Significance of Cigarette Smoking Among Youths with Bipolar Disorder

Benjamin I. Goldstein, MD, PhD,[1] Boris Birmaher, MD,[1] David A. Axelson, MD,[1] Tina R. Goldstein, PhD,[1] Christianne Esposito-Smythers, PhD,[2] Michael A. Strober, PhD,[3] Jeffrey Hunt, MD,[2] Henrietta Leonard, MD,[†] Mary Kay Gill, RN, MSN,[1] Satish Iyengar, PhD,[1,4] Colleen Grimm, BA,[1] Mei Yang, MSc,[1] Neal D. Ryan, MD,[1] Martin B. Keller, MD[2]

[1]Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
[2]Department of Psychiatry and Butler Hospital, Brown University School of Medicine, Providence, Rhode Island
[3]Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, California
[4]Department of Statistics, University of Pittsburgh, Pittsburgh, Pennsylvania

Cigarette smoking among adults with bipolar disorder (BP) correlates with psychosis, substance use disorders (SUD), and suicidality. Little is known regarding smoking among youths with BP. Youths with BP (n = 441) were divided into three smoking groups: Never, Ever, and Daily. Twenty-five percent reported any smoking (11% daily, 14% ever). Ever and Daily subjects had significantly greater lifetime prevalence of suicide attempts, physical abuse, conduct disorder, and SUD compared to Never subjects. Daily heavy smokers had greater prevalence of SUD and suicide attempts, and worse depression versus daily light smokers. Smoking among youths with BP is independently associated with suicide attempts and SUD. (Am J Addict 2008;17:364–371)

BACKGROUND

During the past decade, a growing body of literature has developed regarding the prevalence and correlates of cigarette smoking among adults with bipolar disorder (BP).[1−8]

Epidemiologic data indicate that the lifetime prevalence of daily smoking among adults with BP is 82.5%, more than twice as high compared to that of adults with no mental illness (39.1%), and higher than that of adults with lifetime major depression (59%).[7] Clinical data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD)[1] indicate that approximately one-third of subjects were daily smokers at intake, although the lifetime prevalence of daily smoking in clinical samples of BP subjects may be twice as high.[5] These findings are especially concerning, not only because of the well-known medical consequences of cigarette smoking, but because smoking among adults with BP has been associated with greater severity of BP illness, as manifested by psychosis,[1,4] suicide attempts,[2,6] and comorbid substance use disorders (SUD).[2,5] Smoking may also increase the metabolism of medications such as atypical antipsychotics.[9]

Smoking is the world's leading cause of preventable mortality in general,[10] and it may be an important factor in the premature mortality in BP specifically. In addition to the tremendously increased risk of suicide and accidental death among persons with as compared to without BP, cardiovascular illness may account for the greatest proportion of the excess mortality associated with BP,[11] perhaps more so for females.[12] Kupfer hypothesized that excessive nicotine use may be an important factor leading to early onset of cardiovascular and other medical diseases in BP.[13] Accordingly, the quit rate for adults with BP (16.6%) is substantially lower versus adults with no mental illness (42.5%) or those with lifetime major depression (38.1%).[7] Even short-term exposure to low-level cigarette smoking among adolescents may have atherogenic consequences.[14]

Despite increasing evidence regarding smoking and psychiatric comorbidity in general,[15–17] to our knowledge only one previous study has specifically examined cigarette smoking among youths with BP. Wilens and colleagues examined the prevalence of smoking among 31 adolescent boys with BP (≥12 years of age; mean 14.7 years) ascertained from a controlled study of ADHD (N = 128) and non-ADHD (N = 109) adolescent boys.[18] They found that the prevalence of smoking was significantly greater among boys with BP (35%) versus without BP (12%), that the risk of smoking conferred by BP was similar to that conferred by comorbid conduct disorder, and that youths with BP began smoking at a significantly earlier age as compared to youths without BP. These data suggest that further study of the prevalence and correlates of smoking among youths with BP in larger samples is indicated.

The present report examines the prevalence and correlates of cigarette smoking in a large sample of youths with BP from the multi-center Course and Outcome of Bipolar Youth (COBY) study. Based on the extant literature from adults with BP and from youths with non-BP psychiatric illness, it was hypothesized that cigarette smoking would be associated with increased age, comorbid conduct disorder and SUD, psychosis, and suicide attempts.

