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Diagnosing Alcohol and Cannabis Use Disorders in Adolescents with Bipolar Disorder: A Preliminary Investigation

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Abstract

Objective—The aim of this report was to examine the accuracy of diagnosing substance use disorders in manic adolescents with bipolar disorder.

Methods—The substance use disorder modules of the KSADS-PL were administered to a sample of 80 manic adolescents (12-21 years old) with co-occurring bipolar and substance use disorders. Initial substance use disorder diagnoses obtained from the KSADS-PL were then compared to a best-estimate diagnosis derived from all available information, including a second diagnostic interview, the Child Semi-Structured Assessment for the Genetics of Alcoholism, Adolescent version (C-SSAGA-A).

Results—Relatively low diagnostic agreement was achieved across the initial and the best estimate diagnoses for both alcohol and cannabis use disorders. Age, race, and sex did not predict diagnostic agreement between the two evaluations.

Conclusions—Results of this study call for more research on diagnosing substance use disorders and suggest that a single interview alone may not be accurate for diagnosing substance use disorders in manic adolescents with bipolar disorder.

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DISCLOSURES

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Keywords

adolescents; bipolar disorder; substance use disorders; KSADS-PL; C-SSAGA-A

Early onset bipolar disorder is a serious mental illness that is often associated with periods of substantial impairment. Fairly recent research in the area is producing a better understanding of the etiology and course of this disorder thereby improving treatment of current symptoms and assisting in prevention of future episodes (Pfeifer, Kowatch & DelBello, 2010). Despite this, high rates of comorbid substance use disorders cloud research findings and adversely impact treatment outcomes in bipolar youth (Goldstein & Bukstein, 2010).

Prospective data suggest that bipolar disorder during adolescence is a risk factor for the subsequent development of a substance use disorder (Geller, Tillman, Bolofner & Zimerman, 2008; Goldstein & Bukstein, 2010; Wilens *et al.*, 2008 see Jerrell, McIntyre & Tripathi, 2010 see also Jerrell, McIntyre & Tripathi, 2010) and that adolescents with comorbid bipolar and substance use disorders have significant functional impairment and high suicide risk (Goldstein & Bukstein, 2010). Additionally, these adolescents use more outpatient and acute medical and psychiatric services (Jerrell *et al.*, 2010). Accurate identification of co-occurring substance use disorder and bipolar disorder in adolescents is an initial step to improving research and treatment practices. However, making the diagnosis of bipolar disorder in individuals with substance use disorders is complicated by the fact that secondary affective and behavioral symptoms resulting from substance use may be difficult to distinguish from primary mood disorder symptoms (Schuckit, 2006). Conversely, diagnosing substance use disorders in patients with bipolar disorder may be difficult because alcohol and drug use may be attributed to the impulsivity and poor judgment associated with bipolar disorder.

In order to optimize diagnostic validity and reliability, structured or semi-structured diagnostic interviews are frequently administered in research and, less commonly, in clinical settings. Indeed, Andreas and colleagues (2009) found that psychiatric diagnoses from structured interviews on inpatients with mental disorders were more valid than diagnoses derived from standard clinical interviews. However, in general, there is little research investigating the validity and reliability of structured interviews that assess substance use disorders in adolescents (Deas & Clark, 2009; Bukstein & Winters, 2004). The Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version (KSADS-PL) is a widely used semi-structured interview for assessing psychiatric disorders in youth. This instrument has been used to diagnose substance use disorders in adolescents with mood disorders in several recent research studies (Geller, Tillman, Bolofner & Zimerman, 2008; Duffy, Alda, Hajek, Sherry & Grof, 2010). However, we are unaware of any studies examining the KSADS-PL for diagnosing substance use disorder in youth with bipolar mania.

Moreover, current mood state may also be an important factor to consider when diagnosing substance use disorders in individuals with bipolar disorder. Specifically, during mania insight is more likely to be impaired, which may impact a patient's self-report (Dias, Brissos, Frey & Kapczinski, 2008).

