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Reasons for Substance Use among Adolescents with Bipolar Disorder

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Abstract

We examined whether children and adolescents with Bipolar Disorder (BPD) "self-medicate" with cigarettes, alcohol, or other substances of abuse. 105 adolescents with BPD and 98 controls were comprehensively assessed with a structured psychiatric diagnostic interview for psychopathology and the Drug Use Screening Inventory (DUSI) for self-medication. 13 control (mean ± SD: 15.31 ± 1.18 years) and 27 BPD (15.30 ± 2.09 years) subjects endorsed use of one of the listed drugs in the DUSI Section A within the past year and were included in all analyses. BPD adolescents were more likely than non-mood disordered, substance-using controls to report starting to use their preferred drug for mood-altering effects. There were no differences between groups in motivation for use with respect to starting substances to sleep better or get high, or in continuing substances to change mood, sleep better, or get high. This data may contribute to increased prevention of Substance Use Disorders and to the treatment of adolescent BPD. Further studies clarifying the characteristics of self-medication are necessary.

INTRODUCTION

Pediatric-onset Bipolar Disorder (BPD) has emerged as an increasingly prevalent and difficult to treat chronic psychiatric disorder.[1–4] Broadly defined, BPD affects 1 to 4% of children and adolescents[5] and manifests a high degree of functional impairment.[4,6–8] One of the main sources of resistance and impairment, in regards to BPD treatment, is the frequent co-occurrence of BPD with other psychiatric disorders, specifically, substance use disorders (SUD).[3,9–13]

The nature of the relationship between BPD and SUD is complex and likely bidirectional. Both intrinsic and external factors appear to be related to the development of BPD and SUD comorbidity. For instance, there exists evidence for a familial association between pediatric

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Declaration of Interest

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BPD and SUD,14 raising the possibility that the two might share genetic and other etiologic factors.

In addition to genetic vulnerabilities, BPD may predispose adolescents to the development of SUD through a mechanism of self-medication. It has been speculated that associated features of pediatric BPD such as affective instability, behavioral disinhibition, high impulsivity, sensation seeking, cognitive impairment, and deficient self-regulation traits, may all predispose adolescents with BPD to seek drugs of abuse.15,16

The hypothesis of self-medication posits that individuals may try to manage their overt and covert underlying psychological conflicts and symptoms by modulating them with substances of abuse.17–20 One may further postulate that specific psychopharmacologic effects of the abused substances may target specific core symptoms of the psychiatric disorders, such as BPD.17–19

Evidence in support of this hypothesis includes a study of adults with BPD and SUD which found that two-thirds of subjects reported improvement in at least one BPD symptom as a result of their substance use and nearly all patients initiated substance use because of at least one BPD symptom.21 In another study of Italian adults with BPD, “improving mood, relieving tension, alleviating boredom, achieving/ maintaining euphoria, and increasing energy” were noted as the most frequent reasons for substance use.22 Similarly, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; n=43,093, age 18 years and older) found that 24% of individuals with mood disorders used alcohol or drugs to relieve mood symptoms. Also, relative to all other DSM-IV psychiatric diagnoses, respondents with Bipolar I Disorder reported the highest prevalence of self-medication.23 This aggregate literature suggests that a number of adults with BPD may initiate or continue to use/abuse substances for reasons other than euphoria, highlighting the importance of self-medication as a potential origin of substance abuse.18

Despite the growing literature consistent with the theory of self-medication among BPD adults, there are several reports of conflicting opinions. For example, in a recent meta-analysis of cannabis use and depression, Degenhardt et al. did not find a positive association between cannabis use and later depression, dispelling the self-medication theory.24 Further, in a study that examined post-treatment substance use and psychiatric symptoms among adolescents, McCarthy et al. found evidence of not only self-medication, but also evidence in support of symptom exacerbation.25

With the majority of SUD arising during adolescence,26 we remain unaware of any studies that have investigated self-medication among adolescents with BPD. To this end, we examined the evidence for self-medication in adolescents with BPD. As part of our ongoing, controlled, longitudinal family-based study of youth with BPD, we compared the frequency, motivation, and drug of choice for reported “self-medication” by substance-using adolescents with BPD, relative to non-mood-disordered, substance-using controls. Based on the literature, we hypothesized that self-medication with substances of abuse would be evident and would be related to BPD in adolescents.