METHOD

Participants

The COBY study enrolled 446 subjects, with ages of 7–17 years. Subject assent and parental informed consent was provided for participation in the COBY study. Subjects were primarily recruited through clinical referrals within three academic medical centers (ie, University of Pittsburgh, n = 212; Brown, n = 144; and UCLA, n = 90); community referrals and print advertisements were also utilized to recruit subjects. Institutional Review Board approval was obtained at each site prior to subject enrollment.

Inclusion Criteria

Subjects met the following criteria:

1. DSM-IV bipolar I disorder (BPI), bipolar II disorder (BPII), or study-operationalized criteria for bipolar disorder not otherwise specified (BP NOS);
2. determined to have a primary bipolar disorder (not induced by substance use, medications, or a medical condition); and
3. intellectual functioning within normal limits.

Details regarding the study-operationalized diagnosis of BP-NOS have been previously reported, and COBY data on clinical course and outcome provide preliminary validation for these operationalized BP NOS criteria.[19,20]

Procedures

Procedures for the COBY study have been reported in detail elsewhere,[19,20] and are presented here in summarized format.

All of the information described below was ascertained at the intake assessment.

Diagnosis

All COBY diagnosticians have a bachelor's degree, master's degree, or Ph.D. in a mental health field, and attended K-SADS training sessions. Parents were interviewed about their adolescents, and adolescents were directly interviewed. Mood symptoms were assessed by the mood disorder sections of the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present Episode version (K-SADS-P[21]), plus additional items from the K-SADS-Mania Rating scale (K-SADS-MRS[22]). Non-mood disorders were assessed using the K-SADS Present and Lifetime version (K-SADS-PL[23]). K-SADS symptom ratings and diagnoses were based on consensus ratings incorporating all available data; in the event of conflicting information, summary ratings were guided by clinical judgment. This study examined current (ie, during the two weeks prior to the intake assessment) global functioning (CGAS: Children's Global Assessment Scale) and current symptoms of mania and depression. To maintain reliability, bimonthly conference calls between sites addressed assessment questions and concerns. Based on ratings of 13 study interviews (4–7 raters per case), inter-rater reliabilities for mood disorders were ≥ 0.75 (kappa); kappas for non-mood disorders were ≥ 0.80. The intraclass coefficient (ICC) for the K-SADS-MRS (12 cases) was 0.96, and the K-SADS-P depression section (12 cases) was 0.98.

The age of onset for a subject's BP illness was considered to be when the subject first met DSM-IV criteria for a manic, mixed, hypomanic, or major depressive episode, or when he/she first met COBY criteria for BP NOS. Given that the validity of DSM-IV diagnostic criteria for preschool-aged children has not been established, the minimum age of onset for BP-spectrum illness was set at four years.

Smoking Status

Questions regarding cigarette smoking were administered as part of the K-SADS. Subjects were divided into three groups with respect to smoking: daily smokers ("Daily"), ever smoked but not current daily smokers ("Ever"), and never smoked ("Never"). Subjects were considered daily smokers if they reported smoking at least one cigarette per day at intake; however, no duration criteria were operationalized. Data regarding the frequency/extent of smoking in the ever group (eg, weekly versus monthly) was not available. Other information ascertained regarding smoking included age at first regular use, current cigarettes/day, and greatest lifetime cigarettes/day. Smoking status could not be determined for five subjects, leaving a total of 441 cases for the analyses.

Other Clinical Information

Basic demographic information was obtained at intake. History of sexual and physical abuse was systematically obtained using the K-SADS as well as an interviewer-administered medical history questionnaire (unpublished) developed at the

Western Psychiatric Institute and Clinic Suicide attempt was defined by self-injurious behavior of clinically significant seriousness and/or lethality, as described in greater detail previously.[24]

The parent(s) who attended the assessment were interviewed at intake about their personal psychiatric history using the Schedule for Clinical Interview of DSM-IV (SCID).[25] The parent(s) were also interviewed regarding the psychiatric status of all first- and second- degree relatives using the Family History Screen, which has demonstrated adequate reliability and validity.[26] In addition, the parent was asked about his/her own smoking habits.