At present, there is a gap in the literature on the best practices for diagnosing substance use disorder in adolescents with bipolar disorder. As an initial step to inform future research in this area, and as a first step to assess the validity of current substance use disorder diagnostic procedures, we compared diagnoses derived two different ways and at two different times.

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First, initial substance use disorder diagnoses in manic adolescents with bipolar disorder were obtained using the KSADS-PL semi-structured interview, at the time of initial assessment. Second, best-estimate substance use disorder diagnoses were derived from a consensus conference using all available information, including that obtained from a second diagnostic interview, the Child Semi-Structured Assessment for the Genetics of Alcoholism, Adolescent version (C-SSAGA-A), conducted a few weeks after the initial assessment, after participants were provided with pharmacotherapy. We hypothesized that initial substance use disorder diagnoses in manic adolescents with bipolar disorder would be less valid than best estimate substance use disorder diagnoses derived from all available information, including a second diagnostic interview, and following resolution of mania.

METHODS

Participants

Eighty adolescents, 12 to 21 years of age (median age = 17 years), who had bipolar I disorder in a current mixed or manic episode and co-occurring substance use disorders (i.e., alcohol and/or cannabis use disorders, as determined by administering of the KSADS-PL) were recruited to participate in one of two pharmacotherapy studies. All study participants were fluent in English, had a Young Mania Rating Scale (Young, Biggs, Ziegler & Meyer, 1978) score of 16 or higher, and provided written informed consent following a complete discussion of the study. (Adolescents who were under 18 years of age provided written assent and their legal guardian provided informed consent for study participation). The studies were conducted in accordance with the Declaration of Helsinki and with the approval and oversight of the University of Cincinnati and Cincinnati Children's Hospital Medical Center Institutional Review Boards.

Procedures

KSADS-PL—The KSADS-PL, including the substance use modules, was administered by trained interviewers with documented excellent diagnostic reliability for the instrument (Kappa > 0.9). Reliability was established by each interviewer administering ten interviews concurrently with an established rater, then comparing diagnoses. Established raters were psychiatrists or psychologists with expertise in mood and substance use disorders (MPD, RMA, JLH).

Best-estimate consensus diagnostic procedures—The best-estimate consensus diagnoses were derived from multiple sources of information, including the KSADS-PL; a second diagnostic interview, the Child Semi-Structured Assessment for the Genetics of Alcoholism, Adolescent version (C-SSAGA-A); urine drug screens; adolescent self-report on the Drug Use Screening Inventory (Tarter, 1990); and, when available, parental report. The C-SSAGA-A, an adaptation of the Semi-Structured Assessment for the Genetics of Alcoholism (Bucholz, Cadoret & Cloninger et al., 1994) is a semi-structured diagnostic interview that emphasizes distinguishing substance-induced syndromes from independent symptoms of mood and anxiety disorders, psychosis, and antisocial personality disorder. The substance use section of the CSSAGA-A was administered by a trained interviewer with established diagnostic reliability (Kappa > 0.9). The C-SSAGA-A was administered within two to four weeks of the KSADS-PL interview.

Twice per month a board-certified child psychiatrist (MPD) and a board-certified addiction psychiatrist (RMA), along with the study nurses, coordinators, and therapists met to establish consensus best-estimate diagnoses for each participant using all available information.

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Comparison of the KSADS-PL and C-SSAGA-A—There are two primary construct differences between the interviews: 1) screening criteria, and 2) symptom threshold. Both the KSADS-PL and the C-SSAGA-A have screening criteria which must be met in order to continue with the substance use supplemental module; however, the screening criteria differ. Related to timing of use, the KSADS-PL screener requires use of a substance within the past six months. The other screening criterion relates to extent of use with the C-SSAGA-A setting use of a drug 7 times or more in their life; and the KSADS-PL requiring use of a drug more than once per month during the past 6 months. The other main difference between instruments is what constitutes endorsement of a symptom. The KSADS-PL requires "two or more incidents" as the threshold for the occurrence of any specific substance use disorder symptom criterion, whereas the C-SSAGA-A sets "three or more incidents" as the criterion threshold. For example, the KSADS-PL requires two or more incidents of "recurrent substance use despite persistent interpersonal problems" to meet the threshold for that criterion.