METHODS

The methods of the study are described in full detail elsewhere.27 Briefly, we ascertained 105 probands and 98 non-mood disordered control subjects between the ages of 10–18 years and their first-degree relatives. We ascertained youth at age 10 to examine youth before the age of risk for substance use and to prospectively monitor them through the age of risk. Subjects from both groups were recruited from the same catchment area through newspaper advertisements, Internet postings, clinical referrals to our program (BPD only), and internal

postings within the Partners/Massachusetts General Hospital (MGH) system. These methods were used to collect controls that would also use the Partners/MGH system if they had BPD, representing the same source population as the cases.

We included families with a child (designated the proband) who had at least one parent available to complete interviews about the children. We also recruited the biological siblings, as young as the age of six, of the probands. We excluded potential probands if they had been adopted or if their nuclear family was not available for study. We also excluded any youth with major sensorimotor handicaps that would impede the testing process such as paralysis, deafness, blindness, profound disorders of language such as autism, inadequate command of the English language, or a Full Scale IQ less than 70 (assessed by the Wechsler Abbreviated Scale of Intelligence (WASI)).28 Parents provided written informed consent for their children and children provided written assent to participate. The institutional review board at Massachusetts General Hospital approved this study and a federal certificate of confidentiality was obtained for the study.

A two-stage ascertainment procedure selected subjects, if they were not clinically referred. For BPD probands, the first stage assessed the diagnosis of BPD by screening all children using a telephone questionnaire conducted with their primary caregiver, which queried about symptoms of BPD and study exclusion criteria. The second stage confirmed the diagnosis of BPD using a structured psychiatric interview, as described below. Only subjects who received a positive diagnosis at both stages were included in the study sample. Also, we screened non-mood disordered controls in two stages. First, control primary caregivers responded to the telephone questionnaire, then eligible controls meeting study entry criteria were recruited for the study and received the diagnostic assessment with a structured interview. Only subjects classified as not having any mood disorder at both stages were included in the control group. We excluded controls with any mood disorder because of concerns about potential “manic switching” from dysthymia or unipolar depression to BPD.

Assessments

All diagnostic assessments were made using DSM-IV based structured interviews, by raters with bachelor’s or master’s degrees in psychology who had been extensively trained and supervised by senior investigators (TW). Raters were blind to the ascertainment status of the probands. Psychiatric assessments for subjects under 18 years old relied on the DSM-IV Kiddie Schedule for Affective Disorders-Epidemiologic Version (KSADS-E)29 and were based on independent, indirect interviews with the primary caregivers and direct interviews of probands and siblings. Psychiatric assessments for subjects 18 or older relied on the Scheduled Clinical Interview Diagnosis (SCID).30 For every diagnosis, information was gathered regarding the ages at onset and offset of full syndromatic criteria, and treatment history.

Although standardized algorithms were used to determine each diagnosis, interviewers needed a mechanism to determine the clinical relevance of symptoms when subjects were only able to provide unclear or imprecise information. Thus, a committee of board-certified child and adult psychiatrists who were blind to the subject’s status, referral source and all other data resolved diagnostic uncertainties. Diagnoses presented for review were considered positive only when the committee determined that diagnostic criteria were met to a clinically meaningful degree. We estimated the reliability of the diagnostic review process by computing kappa coefficients of agreement for clinician reviewers. For these diagnoses, the median reliability between individual clinicians and the review committee assigned diagnoses was 0.87. Kappa coefficients for individual diagnoses included: attention deficit hyperactivity disorder (ADHD, 1.0), conduct disorder (CD, 1.0), major depression (1.0),

BPD (0.78), separation anxiety (0.89), agoraphobia (0.80), panic disorder (0.77), substance use disorder (1.0), and Tics/Tourette's (0.68).

