Prevalence and correlates of heavy smoking and nicotine dependence in adolescents with bipolar and cannabis use disorders

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Abstract

The study examined the prevalence and correlates of heavy smoking and nicotine dependence in adolescents with bipolar and cannabis use disorders. Participants were 80 adolescents between 13 and 22 years of age with co-occurring bipolar I disorder and cannabis abuse or dependence who reported ever trying a cigarette. Diagnostic and symptom severity measures were completed as part of the baseline assessments for a clinical trial. Almost half (49%) of these participants who ever tried a cigarette were current heavy smokers (10 cigarettes/day), and 70% met DSM-IV-TR lifetime criteria for nicotine dependence. Heavy smoking was associated with older age, heavier marijuana use and greater compulsive craving, lifetime diagnoses of attention-deficit/hyperactivity disorder, conduct disorder, illicit drug use disorders, and poorer overall functioning. Nicotine dependence was related to White race, higher current mania severity, and poorer overall functioning. These findings suggest that heavy smoking and nicotine dependence were highly prevalent among these adolescents. Although both were associated with greater physical and psychosocial problems, only heavy smoking was linked to a clear pattern of more severe substance-related and psychiatric problems. Further research to elucidate mechanisms and develop interventions to address early, entrenched patterns of co-use of tobacco and marijuana is warranted.

Keywords

Tobacco; Marijuana; Mania; Dual diagnosis; Comorbidity

1. Introduction

Epidemiologic data indicate that over 80% of adults with bipolar disorder have a history of regular tobacco smoking and only 17% of these ever-smokers are able to successfully quit (Lasser et al., 2000), perhaps due to their higher-than-average likelihood of being nicotine

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dependent and smoking heavily (Grant et al., 2004; Diaz et al., 2009). The high prevalence of smoking and low rate of quitting contribute to increased rates of cardiovascular, respiratory, and cancer morbidity and mortality in bipolar disorder (Carney and Jones, 2006; Colton and Manderscheid, 2006; Goldstein et al., 2009). Although adolescence is, by far, the most common age for initiation of tobacco use (Kandel and Logan, 1984), very few studies have focused on the prevalence and correlates of tobacco smoking in adolescents with bipolar disorder (Wilens et al., 2008; Goldstein et al., 2008; Heffner et al., 2008).

In some studies of adolescents with bipolar disorder, cigarette smoking was linked with the presentation of bipolar disorder, including severity of mood symptoms and suicidality, as well as psychiatric comorbidity (Goldstein et al., 2008), but these findings are not uniform (Heffner et al., 2008). The most robust finding from these studies is that there is a strong relationship between tobacco use and other substance use, particularly cannabis. For example, bipolar adolescents who smoke cigarettes are also more likely to use marijuana, to start using it at younger ages, and to develop cannabis use disorders (Goldstein et al., 2008; Heffner et al., 2008, 2012).

Identifying factors associated with cigarette smoking in bipolar adolescents with cannabis use disorders represents a critical step toward understanding the high prevalence of co-use of these two substances as well as identifying shared risk factors (e.g., genetic influences, co-occurring psychiatric disorders) and potential causal factors (e.g., cross-tolerance and cross-sensitization) underlying the relationship. Previous studies examining correlates of cigarette smoking in adolescents with bipolar disorder have not consistently evaluated heaviness of smoking, and none have included a DSM-IV-TR assessment of nicotine dependence. Heavy, regular smoking and nicotine dependence are key considerations in predicting difficulty with quitting (Fiore et al., 2008), as well as in understanding the mechanisms underlying the high prevalence of smoking in bipolar adults.

