 ($SD=8.7$). The average dose of OROS-MPH prescribed at the end of treatment was 68 mg ($SD = 15$ mg). Seventy-five percent of the sample completed treatment. Medication adherence was 86.1% ($SD=19.8$) when defined as percentage of returned pills out of what was expected, and 82.1% ($SD=22.2$) when based on adolescent self-report of medication compliance/medication diaries (i.e., percentage of prescribed pills taken). Average compliance with CBT was 75.7% ($SD=25.0$) based on number of sessions attended of those offered (typically 16). In terms of rates of substance abuse and dependence, the vast majority met criteria for cannabis dependence (66.9%) or abuse (26.4%), followed by alcohol dependence (28.1%) or abuse (28.1%), with much lower rates for other substances (i.e., <10% for sedatives, cocaine, amphetamine, and hallucinogens). It should also be noted that there were no significant differences between OROS-MPH and placebo groups on conduct disorder status, ADHD baseline severity, medication adherence, treatment completion rates, or rates of substance abuse or dependence diagnoses.

We conducted independent sample *t*-tests (for continuous variables) and Chi-square tests (for categorical variables) to evaluate whether there were relationships between the various baseline predictor variables which could potentially confound the findings. We did not find a significant difference in ADHD or SUD baseline severity for individuals with and without conduct disorder or for those who were and were not court ordered to treatment. Similarly, we did not find significant differences in the number of individuals assigned to placebo or OROS-MPH as a function of court ordered status or substance use severity levels.

3.2 Interaction–Effects Models

Results from the interaction effects analyses (examining the interaction of the baseline predictor variables with medication or placebo; Table 1) did not reveal significant predictor by treatment interactions on any outcome variable except for the interaction effect of comorbid conduct disorder by treatment on SUD responder. Participants with comorbid conduct disorder who received OROS-MPH had 3.866 times the predicted odds to achieve a 50% reduction in substance abuse (OR=3.866, 95% CI=1.29–11.58; $p<.05$) than those with comorbid conduct disorder who received placebo (Figure 1).

We also observed some significant main effects, with treatment and the predictor by treatment interaction terms included in the model (models were parameterized for the binary indicators as present vs. absent and at the treatment level of OROS-MPH; Table 1). Specifically, we observed a significant main effect of substance severity, ADHD severity and comorbid conduct disorder on ADHD change score, and a main effect of substance severity and drinks per day on number of negative urine samples. We also observed a significant main effect of court ordered treatment on SUD responder and treatment completer status. Participants who had worse substance severity (i.e., more days substance use in the last 28 at baseline) had less change in their ADHD ratings between baseline and week 16 (regression coefficient = -0.35 , $p=.006$) and had fewer negative urine samples during treatment (regression coefficient = -0.08 , $p<.0001$). Similarly, participants who reported more drinking in the last 28 at baseline had fewer negative urine samples during treatment (regression coefficient = -0.0084 , $p=.0002$). Participants who had greater ADHD severity had greater predicted odds to achieve a 50% reduction in substance abuse (OR=1.06, 95% CI: 1.01 to 1.11, regression coefficient = 0.06 , $p=.009$) and had more change in their ADHD ratings (regression coefficient = 0.64 , $p<.0001$), while participants with comorbid conduct disorder had less change in their ADHD ratings (least squares mean=17.53, SE=1.41) than those without comorbid conduct disorder (least squares mean=22.42, SE=0.98; $t = 2.85$, $p = .004$). Finally, participants who were court mandated to treatment had greater predicted odds to achieve a 50% reduction in substance abuse (OR=3.71, 95% CI: 1.26 to 10.89, regression coefficient = 1.31 , $p=.01$), but had lower predicted odds to complete treatment (OR=0.40, 95% CI: 0.17 to 0.94, regression coefficient = -0.90 , $p=.03$) than those who were not court mandated to treatment.

4.0 Discussion

Recently, we reported that a large sample of adolescents with comorbid ADHD and SUD treated with OROS-MPH or with placebo, in the context of outpatient substance treatment with CBT had inconsistent outcomes in terms of ADHD and SUD treatment response depending on the reporter and measure (Riggs, et al., 2011; Winhusen, et al., 2011). In the current study, we conducted secondary analyses to investigate potential predictors of treatment outcomes in order to add to the clinical base of knowledge regarding treatment of this vulnerable population. Our findings demonstrate that although comorbid conduct disorder predicted worse ADHD outcomes, there was an interaction effect for SUD outcomes, such that adolescents with conduct disorder who were prescribed OROS-MPH had significantly better substance use outcomes than adolescents with conduct disorder who

received placebo. We speculate that this might be due to reductions in impulsive behaviors leading to substance use, since previous work has shown improvement in both ADHD and CD symptomatology with stimulant medication (Klein, et al., 1997). In addition, we found that adolescents with more severe ADHD at baseline had greater reduction in ADHD symptoms (i.e., larger change score) and a greater likelihood of achieving a 50% reduction in substance use, regardless of medication status. In contrast, adolescents with higher substance use severity showed poorer treatment outcomes: they had less reduction in ADHD symptom ratings and fewer negative urine drug screens. Our findings also show that adolescents who were court-mandated to substance treatment had greater reductions in days of substance use but lower rates of treatment completion. This latter finding should be interpreted with caution as we do not have a great deal of information regarding this group.