To assess the reliability of our diagnostic procedures, we computed kappa coefficients of agreement by having three experienced, blinded, board-certified child and adult psychiatrists diagnose subjects from audio-taped interviews made by the assessment staff. Based on 500 assessments from interviews of children and adults, the median kappa coefficient was 0.98. Kappa coefficients for individual diagnoses included: major depression (1.0), mania (0.95), ADHD (0.88), CD (1.0), oppositional defiant disorder (ODD; 0.90), antisocial personality disorder (ASPD; 0.80), and substance use disorder (1.0). Socioeconomic status (SES) was measured using the five-point Hollingshead scale, where higher scores indicated lower SES. 31

Drug Use Screening Inventory

The Drug Use Screening Inventory (DUSI) is a reliable32 self-reporting instrument for assessing drug use frequency, preference, motivation, and problems associated with use. Screening questions divides participants into those that have and have not used specific drugs and the frequency of use of these drugs within the last year prior to the survey. Subjects reported current use as frequency of use within the year prior to the survey. For these same categories, the DUSI asks which substance the respondent preferred and for which drugs the respondent perceived a problem. Only participants who identified "use within last year" responded to the full questionnaire on the DUSI. The DUSI also queries on 15 specific problems related to use in a yes-no survey format and ranks motivation for *Initiation* and *Continuation* of preferred substance use on a Likert Scale from 1 "very true" through 4 "not true at all" to a) change mood, b) aid sleep, c) get high, or D) other.

Statistical Analysis

Any subject who endorsed use within the last year of one of the listed drugs in the DUSI Section A was included in all analyses. As previously reported,33 to ease the analysis of the DUSI motivational categories (to get high, to change mood, to sleep better), we assigned subjects to a particular category if he or she scored that category 1 or 2 on a scale of 1 to 4 (1=very true; 4=not true), with no other category scored as 1. All subjects who failed to answer these questions or rated "other" with a high priority were scored as "unknown." We also characterized family environment with intactness (divorced/separated or intact).

We compared participants with BPD with non-mood-disordered control participants on potentially confounding demographic variables, using Pearson χ^2 tests for categorical variables, a Wilcoxon rank-sum test for socioeconomic status (SES), and Student's t-test for continuous outcomes. To assess the frequency of use, drug preference, and problems related to use, we used Pearson χ^2 tests and used Fisher's exact test in the case of low-frequency responses. We used ordered logistic regression to assess differences in the motivation of use between groups. All statistical tests were two-tailed. We used a p-value threshold of 0.05 to assert statistical significance with p values between 0.1 and 0.05 as *trends*. Data are presented as mean ± standard deviation (SD) unless otherwise specified.

RESULTS

Clinical characteristics of sample

We ascertained 105 adolescents with BPD and 98 non-mood-disordered control participants. Of these 203 total participants, 120 endorsed ever using any substance on the DUSI (67 BPD and 53 control participants). Of these 120 participants, 40 participants (27 BPD and 13

control participants) endorsed use of one of the drugs listed in DUSI Section A - within last year (hereafter "respondents").

Demographics of the sample are summarized in Table 1. Specifically, we found no statistically significant differences between BPD and control adolescents with respect to age, IQ, parental history of BPD, SES, gender, parental history of any SUD or family intactness (all p values >0.1).