With these considerations in mind, the purpose of this study was to examine the prevalence and correlates of heavy smoking and nicotine dependence in bipolar adolescents with co-occurring cannabis use disorders. Based on prior literature examining correlates of smoking in adolescents and adults with bipolar disorder (Waxmonsky et al., 2005; Goldstein et al., 2008; Heffner et al., 2008), our exploratory hypotheses were that heavy smoking and nicotine dependence would be associated with demographics (i.e., older age), symptoms and severity of bipolar disorder, severity of cannabis misuse, co-occurring alcohol and illicit drug use disorders, co-occurring psychiatric disorders (i.e., ADHD and anxiety disorders), and suicidal ideation and behavior. We also examined whether heavy smoking and nicotine dependence were related to physical health and psychosocial functioning.

2. Methods

2.1. Participants

Study participants were 80 adolescents, ages 13 to 22, who met DSM-IV-TR criteria for bipolar I disorder as well as either cannabis abuse or dependence and reported ever trying a cigarette. Participants were a large subsample of adolescents (i.e., 80 of 87; *n*=7 reported never trying a cigarette) enrolled in a study examining the effects of topiramate on cannabis use (NCT#00393978). Because a second aim of the study was to determine the efficacy of topiramate in reducing manic symptoms, all of the participants met criteria for a manic or mixed episode at the time of study enrollment, with a Young Mania Rating Scale (YMRS; Young et al., 1978) score of 16. Potential participants were excluded if they had received treatment for substance use disorders in the month prior to screening, if they were court-ordered for substance abuse treatment, if there were any medical or psychiatric contraindications to taking topiramate and/or quetiapine, or if they reported active suicidal

ideation or a recent suicide attempt at the time of screening. Concurrent substance use disorders and other psychiatric disorders were not exclusionary.

2.2. Assessments

To determine whether the DSM-IV-TR diagnostic criteria for bipolar I disorder were met, and whether there were any co-occurring psychiatric disorders, the Washington University at St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS; Geller et al., 2001) was administered by mastersor doctoral-level clinicians. The substance use disorder sections of the Child Semi-Structured Assessment for the Genetics of Alcoholism—Adolescent version (CSSAGA-A; Bucholz et al., 1994) were also completed by trained raters to assess lifetime substance use disorder symptoms and diagnoses, including nicotine dependence. Diagnostic consensus meetings were conducted to make final best estimate diagnoses (Leckman et al., 1982) and establish age-at-onset of each diagnosis based on information obtained from the WASH-U-KSADS and the SSAGA (Black et al., 2012). The YMRS (Young et al., 1978) and the Children's Depression Rating Scale-Revised (CDRS-R; Poznanski and Mokros, 1996) were administered to rate severity of mood symptoms.

The Smoking Timeline Followback (TLFB; Fals-Stewart et al., 2000) method was used to assess quantity of cigarette smoking and cannabis use over the 28 days prior to study entry, and average daily use was calculated by adding the total number of cigarettes or joints smoked during that time period and dividing by the number of days. Heavy cigarette smoking was defined as smoking 10 cigarettes per day, consistent with prior work in adolescents (e.g., Cornelius et al., 2001). To assess severity of functional problems, we used the Drug Use Screening Inventory— Revised (DUSI; Tarter, 1990), a 159-item measure of health in multiple domains including Substance Use, Behavior Pattern, Health Status, Psychiatric Disorder, Social Competence, Family System, School Performance, Work Adjustment, Peer Relationship, and Leisure/Recreation. The DUSI also contains a Lie scale designed to detect deception. Consistent with prior work (Tarter et al., 2011), we considered DUSI profiles in which the Lie scale score was 7 or greater to be invalid (n=1 participant excluded from analyses involving the DUSI). The Marijuana Craving Questionnaire—Short Form (MCQ; Heishman et al., 2001) is a 12-item measure covering four domains of craving: Compulsivity (loss of control over marijuana use), Emotionality (use of marijuana to relieve withdrawal or negative affect); Expectancy (expectation of positive outcomes from using marijuana) and Purposefulness (intentional use of marijuana to obtain positive outcomes). Two items from the Teen Addiction Severity Index (Teen-ASI; Kaminer et al., 1991) were used to assess history of suicidal ideation and suicide attempts. Supine blood pressure and body mass index are included in this report as indicators of health. Body mass index was calculated and interpreted according to guidelines published by the Centers for Disease Control (2011). Medication history was obtained from interviews with participants and their parents. Prior medications were classified into 5 major categories: antipsychotics, mood stabilizers, stimulants, antidepressants, and medications used in the treatment of tobacco dependence (even if they were not prescribed for that indication—e.g., bupropion, clonidine).