Data Analysis

Substance use disorders were grouped according to Diagnostic and Statistical Manual of Mental Disorders-IV-TR (DSM-IV-TR; American Psychiatric Association, 2000) classification. Given the small number of substance use disorders other than alcohol and cannabis use disorders, diagnostic agreement was explored only for these two diagnostic categories. Cohen's Kappa was calculated as an estimate of diagnostic concordance. Fleiss and Cohen's (1973) agreement guidelines were employed (i.e., poor [0 to 0.4], fair [0.41 to 0.59], good [0.6 to 0.74] and excellent [≥ 0.75]). Additionally, logistic regressions were used to determine whether demographic variables of interest (age, sex, or race) predicted discrepancies in KSADS-PL and best-estimate diagnoses. Young Mania Rating Scale scores were used to examine associations between manic symptoms and self-report during the interviews. Three sets of logistic regression analyses were conduced. First, whether the Young Mania Rating Scale score predicted substance use disorder diagnoses at baseline (pre-treatment; time of KSADS-PL interview). Second, we examined whether Young Mania Rating Scale score predicted substance use disorder diagnoses at time 2, once participants had received treatment and time of the C-SSAGA-A interview. Lastly, we examined whether change in Young Mania Rating Scale score predicted a worsening of substance use disorder diagnosis from baseline to time 2.

RESULTS

Primary findings

Fifty-one percent of study participants were female, and 89% were White. At the time the KSADS-PL was administered, the mean Young Mania Rating Scale score was 24.3, which is consistent with clinically significant symptoms of mania. However, at the time that the C-SSAGA-A was administered, the average Young Mania Rating Scale score was 11.3, indicating a statistically and clinically significant reduction in symptoms of mania, $t(76) = 14.99$, $p < 0.001$.

Table 1 illustrates the rates of cannabis and alcohol use disorder diagnoses using the initial KSADS and the best estimate diagnoses, respectively. Rates of current alcohol and cannabis abuse or dependence differed substantially between the initial KSADS-PL and best estimate; Cohen's Kappa coefficients (Table 2) indicated that diagnostic agreement between the two diagnoses was generally poor. In the case of cannabis abuse, diagnostic agreement was not better than chance ($p = .35$).

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Four logistic regression analyses, one for each diagnosis—cannabis and alcohol abuse and dependence, respectively—were conducted to assess whether age, sex or race predicted diagnostic agreement. In each analysis, none of these demographic variables significantly predicted or indicated a trend of diagnostic agreement levels (all p values > .05).

Lastly, we employed logistic regression to examine whether mania predicted substance use disorder diagnosis, see Table 3 for complete results. In sum, we found mixed results. Time 1 was pre-treatment initiation and the time of KSADS-PL administration. Time 2 was at treatment initiation and the time of C-SSAGA-A administration. For cannabis abuse, there was a trend for participants who endorsed more mania symptoms at Time 1 to be more likely to meet disorder criteria ($p = 0.07$; $OR = 1.09$). In contrast, participants with lower levels of mania were significantly more likely to meet for alcohol abuse ($p = 0.01$; $OR = .90$). As was the case with reduction of mania symptoms from time 1 to time 2 corresponding with higher likelihood to meet cannabis use disorder criteria ($p = 0.08$; $OR = 1.06$). In other words, for the 13 point decrease we saw in our sample, the odds of having a worse cannabis diagnosis at Time 2 were about double.

Differences between KSADS-PL and best-estimate diagnoses

Given the low levels of diagnostic agreement between the KSADS-PL and the best-estimate consensus diagnosis, the latter of which was 100% concordant with C-SSAGA-A diagnoses, we conducted an exploratory examination of reasons for discrepancies. Approximately 86% of discrepant cases were attributable to either differences in the KSADS-PL and C-SSAGA-A screening items that prompt further questioning regarding a specific substance (19%) or to conflicting patient report between the two interviews (67%). The reason for discrepant diagnoses could not be identified with confidence in 14% of the cases. In the sections that follow, we provide a more detailed description of the manner in which interview differences and inconsistencies in patient self-report resulted in discrepant KSADS-PL and best-estimate substance use disorder diagnoses.