Frequency of Substance Use

We first examined the frequency of all current substance use as self-reported on the DUSI. BPD probands were more likely than controls to report greater frequency of “any cigarette use” (BPD: 78% (N=21); Controls: 31% (N=4); χ^2=8.27, p=0.006), and “problem with cigarette use” (BPD: 48% (N=13); Controls: 8% (N=1), χ^2=6.31, p=0.02). There was a trend to statistical significance for cigarette use of “more than 20 times in a year” (BPD: 44% (N=12); Controls: 15% (N=2); χ^2=3.26, p=0.09, *trend*) with BPD probands more likely to report use of “more than 20 times.” There was also a trend for the use of other drugs “more than 20 times a year” with controls more likely to report this frequency of use (BPD: 4% (N=1); Controls: 23% (N=3); χ^2=3.66, p=0.09, *trend*). We did not find any statistically significant differences for use of alcohol or marijuana or for any problems related to alcohol, marijuana, or other drugs (all p values > 0.10).

Motivation for Substance Use

We then examined our primary outcome: the motivation for using the self-reported “preferred” substance or drug of choice. As Table 2 details, we found that according to the 4 DUSI categories that rank motivation for initiation or continuation of preferred substance use, there was a significantly higher self-report of using drugs to attenuate mood in the substance-using BPD group (2.56±1.40) compared to substance-using controls (3.69±0.75, z=−2.41, p=0.02). Likewise, we found a notable trend to significance in the motivation to continue use in order to change mood (Controls: 3.62±0.96, BPD: 2.96±1.34; p=0.1, *trend*). We found no statistically significant differences between groups in regards to the motivation to start or continue to use in order to get high or sleep better (all p values>0.10).

Substance Preference and Problems Related to Substance Use

Twenty-three percent (N=3) of controls endorsed alcohol as their preferred substance, while none of the BPD group endorsed alcohol as their drug of choice (p=0.03). Adolescents with BPD had a trend to significance with a greater drug preference of marijuana (41% vs. 15% in controls, p=0.1, *trend*). Likely related to small sample sizes, we found no statistically significant differences in the frequency of participants preferring other drugs. When we examined problems related to substance use, the BPD group (48%) were more likely than controls to report problems related to cigarette use (8%, χ^2=6.31, p=0.02). No other report of problems was significantly different between the two groups (all p values > 0.10).

DISCUSSION

The results of this controlled study of adolescents with BPD largely support the hypothesis that youth with BPD were self-medicating with substances of abuse. Substance-using adolescents with BPD were significantly more likely than substance-using controls to report “change in mood” as a motivation for starting to use their preferred substance, with a trend towards significance for continuing to use. We did not find differences between substance-using BPD and controls in other motivational categories of substance use.

Our findings indicate that the majority of adolescents with BPD (about 81%) use substances for reasons other than their euphorogenic properties and about 30% of BPD adolescents initiate and continue to use substances specifically to change their mood. These numbers are consistent with NESARC's data which report that 24% of adults with mood disorders comorbid with SUD self-medicate in response to their mood symptoms.23 Our data are also similar to work with other psychiatric disorders in which continued substance use was unrelated to the euphorogenic effects of the identified substance.33

Overall, our findings add to a growing literature on self-medication and its relation with SUD in BPD and other pediatric psychiatric diagnoses (e.g. ADHD). For instance, Lerner and Schiebe34 demonstrated that adolescent substance users were likely to have a substantial comorbidity of ADHD with indications of drug use for self-medication. In our previous work with ADHD, we found that the majority of ADHD youth did not use substances for their euphorogenic effects nor did they differ from controls in their reports of substance use for the attenuation of mood, sleep, or other reasons.33 In contrast to these findings, our current work shows that adolescents with BPD were significantly more likely than controls to report initiating use and there was a trend to significance for continuing to use in order to change mood.

The differences in DUSI profiles between youth with ADHD and youth with BPD are noteworthy since they are consistent with the postulated self-medication specificity among psychiatric diagnoses and "preferred" psychoactive substances.18 Namely, ADHD adolescents unlike BPD adolescents are not expected to report initiating use of their preferred drug for mood-altering reasons since mood is not a part of the cardinal symptom domain in ADHD.