2.3. Procedure

Adolescents with bipolar disorder were recruited from outpatient and inpatient treatment settings in the Greater Cincinnati area as well as through newspaper advertisements. After obtaining informed consent from participants (or guardians, if the participant was younger than 18 years, in which case the adolescent's assent was also obtained), study staff administered the semi-structured diagnostic assessments, symptom measures, and self-report measures of current substance use described previously in order to establish eligibility for

the study. Adolescents were interviewed separately from their parents/guardians regarding substance use, and both adolescents and their parents/guardians understood as part of the informed consent procedures that information provided by the adolescent about his/her substance use would not be shared with the parent/guardian. As an additional measure to protect participants' data, we obtained a Certificate of Confidentiality from the National Institute on Drug Abuse. All study procedures were reviewed and approved by the institutional review boards of the University of Cincinnati and the Cincinnati Children's Hospital Medical Center.

2.4. Data analysis

All analyses compared: (1) adolescents who were current heavy smokers versus those who were not; and (2) adolescents who met lifetime DSM-IV criteria for nicotine dependence versus those who did not. Independent samples t-tests and Fisher's Exact Tests were conducted to compare demographic characteristics. For all other analyses, we used ANCOVA (for continuous variables) or logistic regression (for categorical variables), with age as a covariate. All analyses were twotailed and were conducted using PASW v. 18.0 (SPSS, Inc.; Chicago, IL).

3. Results

The mean age of the adolescents was 17 years (S.D.=2). Boys (n=42; 53%) slightly outnumbered girls. The majority of participants were White (n=71; 89%), and most met criteria for cannabis dependence (n=56; 70%) as opposed to abuse (n=24; 30%). Cooccurring diagnoses of alcohol use disorders (including both abuse and dependence; n=47; 59%) and illicit drug use disorders other than cannabis (n=26; 33%) were also common in this cohort.

Approximately half of the participants (n=39; 49%) reported current, heavy smoking, averaging at least 10 cigarettes per day over the 28 days prior to screening (M=17 per day, S.D.=5). Fiftysix participants (70%) met lifetime criteria for nicotine dependence. Most (n=36; 92%) of the heavy smokers met lifetime nicotine dependence criteria, as did roughly half of those who were not current, heavy smokers (n=20; 49%).

Participants who reported smoking at least 100 cigarettes over their lifetime (n=70; 88%) were asked about interest and experience in trying to quit smoking. A large majority indicated that they often wanted to quit or cut down on tobacco use (79%; n=53 of 67 responses) and that they had ever tried to quit or cut down (75%; n=50 of 67 responses). Of the 50 who indicated that they had ever tried to quit, few reported that they had received treatment to help them (18%; n=9).

3.1. Correlates of heavy smoking

As shown in Table 1, current heavy smoking was associated with older age and lower diastolic blood pressure as well as diagnoses of ADHD, conduct disorder, and illicit drug use disorders (other than cannabis use disorders). Prior use of stimulant medication was also higher in the heavy smokers, consistent with the higher prevalence of lifetime ADHD diagnoses. Heavy smokers also had higher craving scores on the Compulsivity subscale of the MCQ and reported using significantly more marijuana per week than the light- and non-smoking group. Additionally, heavy smokers endorsed worse functioning on numerous domains of the DUSI, including Behavior Pattern, Health Status, School Performance, Peer Relationship, and Leisure/Recreation, as well as the overall DUSI Problem Density Index—the value of which indicates the proportion of items endorsed as problematic. These scores suggest high levels of functional difficulties in both groups, with heavy smokers endorsing

more difficulty than light/nonsmokers (59% for heavy smokers versus 51% for light-/non-smokers).