Interview Differences

Some of the discordant cases were attributed to structural differences between the two interviews in terms of screening criteria and symptom thresholds. Three percent of discordant cases were due to participants not reporting using a substance within the past six months during the KSADS-PL interview. Another 14% of discrepant cases were due to patients not reporting using substances regularly enough to prompt further questioning on the KSADS-PL. Specifically, the KSADS-PL sets > 1 use per month over the past 6 months, whereas the C-SSAGA-A uses ≥ 7 times in one's lifetime as its screening threshold to prompt further questioning for substance use disorder diagnoses. Thus, the KSADS-PL screening items have more stringent requirements regarding the timing and regularity of use, resulting in fewer substance use disorder diagnoses than the best estimate diagnoses, which was largely based upon the additional information obtained during the C-SSAGA-A interview. Conversely, the symptom threshold is less stringent in the KSADS-PL, where only two or more incidents are the threshold for substance use disorder symptom endorsement, whereas the C-SSAGA-A sets three or more incidents as the criterion threshold. This structural difference resulted in only one identified discrepant case: a diagnosis of cannabis abuse on the best estimate diagnosis and a diagnosis of cannabis dependence on the KSADS-PL.

Differences in Self-Reported Use and Symptoms

Variability in patient self-report was a major source of discrepancy in substance use disorder diagnoses between diagnostic interviews. Variance in the number of symptoms reported across the two interviews, which in turn affected diagnostic threshold, accounted for 62% of

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the discrepant cases, with youth consistently reporting more symptoms on the second interview. Similarly, 5% of discrepant cases were due to patients reporting that they never used a drug on the KSADS-PL, then reporting use and clinically significant symptoms of abuse or dependence on the C-SSAGA-A.

DISCUSSION

Our primary finding from this preliminary study is that the validity of an initial diagnosis of alcohol and cannabis use disorders in adolescents with bipolar disorder who present in a manic or mixed state is low. Notably, in the case of cannabis abuse, agreement between the initial substance use disorder diagnosis, obtained by KSADS-PL interview, and the best-estimate consensus diagnoses was not significantly better than chance. Based on our exploratory analysis of the reasons for poor agreement, it appears that the majority of diagnostic disagreements resulted from limitations in patient report during the initial interview. Several factors may have led to this poor self-reporting. Given that concerns about confidentiality are known to impact adolescents' disclosure (Ford, Millstein, Halpern-Felsher & Irwin, 1997), the participants may have been less open about the extent of their substance use during the initial assessment, prior to the development of a trusting relationship with the interviewers. Consistent with this, we observed that participants frequently disclosed less information during the KSADSPL than during the C-SSAGA-A. Research suggests that reports of higher rates of substance use in adolescents are typically more accurate (Gans & Brindis, 1995; Turner, Ku, Rogers, Lindberg, Pleck & Sonenstein, 1998). Thus, our findings highlight the importance of establishing a good rapport and trust between the interviewer and the adolescent as a critical step toward obtaining accurate reports of substance use.

Clinical factors associated with bipolar I disorder may also have impacted patient report. The initial interview was administered during a manic or mixed mood state. Impaired insight often accompanies manic states, which can affect the validity of self-report (Dias, Brissos, Frey & Kapczinski, 2008; Gazalle, Frey & Hallal *et al.*, 2007). The best estimate substance use disorder diagnoses included information from the C-SSAGA-A, which was administered while the patients were, in general, less manic. These findings suggest that mood state may also be a factor in limiting the accuracy of self-report of substance use symptoms in adolescents with bipolar disorder. However, due to conflicting findings (see Table 3), we are not able to draw any conclusions based on our study's results.

There are several limitations to consider when interpreting our findings. First, generalization of results should be done with caution as adolescents without a cannabis or alcohol use disorder diagnosis on the KSADS-PL would have been excluded from the treatment studies, and thus, not included in this analysis. Similarly, future studies controlling for the potential confounding influence of interview order effects and mood effects would likely be helpful to eliminate alternative reasons for poor KSADS-PL and best-estimate diagnostic reliability. Without exploration of these potential confounds, at present it cannot be determined that the KSADS-PL contributed to self-report discrepancies. Finally, studies should ideally control for possible interviewer effects in order to better explore the importance of rapport in this high-risk population.