The results of our study also show that the frequency and level of severity of current cigarette use differs between adolescents with BPD and controls. Specifically, adolescents with BPD were more likely than controls to self-report a greater frequency of any cigarette use (78% BPD vs. 31% Controls, p=0.006) and problems with cigarette use (48% BPD vs. 8% Controls, p=0.02), with a trend to significance for cigarette use of "more than 20 times" (44% BPD vs. 15% Controls, p=0.09). Of interest, our findings are similar to recently reported findings of higher cigarette use and correlates in BPD compared to non-mood disordered controls.35 Given the public health implications of smoking cigarettes, the link between BPD and nicotine dependence from a self-medication perspective requires further investigation.

Another finding was the trend to significance for the preferred marijuana use in BPD adolescents compared to controls (41% vs. 15%, p=0.1, *trend*). While a trend, this finding is consistent with the literature argument that cannabis may have potent mood effects.36 Contrary to previous research (i.e. Weiss et al.37) that found an improvement in psychiatric symptoms regardless of drug choice, our results further highlight the importance of self-selection of specific compounds in context to self medication.18

Our current findings have important implications. Self-medication with substances of abuse has been linked with high rates of affective and other BPD symptoms,17,18,23 which is an important finding since mood and substance use are interconnected.38 Because of these facts, it is reasonable to suggest that early identification and treatment of severe affective dysregulation within pediatric BPD may result in reduced subsequent substance use and abuse. Specifically, attenuation of the need to self-medicate may advance primary and secondary prevention of substance abuse within BPD. For example, in one controlled study of substance abusing adolescents with BPD spectrum illness, lithium resulted in significant reductions in substance use as well as an improvement in global functioning.39 Likewise, in

a study of substance abusing adults with BPD, those who had reported substance-induced improvement in BPD symptoms prior to therapy were the ones who had the greatest decrease in substance use as a result of interpersonal group therapy that challenged and dispelled the flawed logic behind their assumption.21 Further longitudinal data examining this important issue is necessary.

There are a number of important methodological limitations in the current study. Our study consisted of a largely middle class Caucasian sample ascertained from outpatient clinical referrals and advertisements. Hence, this sample may not be generalizeable to other socio-demographic groups. Although our overall sample was relatively large, the subgroup of adolescents with self-reported substance use was relatively small - limiting our sample size and statistical power. This limitation was particularly pronounced in controls and in the analysis subdivided according to preferred substances. Our assessment of the motivation for use and hence self-medication was limited to only four items on the DUSI. While valid and reliable, the DUSI does not cover all possible motivations for use, such as parental/community modeling, peer pressure, stress, and other psychiatric symptoms (anxiety, inattention, impulsivity, etc). In addition, the DUSI provides only subjective, self-report data; and the validity of differentiating between “use to get high” versus “use to change mood” is not well delineated in the literature. We also chose not to control for multiple comparisons. Using the Bonferroni adjustment alters the statistical inference of a study from the testing of a number of specific hypotheses to a test of the universal null hypotheses.40–42 This method increases the Type II error rate40,41 and raises the issue of the amount of tests to be included in the adjustment.40 We did not control for psychiatric comorbidity due to our small sample size and the high comorbidity of BPD with ADHD and CD in our sample: 16 (89%) of BPD subjects had comorbid ADHD and 19 (83%) of BPD subjects had comorbid CD. We also restricted our analyses to data derived only from the DUSI; and hence, we did not examine structured interview-derived substance abuse and dependence data for probands in addition to the DUSI. However, the DUSI has proven to be a valid and reliable measure with psychometric properties studied independently in assessing substance use, reasons for use, and problems related to the use.43,44 Despite the use of structured diagnostic interviews in this study, the diagnostic criteria for juvenile BPD remain controversial.45 However, all participants in this study underwent a two-stage diagnostic assessment as well as confirmation of the diagnosis of BPD by clinical interview. Such high level of scrutiny provides us with a significant degree of reassurance.

Despite these important methodological shortcomings, our study in context to the literature provides further evidence that BPD among adolescents is a major risk factor for substance abuse that appears to be in part related to the self-medication of mood symptomatology. These data highlight the importance of examining substance use in adolescents with serious mood dysregulation. Future studies clarifying the characteristics of substance use in context to self-medication and other intrinsic and extrinsic factors are necessary to provide more data on the prevention of SUD in BPD and other mood dysregulated states.