3.2. Correlates of nicotine dependence

We found significant differences in nicotine dependence by race, with White adolescents more likely to be classified as nicotine dependent than non-White patients. Nicotine dependent adolescents also had significantly higher baseline YMRS scores, although average scores in both groups were indicative of severe symptoms of mania. There were no significant associations between nicotine dependence and other psychiatric characteristics or history/severity of cannabis use. On the DUSI, nicotine dependent adolescents reported poorer functioning overall, and specifically in the areas of Behavior Pattern and Social Competence.

4. Discussion

Current heavy smoking (49%) and lifetime nicotine dependence (70%) were both highly prevalent in these treatment-seeking adolescents with bipolar and cannabis use disorders who had ever tried a cigarette. The severity of smoking observed in these adolescents is considerably higher than that seen in the general population of U.S. adolescents. For example, in the recent Adolescent National Comorbidity Survey, only approximately 33% of those who ever tried smoking progressed to daily use, and only 20% met criteria for nicotine dependence (Dierker et al., 2012). Data from the Youth Risk Behavior Surveys also suggest that only a small portion (~8%) of adolescents who smoke are heavy smokers (Jones et al., 2011). Thus, adolescents with bipolar and cannabis use disorders appear to be at considerably greater risk for progression to more entrenched patterns of tobacco use than adolescents without psychiatric disorders. However, whether it is either the bipolar disorder or cannabis abuse disorder alone, or the combination, that contributes to the increased risk cannot be determined from this study in the absence of non-comorbid samples of each condition.

As an indicator of smoking severity, heavy smoking exhibited the expected pattern of relationships with the severity and extent of psychiatric and substance-related problems, including a relationship with comorbid ADHD and conduct disorder, illicit substance use disorders, and the quantity of cannabis use. These patterns were either weaker or non-existent when using lifetime DSM-IV diagnosis of nicotine dependence as the indicator, although both heavy smoking and nicotine dependence were associated with poorer physical and/or psychosocial health on the DUSI-R. Of note, although most of the heavy smokers met criteria for nicotine dependence, the inverse was not true, as many of those who met criteria for nicotine dependence were not heavy smokers. The discrepancies noted here between heaviness of smoking and DSM-IV-TR diagnosis of nicotine dependence reinforce previous findings that adolescents may begin to show signs of nicotine dependence even at relatively low levels of smoking (DiFranza et al., 2002; Rose et al., 2010), making early intervention all the more important.

Despite these differences between indicators of smoking severity, our findings support the notion that extent of cigarette smoking is associated with poorer physical and psychosocial functioning in youth with co-occurring bipolar and cannabis use disorders and may be related to the presence of other substancerelated and psychiatric disorders. Causality cannot be determined from our findings of association, but there is evidence from prior studies to suggest that relationships between cigarette smoking and the presence or severity of substance-related and other psychiatric disorders may be bidirectional or driven by third factors, such as a common genetic or environmental influences (see review by Heffner et al. (2011)). Longitudinal studies of youth with bipolar disorder are needed to begin to

understand how these relationships emerge over time and how best to intervene to prevent progression of cigarette smoking.