Nonetheless, the present findings emphasize the importance of developing and evaluating methods to more efficiently diagnose substance use disorder in adolescents with bipolar disorder. Some of the discrepancies between KSADS-PL and best estimate diagnoses appear to be attributable to the structural differences between the KSADS-PL and the C-SSAGA-A. Therefore, more systematic research evaluating the psychometric properties of the substance use disorder modules of the KSADS-PL and the C-SSAGA-A is warranted. For example,

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examination of the test-retest reliability of substance use disorder diagnoses obtained from structured and semi-structured diagnostic instruments might be useful to determine which instruments more accurately diagnose substance use disorder early in illness course.

In summary, we found significant discrepancies in substance use disorder diagnoses obtained using an initial KSADS interview in manic adolescents with bipolar disorder and a best-estimate consensus diagnosis, that relied primarily on a C-SSAGA-A interview, conducted following treatment of mania. A noteworthy implication of our findings it that the information provided by manic adolescents during an initial assessment may be less accurate than information provided after a relationship with the interviewer has been established and/or when the patient has fewer manic symptoms, suggesting the utility of conducting repeat assessments of substance use disorder in adolescents with bipolar disorder. Although we are unable to determine whether the differences in substance use disorder diagnoses are due to differences in the timing of assessments, mood states, or the interview structure, substance use disorder diagnoses were often characterized as less severe or sometimes were not captured at all with the initial assessment, which in clinical settings might lead to a missed opportunity for treatment.

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Table 1

Demographic information (Total $N = 80$)

Age, mean (SD), years	17.0 (2.0)
Sex, *n* (%), female	41 (51%)
Race, *n* (%),White	71 (89%)
Cannabis abuse or dependence *n* (%)	70 (87%)
Alcohol abuse or dependence *n* (%)	51 (64%)
Nicotine dependence *n* (%)	50 (62%)
Other drug abuse or dependence *n* (%)	20 (25%)
YMRS score at KSADS-PL diagnosis	24.3 (5.4)
YMRS score at C-SSAGA-A diagnosis	11.3 (7.6)

Note. YMRS = Young Mania Rating Scale; KSADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version; C-SSAGA-A = Child Semi-Structured Assessment for the Genetics of Alcoholism, Adolescent version.

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Table 2

Comparison and Concordance of KSADS-PL and Best-Estimate Substance Use Disorder Diagnoses

	KSADS-PL	Best-Estimate	Kappa	*p*	Participants with the Same Diagnosis at KSADS-PL and Best-Estimate (*n*)	
	n (%)	*n (%)*			Positive	Negative
Abuse						
Alcohol	13 (16)	22 (28)	0.25	0.02	7	52
Cannabis	20 (25)	18 (23)	0.10	0.35	6	48
Dependence						
Alcohol	14 (18)	28 (35)	0.50	0.00	13	51
Cannabis	41 (51)	52 (65)	0.37	0.00	34	21

Note: KSADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version.

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Table 3

Mania symptoms predicting substance use disorder diagnosis (*p*-values)

	Time 1 Pre-Treatment	**Time 2 Treatment Initiation**
Alcohol Abuse	0.29	0.01* (*OR* = .90)
Cannabis Abuse	0.07* (*OR* = 1.09)	0.95
Alcohol Dependence	0.44	0.27
Cannabis Dependence	0.74	0.24
Change in mania from Time 1 to Time 2 (reduction)		
Alcohol Use Disorder (abuse and dependence)	0.7	
Cannabis Use Disorder (abuse and dependence)	0.08* (*OR* = 1.06)	

Note. KSADS-PL was administered at Time 1 and C-SSAGA-A was administered at Time 2. KSADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version; C-SSAGA-A = Child Semi- Structured Assessment for the Genetics of Alcoholism, Adolescent version. *OR* = Odds Ratio.

*Indicates a significant result.