REFERENCES

1. Kowatch RA, Youngstrom EA, Danielyan A, Findling RL. Review and meta-analysis of the phenomenology and clinical characteristics of mania in children and adolescents. Bipolar Disord. 2005; 7:483–496. [PubMed: 16403174]
2. Weller EB, Weller RA, Fristad MA. Bipolar disorder in children: Misdiagnosis, underdiagnosis, and future directions. J Am Acad Child Adolesc Psychiatry. 1995; 34:709–714. [PubMed: 7608043]
3. Wozniak J, Biederman J, Kiely K, et al. Mania-like symptoms suggestive of childhood-onset bipolar disorder in clinically referred children. J Am Acad Child Adolesc Psychiatry. 1995; 34:867–876. [PubMed: 7649957]

4. Geller B, Tillman R, Craney JL, Bolhofner K. Four-year prospective outcome and natural history of mania in children with a prepubertal and early adolescent bipolar disorder phenotype. Arch Gen Psychiatry. 2004; 61:459–467. [PubMed: 15123490]
5. Lewinsohn PM, Klein DN, Seeley JR. Bipolar disorders in a community sample of older adolescents: prevalence, phenomenology, comorbidity, and course. J Am Acad Child Adolesc Psychiatry. 1995; 34:454–463. [PubMed: 7751259]
6. Birmaher B, Axelson M, Strober M, et al. Clinical course of children and adolescents with bipolar spectrum disorders. Arch Gen Psychiatry. 2006; 63:175–183. [PubMed: 16461861]
7. Geller B, Tillman R, Bolhofner K, et al. Controlled, blindly rated, direct-interview family study of a prepubertal and early-adolescent bipolar I disorder phenotype: morbid risk, age at onset, and comorbidity. Arch Gen Psychiatry. 2006; 63:1130–1138. [PubMed: 17015815]
8. Axelson D, Birmaher B, Strober M, et al. Phenomenology of children and adolescents with bipolar spectrum disorders. Arch Gen Psychiatry. 2006; 63:1139–1148. [PubMed: 17015816]
9. West SA, Strakowski SM, Sax KW, et al. Phenomenology and comorbidity of adolescents hospitalized for the treatment of acute mania. Biological Psychiatry. 1996; 39:458–460. [PubMed: 8679794]
10. Strober M, DeAntonio M, Schmidt-Lackner S, et al. Early childhood attention deficit hyperactivity disorder predicts poorer response to acute lithium therapy in adolescent mania. J Affect Disord. 1998; 51:145–151. [PubMed: 10743847]
11. Kovacs M, Pollock M. Bipolar disorder and comorbid conduct disorder in childhood and adolescence. J Am Acad Child Adolesc Psychiatry. 1995; 34:715–723. [PubMed: 7608044]
12. Biederman J, Faraone SV, Hatch M, et al. Conduct disorder with and without mania in a referred sample of ADHD children. J Affect Disord. 1997; 44:177–188. [PubMed: 9241578]
13. Carlson G, Bromet E, Jandorf L. Conduct disorder and mania: What does it mean in adults. J Affect Disord. 1998; 48:199–205. [PubMed: 9543210]
14. Wilens T, Biederman J, Adamson JJ, et al. Association of bipolar and substance use disorders in parents of adolescents with bipolar disorder. Biological Psychiatry. 2007; 62:129–134. [PubMed: 17481590]
15. Faraone SV, Biederman J, Mennin D, Wozniak J, Spencer T. Attention-deficit hyperactivity disorder with bipolar disorder: a familial subtype? Am Acad Child Adolesc Psychiatry. 1997; 36:1378–1387. discussion 1387–1390.
16. Wilens TE, Biederman J, Millstein R, et al. Risk for substance use disorders in youth with child- and adolescent-onset bipolar disorder. J Am Acad Child Adolesc Psychiatry. 1999; 38:680–685. [PubMed: 10361785]
17. Khantzian EJ. The self-medication hypothesis of addictive disorders: Focus on heroin and cocaine dependence. Am J Psychiatry. 1985; 142:1259–1264. [PubMed: 3904487]
18. Khantzian EJ. The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. Harv Rev Psychiatry. 1997; 4:231–244. [PubMed: 9385000]
19. Pandina, R.; Johnson, V.; Labouvie, E. Affectivity: A central mechanism in the development of drug dependence. In: Glantz, M.; Pickens, R., editors. Vulnerability to Drug Abuse. Washington, DC: American Psychological Association Press; 1992. p. 179-210.
20. Reich LH, Davies RK, Himmelhoch JM. Excessive alcohol use in manic-depressive illness. Am J Psychiatry. 1974; 131:83–86. [PubMed: 4808436]
21. Weiss RD, Kolodziej M, Griffin ML, et al. Substance use and perceived symptom improvement among patients with bipolar disorder and substance dependence. J Affect Disord. 2004; 79:279–283. [PubMed: 15023508]
22. Bizzarri JV, Sbrana A, Rucci P, et al. The spectrum of substance abuse in bipolar disorder: reasons for use, sensation seeking and substance sensitivity. Bipolar Disord. 2007; 9:213–220. [PubMed: 17430295]
23. Bolton JM, Robinson J, Sareen J. Self-medication of mood disorders with alcohol and drugs in the National Epidemiologic Survey on Alcohol and Related Conditions. J Affect Disord. 2009; 115:367–375. [PubMed: 19004504]
24. Degenhardt L, Hall W, Lynskey M. Exploring the association between cannabis use and depression. Addiction. 2003; 98:1493–1504. [PubMed: 14616175]