It is interesting to note that some of the characteristics that have been linked to smoking in other studies of adolescents and adults with bipolar disorder, including earlier age at onset of bipolar disorder (Waxmonsky et al., 2005; Goldstein et al., 2008) and suicidality (Waxmonsky et al., 2005; Ostacher et al., 2006; Goldstein et al., 2008) were not identified as correlates of heavy smoking and nicotine dependence in the present study. It may be that, in this high-risk subpopulation of bipolar adolescents with at least one co-occurring substance use disorder, the risks of heavy and/or dependent smoking are so great that some of the relationships between smoking and other clinical or demographic characteristics that have been reported in prior studies are obscured. Examining these issues in mixed samples of adults and adolescents with bipolar disorder, as has been the case in most prior studies, may also bias findings toward conclusions that are more relevant to adults, since younger adolescents (ages 12–14) are usually excluded from these studies (e.g., Ostacher et al., 2006; Waxmonsky et al., 2005). Prior studies (e.g., Waxmonsky et al., 2005; Ostacher et al., 2006) have also tended to use a binary indicator of current smoking (yes/no) as the indicator of smoking rather than focusing on gradations of severity like heavy smoking (Goldstein et al., 2008) or nicotine dependence, which decreases comparability of our findings with those published previously. Regardless of the cause of the discrepant findings, the high rates of lifetime suicidal ideation and attempts that we observed across groups (i.e., 50–55% for ideation and 37–47% for attempts), which is consistent with prior studies of bipolar adolescents (e.g., Goldstein et al., 2008), serve as a reminder that safety assessments are of paramount importance in working with these adolescents, whether that is in the context of tobacco treatment or treatment of psychiatric and/or other substance use disorders.

Several limitations should be noted in interpreting the findings from this study. First, because we were interested in factors associated with progression from experimentation with cigarette smoking to more entrenched patterns of use, we excluded all participants who never tried smoking. However, this number was quite small in this sample (*n*=7), which is further demonstration of the strong relationship between cannabis use and cigarette smoking in these bipolar adolescents. Additionally, this was a clinical sample of adolescents who, with the consent of their parents, agreed to be treated with pharmacotherapy and a brief behavioral intervention for their bipolar disorder and cannabis use. The results may therefore not be generalizable to nontreatment-seeking youth with bipolar and cannabis use disorders. Additionally, because tobacco use was not the focus of the larger study, we did not biochemically verify current smoking status. However, prior studies have supported the validity of self-reports of smoking in general population samples of adolescents (Harrison et al., 2007) as well as in samples of adults with severe psychiatric symptoms (de Beaurepaire et al., 2007). Finally, since our analyses were exploratory, we conducted a large number of statistical tests without control for multiple comparisons, increasing the likelihood of a Type I error; and results should be viewed as hypothesis-generating, rather than hypothesis testing. Despite these limitations, our study is one of only a very few to examine correlates of cigarette smoking severity in bipolar adolescents, and the first, to our knowledge, to incorporate an assessment of the DSM-IV diagnosis of nicotine dependence.

This examination of smoking severity and its clinical correlates in adolescents with co-occurring bipolar and cannabis use disorders has the potential to shed light on the mechanisms underlying the highly prevalent co-occurrence of cannabis and tobacco use in this group, which could lead to improved prevention and treatment. Although further research is needed to determine how to best intervene with these teens who have co-occurring psychiatric and substance use disorders, the importance of providing cessation interventions that have been found to be effective among adolescents in general is

highlighted by: (1) the observed high prevalence of heavy smoking and nicotine dependence, and, (2) the finding that the majority of these adolescent smokers expressed interest in quitting but that few had received cessation support. Current evidence-based treatment for adolescent smoking cessation include behavioral treatments incorporating motivational enhancement, cognitive-behavioral skills training, and/or social influence approaches (Peterson et al., 2009; Sussman et al., 2006). Pharmacotherapy could also have some benefit for these heavy-smoking teens, but it should be noted that the three FDAapproved, first-line pharmacotherapies for smoking cessation (i.e., nicotine replacement therapy, bupropion, and varenicline) are not currently approved for use in children and adolescents (Fiore et al., 2008). Additional research is needed to determine the safety and efficacy of these medications in children and teens, and specifically in children and teens with psychiatric disorders. The extent to which medications used to treat psychiatric and/or substance use disorders also reduce cigarette smoking should also be explored. For example, topiramate has preliminarily shown efficacy for smoking reduction or cessation in some subgroups of smokers (Johnson et al., 2005; Anthenelli et al., 2008); consequently, we plan to examine the effect of topiramate on cigarette smoking using data from the parent study described in this report. As noted previously, longitudinal studies which incorporate not only phenotypic information, but also genotype, would improve understanding of the causes of the associations among bipolar disorder, cannabis use disorders, and cigarette smoking.