As demonstrated by current and prior findings (Crowley, et al., 1998; Moffitt, 1990), adolescents with ADHD, SUD, and conduct disorder are among the most difficult to treat and offer a particular challenge to providers. Importantly, our results, combined with prior findings that demonstrated that OROS-MPH can be safely utilized in these comorbid adolescents (Riggs, et al., 2011), suggest that OROS-MPH may be a useful and effective approach when combined with cognitive behavioral therapy for reducing drug and alcohol use in these adolescents. While the current findings are still somewhat preliminary, the identification of any therapeutic tool that may reduce substance use in these difficult to reach adolescents is important. The failure to find an interaction between medication treatment and ADHD response was somewhat surprising, particularly in the context of the MTA findings that individuals with ADHD-only and ADHD with comorbid oppositional defiant disorder and conduct disorder responded best to treatment with stimulant medication on ADHD outcomes compared to placebo, with or without behavior therapy (Jensen, et al., 2001). In addition, others have shown that the added comorbidity of SUD in adolescents with conduct disorder does not affect response to stimulants in regard to ADHD (Thompson, et al., 1996).

Consistent with our hypothesis that individuals with worse substance use severity at baseline would have poorer treatment outcomes, we found that individuals with more substance use days at baseline had smaller reductions in ADHD symptomatology and individuals with more substance use days and more drinks in the past 28 at baseline had fewer negative urine samples. The literature suggests pretreatment level of substance use is a consistent baseline predictor of outcome (Adamson, et al., 2009; Brewer, Catalano, Haggerty, Gainey, & Fleming, 1998; Ciraulo, Piechniczek-Buczek, & Iscan, 2003; McKay & Weiss, 2001). Thus, for adolescents with more severe alcohol or drug use problems, a more intensive treatment approach may be required. While the current study offered one outpatient cognitive behavioral therapy counseling session per week in addition to medication (either OROS-MPH or placebo), adolescents with more severe alcohol or drug use may require intensive outpatient, day treatment, or residential care for better outcomes. Still, it is important to note that the majority of adolescents showed significant improvements even at this modest level of care (Riggs, et al., 2011).

We found that more severe ADHD at baseline predicted more change in ADHD symptoms (possibly because they had more room to move), but we did not observe an interaction with medication treatment for ADHD severity which we would have anticipated given reports that individuals with less severe ADHD respond better to treatment with stimulant medication (Buitelaar, et al., 1995). A secondary analysis of a NIDA CTN trial of OROS-MPH in adult smokers with ADHD (Winhusen, et al., 2010) revealed a significant baseline ADHD severity by treatment interaction, which indicated that individuals with more severe baseline ADHD symptoms were more likely to have a better smoking outcome when treated with OROS-MPH than with placebo (Nunes, et al., 2011, under review). While the present

study did not find increased medication response in those with more severe ADHD, those with more severe ADHD did evidence greater reduction in ADHD symptoms and this reduction could, in turn, have resulted in several positive changes, including ability to benefit from cognitive behavioral therapy that could impact SUD outcomes. There may be a specific subset of adolescents for whom ADHD is the primary problem and attention problems (such as increased impulsivity) may drive substance use. For clinicians who are faced with adolescents with severe ADHD, it may be most appropriate to address the ADHD with an approach that includes cognitive behavioral therapy, since it appears that adolescents with more severe ADHD show robust, global improvements when provided with this type of treatment.