Statistical Analysis

The three smoking groups were compared using omnibus chi-square tests for categorical variables and one-way analysis of variance for continuous variables. Due to the large age differences between the smoking groups, and given the association of age with other predictor variables, clinical variables were only entered into dichotomous logistic regression models if the omnibus analysis remained significant after controlling for age and for multiple comparisons (0.05/20 = 0.003). Family history variables were only entered into regression models if the omnibus analysis remained significant after controlling for multiple comparisons (0.05/8 = 0.006). All p values are based on two-tailed tests with $\alpha = 0.05$. Results are presented in Tables 1–3. Regression analyses were computed with and without parental smoking history, as detailed below. Statistical analyses were performed using the Statistical Package for the Social Sciences Version 14 (SPSS).

RESULTS

Prevalence of Cigarette Smoking

Seventy-five percent of subjects (N = 333) had never smoked cigarettes, and comprised the Never group. The Ever group, (N = 61; 14%), was comprised of 43 subjects (10%) with, and 18 subjects (4%) without, a history of daily smoking. Eleven percent of subjects (N = 47) were in the Daily group. Therefore, among subjects with any lifetime cigarette use, 44% (47/108) were daily smokers. Mean current cigarette use among Daily subjects was 10.6 ± 14.7 cigarettes/day, whereas mean greatest lifetime cigarette use in this group was 17.9 ± 12.8 cigarettes/day. The mean age at first regular cigarette use among subjects in the Daily group was 12.9 ± 2.2 years, spanning the range of 7–16 years. Temporal priority of BP onset and onset of regular smoking could be determined for nearly all Daily subjects (45/47). Onset of regular smoking occurred within the same year as BP onset among 25% of this group, whereas smoking onset preceded BP onset among 31% and BP onset preceded smoking onset among 44%.

Demographic Characteristics

Demographic characteristics are depicted in Table 1. Subjects in the Daily group were significantly older as compared to Ever subjects, who were in turn significantly older as compared

to Never subjects. The Ever group had the lowest percentage of Caucasian subjects. The proportion of subjects living with both biological parents in the Daily group was significantly lower as compared to the Never group. There were no significant differences in sex or SES.

Clinical Characteristics

Clinical characteristics for subjects in each of the smoking groups are summarized in Table 2. Subjects in the Never group had significantly younger age of onset of BP as compared to the other two smoking groups. The distribution of BP subtype among Ever subjects differed significantly in comparison to the other two groups; Ever subjects showed a greater prevalence of BP-I and lower prevalence of BP-NOS as compared to the other groups. Lifetime prevalence of suicide attempts, physical abuse, conduct disorder, and SUD were significantly greater in the Daily and Ever groups as compared to the Never group, and the lifetime prevalence of sexual abuse was significantly greater among Ever subjects as compared to Never subjects. History of psychiatric hospitalization was significantly more prevalent among Daily as compared to Never subjects. There were no significant between-group differences in any other clinical characteristics, including comorbid anxiety, ADHD, or ODD.

Family History

Positive family history of depression among first-degree relatives was lowest among Never subjects, and significantly lower as compared to Daily subjects. Positive first-degree family history of schizophrenia was significantly greater in the Ever and Daily groups as compared to the Never group. Subjects in the Never group had the lowest positive family history of SUD among first-degree relatives, significantly lower as compared to Ever subjects. For second-degree relatives, positive family history of ADHD was significantly more common among Never and Ever subjects as compared to Daily subjects. Finally, second-degree positive family history of SUD was least prevalent among Never subjects, and significantly less prevalent as compared to Daily subjects.

Data regarding parental smoking were available for 384 subjects (86% of the sample). Parental history of smoking was positive among 26% of subjects overall, and among 23% of Never subjects, 40% of Ever subjects, and 33% of Daily subjects ($\chi^2 = 6.9$, df = 2, $p = 0.03$). Post-hoc pairwise comparisons indicated that the difference between Never and Ever subjects was significant ($\chi^2 = 6.7$, df = 1, $p = 0.01$). A comparison of the demographic characteristics of subjects with present as compared to missing parental history of smoking indicated that subjects for whom information regarding parental smoking was missing were of significantly lower mean SES (3.1 ± 1.3 versus 3.5 ± 1.2, t = 2.4, $p = 0.02$) and were significantly more likely to be of non-Caucasian race (29% versus 17%, $\chi^2 = 5.1$, $p = 0.02$). These groups did not differ significantly with respect to mean age, sex, or living with intact family.