Acknowledgments

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Table 1

Demographic, health, psychiatric, substance-related, and psychosocial characteristics, by heavy smoking and nicotine dependence status. Bolded values are those that are statistically significant (i.e. $p<.05$).

Variable	Current heavy smoker (n=39)	Current light/non-smoker (n=41)	P	Nicotine dependent (n=56)	Not nicotine dependent (n=24)	P
Demographics						
Age	18.0 (2.2)	16.9 (2.0)	**0.03**	17.4 (2.1)	17.5 (2.2)	0.83
Sex (male)	19 (48.7)	23 (56.1)	0.66	29 (51.8)	13 (54.2)	0.99
Race (White)	36 (92.3)	35 (85.4)	0.48	53 (94.6)	18 (75.0)	**0.02**
Health						
BMI—overweight or obese	15 (40.5)	10 (24.4)	0.15	18 (33.3)	7 (29.3)	0.80
Blood pressure, systolic	112.7 (10.4)	114.4 (10.2)	0.37	114.2 (10.6)	112.2 (9.4)	0.44
Blood pressure, diastolic	67.1 (9.3)	70.4 (7.8)	**0.05**	68.3 (8.9)	70.1 (8.2)	0.39
Symptoms and co-occurring disorders						
Age at onset of BD	13.5 (2.7)	14.3 (2.1)	0.08	13.7 (2.6)	14.4 (2.1)	0.25
Mixed episode at baseline	33 (84.6)	35 (85.4)	0.99	48 (85.7)	20 (83.3)	0.79
Psychosis	11 (28.2)	7 (17.1)	0.33	13 (23.2)	5 (20.8)	0.79
YMRS	24.9 (5.9)	23.7 (5.1)	0.34	25.1 (5.8)	22.4 (4.3)	**0.04**
CDRS-R	37.3 (9.6)	35.4 (9.2)	0.54	35.5 (9.2)	38.3 (9.8)	0.24
History of suicidal ideation	19 (52.8)	21 (51.2)	0.91	27 (50.9)	13 (54.2)	0.82
History of suicide attempt	17 (47.2)	15 (36.6)	0.46	22 (41.5)	10 (41.7)	0.98
ADHD[a]	25 (64.1)	17 (41.5)	**0.04**	31 (55.4)	11 (45.8)	0.44
Conduct disorder[a]	23 (59.0)	12 (29.3)	**0.01**	28 (50.0)	7 (29.2)	0.09
Anxiety disorder[a]	18 (46.2)	13 (31.7)	0.53	22 (39.3)	9 (37.5)	0.88
Alcohol use disorder[a]	25 (64.1)	22 (53.7)	0.84	35 (62.5)	12 (50.0)	0.25
Illicit drug use disorder[a]	19 (48.7)	7 (17.1)	**0.01**	21 (37.5)	5 (20.8)	0.12
History and severity of cannabis use						
Age at onset of regular cannabis use	13.0 (2.1)	13.3 (1.7)	0.42	13.1 (1.8)	13.1 (1.8)	0.96
Age at onset of cannabis abuse/dep.	14.8 (2.5)	14.9 (1.5)	0.16	14.8 (2.1)	15.0 (1.7)	0.62
Cannabis dependent	29 (74.4)	27 (64.9)	0.97	38 (67.9)	18 (75.0)	0.55
Years from onset of regular cannabis use to abuse/dep.	1.7 (2.1)	1.7 (1.8)	0.97	1.6 (1.9)	1.9 (2.1)	0.53