25. McCarthy DM, Tomlinson KL, Anderson KG, Marlatt GA, Brown SA. Relapse in alcohol- and drug-disordered adolescents with comorbid psychopathology: changes in psychiatric symptoms. Psychol Addict Behav. 2005; 19:28–34. [PubMed: 15783275]
26. Perlis R, Miyahara S, Marangell L, et al. Long-Term implications of early onset in bipolar disorder: data from the first 1000 participants in the systematic treatment enhancement program for bipolar disorder (STEP-BD). Biological Psychiatry. 2004; 55:875–881. [PubMed: 15110730]
27. Wilens TE, Biederman J, Adamson JJ, et al. Further evidence of an association between adolescent bipolar disorder with smoking and substance use disorders: a controlled study. Drug Alcohol Depend. 2008; 95:188–198. [PubMed: 18343050]
28. Wechsler, D. Wechsler Abbreviated Scale of Intelligence (WASI). 4th ed.. San Antonio, Tx: The Psychological Corporation; 1999.
29. Ambrosini PJ. Historical development and present status of the schedule for affective disorders and schizophrenia for school-age children (K-SADS). J Am Acad Child Adolesc Psychiatry. 2000; 39:49–58. [PubMed: 10638067]
30. First, M.; Spitzer, R.; Gibbon, M.; Williams, J. Structured Clinical Interview for DSM-IV Axis I Disorders. Washington, DC: American Psychiatric Press; 1997. p. 84
31. Hollingshead, AB. Four factor index of social status. New Haven, CT: Yale University Press; 1975.
32. Tarter RE, Kirisci L. The Drug Use Screening Inventory for adults: psychometric structure and discriminative sensitivity. Am J Drug Alcohol Abuse. 1997; 23:207–219. [PubMed: 9143634]
33. Wilens T, Adamson J, Sgambati S, et al. Do individuals with ADHD self medicate with cigarettes and substances of abuse results from a controlled family study of ADHD. Am J Addict. 2007; 16 Suppl 1:14–23. [PubMed: 17453603]
34. Horner B, Scheibe K. Prevalance and implications of ADHD among adolescents in treatment for substance abuse. J Am Acad Child Adolesc Psychiatry. 1997; 36:30–36. [PubMed: 9000778]
35. Goldstein BI, Birmaher B, Axelson DA, et al. Significance of cigarette smoking among youths with bipolar disorder. Am J Addict. 2008; 17:364–371. [PubMed: 18770078]
36. Gruber AJ, Pope HG Jr, Brown MW. Do patients use marijuana as an antidepressant? Depression. 1996; 4:77–80. [PubMed: 9160645]
37. Weiss RD, Griffin ML, Mirin SM. Drug abuse as self-medication for depression: an empirical study. Am J Drug Alcohol Abuse. 1992; 18:121–129. [PubMed: 1562010]
38. Strakowski SM, DelBello MP, Fleck DE, et al. Effects of co-occurring alcohol abuse on the course of bipolar disorder following a first hospitalization for mania. Arch Gen Psychiatry. 2005; 62:851–858. [PubMed: 16061762]
39. Geller B, Cooper T, Sun K, et al. Double-blind and placebo controlled study of lithium for adolescent bipolar disorders with secondary substance dependency. J Am Acad Child Adolesc Psychiatry. 1998; 37:171–178. [PubMed: 9473913]
40. Perneger TV. What's wrong with Bonferroni adjustments. BMJ. 1998; 316:1236–1238. [PubMed: 9553006]
41. Rothman K. Noadjustments are needed for multiple comparisons. Epidemiology. 1990; 1:43–46. [PubMed: 2081237]
42. Savitz DA, Olshan AF. Multiple comparisons and related issues in the interpretation of epidemiologic data. Am J Epidemiol. 1995; 142:904–908. [PubMed: 7572970]
43. Tarter RE, Hegedus AM. The drug use screening inventory: Its applications in the evaluation and treatment of alcohol and other drug abuse. Alcohol Health and Research World. 1991; 15:65–75.
44. Tarter RE, Kirisci L, Mezzich A. The drug use screening inventory: School adjustment correlates of substance abuse. Measurement and Evaluation in Counseling and Development. 1996; 29:25–34.
45. Leibenluft E, Charney DS, Towbin KE, Bhangoo RK, Pine DS. Defining clinical phenotypes of juvenile mania. Am J Psychiatry. 2003; 160:430–437. [PubMed: 12611821]