Logistic Regression Analyses

The clinical characteristics and family psychiatric history variables for which between-group differences in univariate comparisons had $p < 0.1$ were included in dichotomous logistic regression analyses to examine their unique contribution to variance in smoking status. Given the high degree of similarity between Ever and Daily groups, these groups were collapsed into a single smoking group for the purpose of dichotomous regression analyses.

The logistic regression analysis comparing subjects with versus without a history of smoking included the following variables: age, sex, race, intact family, BP diagnosis, lifetime psychiatric hospitalization, conduct disorder, panic disorder, suicide attempt, suicidal ideation, physical abuse, sexual abuse, and SUD; first-degree family history of depression, schizophrenia, suicide attempt and SUD; and second-degree family history of ADHD and SUD. The variables most significantly associated with smoking were older age ($\chi^2 = 29.1$, df = 1, $p < 0.001$), lifetime SUD (OR 22.8, 95% CI 6.2–84.2; $p < 0.001$), lifetime suicide attempt (OR 3.0, 95% CI 1.7–5.5; $p = 0.001$), first-degree (OR 2.9, 95% CI 1.6–5.4; $p < 0.001$) and second-degree (OR 2.2, 95% CI 1.1–4.2; $p < 0.001$) family history of SUD.

Exploratory Analyses

In order to examine in exploratory fashion the association of quantity of cigarette smoking within the Daily group, univariate analyses were repeated comparing heavy smokers (≥ 10 cigarettes/day; N = 21) and non-heavy smokers (<10 cigarettes/day; N = 26). Heavy smokers comprised 45% (21/47) of Daily smokers, and had significantly greater lifetime prevalence of suicide attempts (68% versus 35%; $\chi^2 = 4.8$, df = 1, $p = 0.03$) and lifetime SUD (62% versus 27%; $\chi^2 = 5.8$, df = 1, $p = 0.02$) and significantly greater depressive severity at intake (20.4 ± 8.2 versus 14.0 ± 10.3; t = 2.3, df = 1, $p = 0.03$) in comparison to non-heavy smokers. A logistic regression analysis that included these variables and controlled for age, race, sex, and intact family showed that heavy smoking was significantly associated with lifetime SUD (OR 4.8, 95% CI 1.2–19.0; $p = 0.03$), whereas the association of heavy

smoking with lifetime suicide attempt (OR 3.5, 95% CI 0.9–13.5; $p = 0.07$) and with depressive severity at intake ($\chi^2 = 3.5$, df = 1, $p = 0.06$) was nearly significant. The estimated effect size for the association between heavy smoking and history of suicide attempt was found to be $d = 0.7$, consistent with a moderate-to-large effect size.[27]

Finally, binary logistic regression analyses were repeated with parental history of smoking as an additional variable, as there was a significant between-group difference in the univariate analysis among subjects for whom this information was available (N = 358). Parental smoking history was independently significantly associated with subject smoking (OR 2.3, 95% CI 1.1–4.6; $p = 0.02$). Moreover, the same five predictors remained significantly associated with smoking when parental history was included in the analysis.

DISCUSSION

In this study of youths with BP, 25% have smoked cigarettes. Among subjects with any lifetime history of smoking, nearly half (44%) were daily smokers, of whom nearly half (45%) were heavy smokers (≥ 10 cigarettes per day). Smoking among COBY subjects is associated with greater age and with markers of psychiatric burden. As compared to subjects in the Never group, subjects in the Ever and Daily groups had significantly greater lifetime prevalence of suicide attempts, physical abuse, conduct disorder, and SUD. Subjects in the Never group differed significantly from those in the other groups in terms of several domains of family psychiatric history. Regression analyses comparing Never subjects to those in the other smoking groups found that age, lifetime SUD, lifetime suicide attempt, and first- and second-degree family history of SUD were most robustly associated with smoking. In a subset of subjects with information regarding parental smoking, this variable was also independently associated with smoking. Compared to Daily smokers without heavy use (<10 cigarettes per day), those with heavy use (≥ 10 cigarettes per day) had greater lifetime prevalence of SUD and of suicide attempts, and greater

TABLE 1. Demographic Characteristics of Youths with Bipolar Disorders by Cigarette Smoking Status