Variable	Current heavy smoker (n=39)	Current light/non-smoker (n=41)	P	Nicotine dependent (n=56)	Not nicotine dependent (n=24)	P
Joints per week, past month	22.7 (17.4)	14.2 (13.9)	**0.03**	20.4 (17.7)	13.6 (11.0)	0.08
MCQ general	4.5 (1.1)	4.2 (0.9)	0.28	4.4 (1.0)	4.3 (1.0)	0.68
MCQ compulsivity	3.3 (1.4)	2.7 (1.3)	**0.04**	3.0 (1.4)	3.0 (1.4)	0.89
MCQ emotionality	6.0 (1.1)	5.9 (1.4)	0.59	6.0 (1.3)	5.8 (1.2)	0.51
MCQ expectancy	5.2 (1.4)	5.0 (1.5)	0.88	5.2 (1.3)	4.9 (1.7)	0.36
MCQ purposefulness	4.9 (2.0)	4.5 (1.8)	0.81	4.7 (1.9)	4.7 (1.9)	0.90
Overall and domain-specific functioning						
DUSI overall problem density index	59.3 (9.5)	50.5 (11.6)	**0.003**	56.4 (11.3)	49.8 (10.8)	**0.02**
DUSI substance use	48.0 (24.0)	42.9 (22.9)	0.62	47.5 (24.5)	39.9 (20.2)	0.20
DUSI behavior pattern	62.5 (14.6)	53.8 (18.6)	**0.04**	60.8 (15.7)	50.4 (19.0)	**0.02**
DUSI health status	49.3 (17.0)	37.3 (17.7)	**0.01**	45.1 (18.3)	36.9 (17.4)	0.09
DUSI psychiatric disorder	63.8 (16.1)	54.5 (18.3)	0.11	61.1 (16.4)	53.1 (20.0)	0.07
DUSI social competence	38.6 (19.5)	30.5 (18.2)	0.13	37.1 (19.6)	27.2 (16.4)	**0.045**
DUSI family system	56.7 (22.8)	58.8 (15.9)	0.43	59.0 (18.7)	54.4 (22.8)	0.40
DUSI school performance	69.0 (15.8)	55.1 (16.3)	**0.001**	62.0 (17.4)	59.3 (17.8)	0.56
DUSI work adjustment	34.0 (25.3)	24.6 (18.8)	0.40	29.8 (23.1)	26.5 (20.3)	0.43
DUSI peer relationship	72.1 (12.3)	60.9 (16.9)	**0.002**	68.3 (15.3)	60.8 (16.5)	0.08
DUSI leisure/recreation	60.2 (16.8)	49.8 (20.0)	**0.04**	54.7 (20.3)	54.2 (16.8)	0.93
Medication history						
Antipsychotic	19 (48.7)	13 (31.7)	0.20	24 (42.9)	8 (33.3)	0.40
Mood stabilizer	12 (30.8)	6 (14.6)	0.13	12 (21.4)	6 (25.0)	0.75
Stimulant	21 (53.8)	14 (34.1)	**0.05**	27 (48.2)	8 (33.3)	0.23
Antidepressant	17 (43.6)	9 (22.0)	0.07	20 (35.7)	6 (25.0)	0.33
Smoking cessation agent	6 (15.4)	3 (7.3)	0.33	5 (8.9)	4 (16.7)	0.33

Note: Heavy smoking is based on current use, whereas nicotine dependence is based on meeting lifetime criteria. Values in table are mean (S.D.) or *n* (%). All analyses except demographics controlled for age. BMI=body mass index; BD=bipolar disorder; YMRS=Young Mania Rating Scale; CDRS-R=Children's Depression Rating Scale-Revised; ADHD=attention-deficit/hyperactivity disorder; MCQ=Marijuana Craving Questionnaire; DUSI=Drug Use Screening Inventory, Revised. Values for DUSI subscales represent percentage of items endorsed positive, where positive responses reflect problems in that area.

[a] Lifetime DSM-IV diagnoses.