With regards to our hypothesis that we might observe a differential treatment response in participants who were court-mandated to treatment, we in fact found that those who were court-mandated to treatment had lower treatment completion rates, but better SUD outcomes in those who completed treatment. In a review of the coercion literature, Klag and colleagues reported “reviews of three decades of research into the effectiveness of coerced substance user treatment have yielded a mixed, inconsistent, and inconclusive pattern of results” pp. 1882 (Klag, et al., 2005). Our data only addressed a legal definition of coercion (i.e., court-mandated to treatment) and does not address potential individual differences in terms of other sources of coercion (e.g., family pressure) nor were we able to investigate whether the length of court mandated treatment corresponded with attendance and/or attrition. It may be that the greater reduction in days of substance use could be related to frequent urine checks (external to the study) or some other evaluation of substance use with resulting consequences of evidence of substance use adverse enough for persons to stop using while in the program. Further, it is unclear if lower completion rates are due to participants quitting treatment as soon as the mandate expires, or use of substances while in treatment and being removed from the program or some other consequence. It should be noted, however, that we did verify that the court-mandated and non-court-mandated participants did not differ on baseline ADHD or substance use severity. Our results suggest that mandating adolescents with ADHD and SUD to treatment might be beneficial for reducing substance use but that additional efforts might be necessary to promote retention and prevent attrition, as this group is more likely to drop out of treatment. Replication is warranted to verify this hypothesis.

Although our sample size was large, there are some limitations. The primary study did not include a group that did not receive cognitive behavioral therapy precluding our ability to investigate potential interactions between treatment modalities. Further, we did not have data regarding content of the treatment sessions; it may be that those with conduct disorder responded differently during the session than those who did not have conduct disorder. In addition, it would have been interesting to know what the diagnostic status of participants was post-treatment to further interpret the conduct disorder findings; however, the K-SADS-E was not re-administered at outcome.

The current paper contributes significantly to the literature in that there is limited knowledge regarding predictors of treatment outcome in well-diagnosed comorbid ADHD and SUD adolescent populations. Our results suggest that individuals with ADHD and SUD who are also diagnosed with conduct disorder could benefit from concurrent treatment with OROS-MPH in addition to treatment for SUD. We also showed evidence that individuals with more severe ADHD but less severe SUD have better treatment outcomes. With regards to mandating treatment, we found better SUD outcomes in adolescents court-mandated to receive treatment, but there were also lower treatment completion rates in the court-mandated group. Thus, particular focus on treatment retention efforts might be important for this group in order to achieve better SUD outcomes.

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Figure 1.
Significant Substance Use Severity X Treatment Interaction
* = Significant difference between medication and placebo condition for participants with comorbid conduct disorder

Table 1

Interaction Effects Models

	ADHD Change Score	SUD Responder	Treatment Completer	# negative urine samples
	F (p value)	χ^2 (p value)	χ^2 (p value)	χ^2 (p value)
	(n=223)	(n=218)	(n=299)	(n=293)
Days Substance Use	7.69 (.006) *	.08 (.77) *	0.26 (.61)	28.21 (<.0001) *
Treatment	.17 (.68)	1.29 (.26)	.06 (.81)	.90 (.34)
Days Substance Use $\times$ Treatment	1.40 (.24)	.42 (.52)	1.07 (.30)	.22 (.64)
Joints per day	.18 (.67)	.92 (.34)	.33 (.57)	2.39 (.12)
Treatment	.21 (.65)	.03 (.86)	.81 (.37)	2.57 (.11)
Joints per day $\times$ Treatment	.58 (.45)	.59 (.11)	.37 (.54)	.54 (.46)
Drinks per day	1.67 (.20)	.12 (.73)	2.64 (.10)	13.68 (.002)
Treatment	.28 (.60)	1.04 (.31)	1.53 (.22)	.14 (.70)
Drinks per day $\times$ Treatment	.21 (.64)	.10 (.75)	.13 (.72)	1.25 (.26)
ADHD Severity	45.39 (<.0001) *	6.84 (.01) *	1.65 (.19)	.58 (.44)
Treatment	.26 (.61)	.66 (.42)	.64 (.42)	.14 (.71)
ADHD Severity $\times$ Treatment	.19 (.66)	1.27 (.26)	.30 (.58)	.003 (.97)
Comorbid CD	8.13 (.004) *	1.72 (.18)	.03 (.85)	0.80 (.37)
Treatment	0.20 (.65)	.15 (.70)	1.47 (.22)	.86 (.35)
Comorbid CD $\times$ Treatment	.54 (.46)	5.16 (.02) *	.03 (.86)	.26 (.61)
Court ordered	3.21 (.07)	5.68 (.01) *	4.36 (.03) *	0.03 (.87)
Treatment	0.12 (.72)	.27 (.60)	1.69 (.19)	1.84 (.17)
Court Ordered $\times$ Treatment	1.14 (.29)	1.46 (.23)	.17 (.68)	.05 (.82)

Note. A separate interaction-effects model was conducted for each predictor on each outcome measure.

χ^2 = Chi-Square Statistic for Type 3 analysis of effects. SUD = Substance Use Disorder; ADHD = Attention-Deficit/Hyperactivity Disorder; CD= Conduct Disorder; Treatment = OROS vs. placebo;

* significant finding (p<.05). Models were parameterized for the binary indicators as present vs. absent and at the treatment level of OROS-MPH.