	Smoking status				
Demographic characteristics	Never (N = 333; 75%)	Ever (N = 61; 14%)	Daily (N = 47; 11%)	Statistic df = 2	p
Age	11.9 ± 3.2^a	14.4 ± 2.3^b	15.7 ± 1.6^c	F = 44.9	<0.001
SES	3.4 ± 1.2	3.4 ± 1.1	3.5 ± 1.2	F = 0.1	0.86
Sex (% male)	56	43	45	$\chi^2 = 5.3$	0.07
Caucasian	83^a	69^b	83^{ab}	$\chi^2 = 7.0$	0.03
Intact family	45^a	36^{ab}	26^b	$\chi^2 = 7.4$	0.03

Never = no history of ever smoking; Ever = history of smoking, but not of daily smoking; daily = history of daily smoking.
[a,b,c] Values with different superscript letters were significant at p values $\leq .05$.

TABLE 2. Clinical Characteristics and Comorbidities of Youths with Bipolar Disorders, by Cigarette Smoking Status

	Smoking status				
	Never (N = 333; 75%)	Ever (N = 61; 14%)	Daily (N = 47; 11%)	Statistic (df = 2)	p
Clinical characteristics, M ± SD					
BP onset age	8.7 ± 3.8^a	10.4 ± 3.5^b	11.8 ± 3.7^b	F = 17.2	<0.001*
Current depression score[‡]	14.1 ± 10.0	16.6 ± 11.3	16.9 ± 9.9	F = 2.6	0.08
Current mania score[§]	22.7 ± 12.3	21.6 ± 11.1	24.5 ± 12.1	F = 0.7	0.47
Current CGAS[‖]	54.9 ± 12.6	53.9 ± 10.7	54.0 ± 10.7	F = 0.2	0.79
BP diagnosis, %				$\chi^2 = 11.2$	0.02[†]
BP-I	58^a	72^b	45^a		
BP-II	6	8	13		
BP-NOS	36	20	43		
Psychosis, %	27	28	28	$\chi^2 = 0.0$	0.99
Mixed episodes, %	26	36	23	$\chi^2 = 3.1$	0.21
Suicide attempt, %	23^a	53^b	49^b	$\chi^2 = 30.2$	<0.001*[†]
Suicidal ideation, %	72^a	82^{ab}	92^b	$\chi^2 = 10.0$	0.007[†]
Self-injurious behavior, %	35	48	43	$\chi^2 = 4.1$	0.13
Hospitalization, %	49^a	61^{ab}	64^b	$\chi^2 = 6.4$	0.04
Physical or sexual abuse, %	16^a	36^b	36^b	$\chi^2 = 20.1$	<0.001*[†]
Physical abuse, %	9^a	26^b	30^b	$\chi^2 = 23.6$	<0.001*[†]
Sexual abuse, %	9^a	25^b	13^{ab}	$\chi^2 = 12.3$	0.002[†]
Comorbidity, %					
Any anxiety	41	38	45	$\chi^2 = 0.6$	0.76
Panic disorder	5	13	13	$\chi^2 = 5.0$	0.08
ADHD	61	61	55	$\chi^2 = 0.6$	0.76
Oppositional defiant disorder	39	46	38	$\chi^2 = 1.1$	0.56
Conduct disorder	8^a	21^b	34^b	$\chi^2 = 29.7$	<0.001*[†]
Substance use disorder	1^a	26^b	43^b	$\chi^2 = 115.2$	<0.001*[†]

Never = no history of ever smoking; ever = history of smoking, but not of daily smoking; daily = history of daily smoking.
*Corrected $p < 0.05$ after controlling for multiple comparisons.
[†]Corrected $p < 0.05$ after controlling for age.
[‡]KSADS-DEP-P valid N = 431.
[§]KSADS-MRS valid N = 435.
[‖]valid N = 434.
[a,b,c]Values with different superscript letters were significant at $p \leq .05$.

depressive severity at intake, although the latter two findings were reduced to near-significance in regression analyses.