Table 1

Sample characteristics (N=40)

	Control (N=13)	**BPD (N=27)**		
	Mean ± SD	Mean ± SD	t-value	p-value
Age	15.31 ± 1.18	15.30 ± 2.09	0.02	1.0
IQ	105.23 ± 10.37	99.81 ± 2.70	1.25	0.22
	Mean ± SD	Mean ± SD	z-value	p-value
SES	1.83 ± 1.17	2.11 ± 1.15	0.60	0.5
	N (%)	N (%)	χ^2	p-value
Gender	7 (54)	18 (67)	0.62	0.4
Intact Family	3 (50)	4 (57)	0.07	0.8
Parental History of BPD	1 (8)	6 (22)	1.28	0.39
Parental History of any SUD	8 (62)	18 (67)	0.10	0.75

Table 2

Motivation for Substance Use, Likert Scale from 1 “very true” through 4 “not true at all” (N=40)

	Control (N=13)	**BPD (N=27)**		
	Mean±SD	Mean±SD	z-score	p-value
Start Drug ToChange Mood	**3.69±0.75**	**2.56±1.40**	**−2.41**	**0.02**
Start Drug To Sleep Better	3.92±0.28	3.70±0.82	−0.67	0.5
Start Drug To Get High	2.77±1.36	2.93±1.33	0.45	0.7
Cont. Drug To Change Mood	3.62±0.96	2.96±1.34	−1.55	0.1
Cont. Drug To Sleep Better	3.92±0.28	3.81±0.62	−0.36	0.7
Cont. Drug To Get High	3.23±1.09	2.85±1.43	−0.71	0.5