This study found that age was significantly and directly associated with smoking. Previous estimates of smoking prevalence among youths similarly vary with age. Less than 10% of 10–11-year-old participants in a Canadian epidemiologic study had ever tried smoking, as compared to approximately one-third of 12–13-year-olds and half of 16–17-year-olds.[28] The equivalent values in the present study were highly similar: 9%, 32%, and 46% for these respective age groups. Recent representative data from the United States indicate that the prevalence of daily smoking is 4.4% among eighth graders and 8.3% among tenth graders (see http://www.monitoringthefuture.org). A previous epidemiologic study found that 7% of adolescents 14–18 years old were daily smokers.[29] The prevalence of daily smoking at intake in the present study was 11%, despite the younger mean age of subjects as compared to the above-cited studies. Moroever, 44% of subjects in the present study who had ever smoked were daily smokers at intake, whereas the equivalent figure in the study by Lewinsohn and colleagues was 19%.[29] These findings suggest that youths with BP may demonstrate increased prevalence of daily smoking, whereas the lifetime prevalence of ever smoking is similar to that of non-clinical samples. Similarly, others have found that the presence of psychiatric disorders among youths is associated with increased prevalence of heavy smoking but is not with increased risk of experimentation.[17]

Cigarette smoking among youths has also been previously associated with depressive symptoms.[16,30–32] Epidemiologic data from older adolescents suggests that smoking is independently associated with incident depression, after controlling for

TABLE 3. Family History Variables of Youths with Bipolar Disorders by Cigarette Smoking Status

	Smoking status				
	Never (N = 333; 75%)	Ever (N = 61; 14%)	Daily (N = 47; 11%)	Statistic df = 2	p
Family history, first-degree					
Mania	33	47	38	$\chi^2 = 4.3$	0.12
Depression	68^a	79^{ab}	87^b	$\chi^2 = 8.5$	0.01
ADHD	27	38	31	$\chi^2 = 3.0$	0.23
Conduct disorder	18	26	27	$\chi^2 = 3.8$	0.15
Schizophrenia	0.3^a	3^b	4^b	$\chi^2 = 8.6$	0.01
Anxiety	50	57	51	$\chi^2 = 1.1$	0.59
Suicide/attempt	21	33	16	$\chi^2 = 5.0$	0.08
Substance use disorder	38^a	62^b	51^{ab}	$\chi^2 = 13.3$	0.001*
Family history, second-degree					
Mania	35	38	40	$\chi^2 = 0.5$	0.79
Depression	71	68	62	$\chi^2 = 1.4$	0.51
ADHD	25^a	36^a	7^b	$\chi^2 = 11.6$	0.003*
Conduct disorder	21	29	27	$\chi^2 = 1.8$	0.41
Schizophrenia	4	7	9	$\chi^2 = 2.9$	0.23
Anxiety	47	39	51	$\chi^2 = 1.6$	0.44
Suicide/attempt	31	36	31	$\chi^2 = 0.5$	0.78
Substance use disorder	59^a	70^{ab}	78^b	$\chi^2 = 7.5$	0.02

Never = no history of ever smoking; ever = history of smoking, but not of daily smoking; daily = history of daily smoking.

*Denotes statistical significance after correction for multiple comparisons.

[a,b,c]Values with different superscript letters were significant at p values ≤ .05.

other disorders, and that lifetime major depression at baseline was the only predictor of smoking onset after controlling for other disorders.[30] Another epidemiologic study of 8–14-years-olds at intake found that tobacco smoking was a predictor of subsequent depressed mood, but that antecedent depressed mood was not a predictor of smoking initiation.[30] Data from the prospective National Longitudinal Study of Adolescent Health indicate that current cigarette smoking at baseline was the strongest predictor of incident high depressive symptoms, conferring a nearly four-fold risk.[31] Finally, depressive disorders among inpatient youths in a psychiatric unit were associated with a four-fold increased risk of being a current smoker.[16] Future prospective studies from the COBY sample will examine whether smoking is predictive of depressive recurrence, as well as whether the burden of depressive symptoms predicts incident smoking.

The findings of this study suggest that smoking may be independently associated with suicide attempts, and that heavy smoking is more strongly associated with suicide attempts in comparison to non-heavy smoking. The difference in lifetime prevalence of suicide attempts among Never and Ever subjects remained significant after controlling for potential confounds, whereas the difference between Daily and Never subjects was no longer significant. The finding of an association between smoking and suicide attempts replicates previous findings from adults with BP.[2,6] Ostacher and colleagues reported that smoking was independently associated with a two-fold increased risk of lifetime history of a suicide attempt after controlling for potential confounds.[2] Oquendo and colleagues examined predictors of incident suicide attempts in a two-year prospective study of 308 patients who had experienced a major depressive episode (21% of the sample had BP).[6] Cigarette smoking was one the three most powerful predictors of suicidal acts, associated with a two-fold increased risk. A study of adolescent psychiatric inpatients found a four-fold risk of suicide attempts among daily smokers as compared to non-daily smokers after controlling for potential confounds.[33] Another study found that heavy daily smoking was independently associated with a two-fold increased risk of suicide attempt among adolescent psychiatric inpatients.[34] In contrast to the findings regarding suicide attempts, previous studies have either failed to demonstrate a significant association between smoking and suicidal ideation,[34] or, as in the present study, have found that the association between suicidal ideation and smoking is confounded by other factors.[35] Neither the present nor previous findings regarding smoking and suicidality address causality; however, the repeated association of these variables by different research groups examining subjects in different age groups and employing different methodologies suggests that this topic merits further examination. Although we attempted to control for potential confounds of the association between smoking and suicide attempts, such as depressive severity and SUD, future prospective studies from COBY will be better able to examine the direction of this association as well as the potential impact of moderators and mediators.

The significant association between smoking and SUD is consistent with previous findings from adults with BP.[1,2,5] For adolescents in the community, lifetime smoking of any quantity or frequency is associated with increased prevalence of subsequent SUD in young adulthood.[36] Similarly, among inpatient youths in a psychiatric unit, SUD were the strongest predictors of being a current smoker.[16]

Contrary to the study's hypotheses, the lifetime prevalence of psychosis was nearly identical across the three smoking groups. The possibility that this was due to the inclusion of BP-NOS was explored by examining the association between psychosis and smoking among subjects with BP-I only; however, between-group differences in psychosis remained non-significant ($p = 0.99$). Two previous studies of adults with BP have found an association between smoking and psychosis[1,4]; however, a third study found no such association.[3] Therefore, the question of whether psychosis is associated with smoking in BP requires further study.

The strength of the association between smoking and conduct disorder was also less than expected. Although the lifetime prevalence of conduct disorder was significantly lower in the Never group as compared to the other groups, the difference was not significant in the regression analyses. In addition, and in contrast to the findings regarding suicide attempts, SUD, and depressive severity, the association between conduct disorder and severity of smoking was non-significant. Family history of conduct disorder was also not significantly associated with smoking. Similarly, there were no significant between-group differences in the prevalence of ADHD or anxiety disorders. A previous study of adults with BP found that the lifetime prevalence of comorbid anxiety disorders is greater among subjects with, versus without, a history of daily smoking (68% vs. 53%), albeit that this difference was no longer significant in multivariate analyses.[2] Prospective data are needed in order to clarify the nature of the association of smoking with psychosis, disruptive behavior disorders, and anxiety disorders among BP youths.

These findings must be interpreted in the context of the methodologic limitations of this study. First, this study is based on cross-sectional and retrospective data, which may be subject to recall bias. However, the current sample is being followed longitudinally, and future reports will allow prospective evaluation of the incidence, prevalence, risk factors, and correlates of smoking. Second, the extent of current smoking in the Ever group could not be determined. Smoking frequency in this group may have ranged from infrequent experimentation to regular, but not daily, smoking. Third, family history of smoking was not ascertained in the same method as psychiatric disorders. Therefore, information regarding smoking among non-interviewed parents, siblings, and other relatives was not systematically ascertained. Fourth, detailed information regarding potential peer-group influence on smoking behavior was not collected. Finally, this study cannot provide an estimate of the prevalence of nicotine dependence in this population, as symptoms of dependence are not ascertained systematically in the KSADS.

Taken together, the findings of this study suggest that cigarette smoking is prevalent among youths with BP beginning in childhood, and that daily smoking may be disproportionately prevalent as compared to community samples. Similar to adults with BP, smoking is independently associated with suicide attempts and SUD. Moreover, among daily smokers, heavy smoking may be associated with greater depressive severity, SUD, and suicide attempts. Unfortunately, few youths in psychiatric treatment settings receive smoking cessation treatment.[15] The far lower prevalence of daily smoking as compared to adults with BP[1] underscores the important opportunity for prevention that exists. Despite the acknowledged limitations of the present study, and pending the availability of prospective data, these findings suggest that further efforts guided toward smoking prevention and cessation among youths with BP are needed.

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