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RESEARCH ARTICLE

Dimensional and Categorical Correlates of Substance Use Disorders among Canadian Adolescents with Bipolar Disorder

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Abstract

Objectives: Despite increasing evidence of excessive substance use disorder (SUD) prevalence among adolescents with bipolar disorder (BP), little is known about this topic among Canadian adolescents with BP. We therefore sought to examine the clinical characteristics and dimensional measures of psychopathology associated with comorbid SUD among Canadian BP adolescents. **Method:** Participants were 100 adolescents, ages 13-19 years, with BP I, II, or not otherwise specified (NOS). Diagnoses (current and lifetime) were determined via the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present and Lifetime version (KSADS-PL). Participants were considered to have lifetime SUD if they met DSM-IV criteria for abuse of or dependence on alcohol or any drug other than nicotine. Chi-square analyses and independent samples t-tests were followed by logistic regression analyses. **Results:** The lifetime prevalence of SUD was 33% (primarily alcohol and cannabis use disorders). In univariate analyses, SUD was associated with greater lifetime prevalence of conduct disorder, oppositional defiant disorder, panic disorder, assault of others, and a greater number of stressful life events. SUD was significantly associated with greater self-reported impulsivity and parent-report of anger/depression in the adolescent. In multivariable analyses, SUD was associated with panic disorder and oppositional defiant disorder. **Conclusion:** SUD is highly prevalent among Canadian adolescents with BP and is associated with anxiety disorders, behavioural disorders, and trait impulsivity. Targeting these clinical characteristics may help guide preventative and treatment strategies for this population.

Key Words: bipolar disorder, substance use disorder, adolescents, drug, alcohol, predictor

Résumé

Objectifs: Malgré des preuves croissantes de la prévalence excessive du trouble d'utilisation de substances (TUS) chez des adolescents souffrant de trouble bipolaire (TB), ce sujet est très peu connu des adolescents canadiens souffrant de TB. Nous avons donc cherché à examiner les caractéristiques cliniques et les mesures dimensionnelles de la psychopathologie associée au TUS comorbide chez les adolescents canadiens souffrant de TB. **Méthode:** Les participants étaient 100 adolescents de 13 à 19 ans souffrant de TB I, II, ou non spécifié ailleurs (NSA). Les diagnostics (actuels et de durée de vie) ont été déterminés par le tableau des troubles affectifs et de la schizophrénie pour les enfants d'âge scolaire, version actuelle et de durée de vie (KSADS-PL). Les participants étaient évalués avoir un TUS de durée de vie s'ils satisfaisaient

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aux critères du DSM-IV en matière d'abus ou de dépendance à l'alcool ou à toute autre drogue que la nicotine. Les analyses chi-carré et les tests t d'échantillons indépendants ont été suivis d'analyses de régression logistique. **Résultats:** La prévalence de durée de vie du TUS était de 33 % (principalement des troubles d'utilisation d'alcool et de cannabis). Dans les analyses univariées, le TUS était associé à une prévalence de durée de vie plus marquée du trouble des conduites, du trouble oppositionnel avec provocation, du trouble panique, d'agression physique et d'un plus grand nombre d'événements de la vie stressants. Le TUS était significativement associé à une plus grande impulsivité auto-déclarée et à des rapports des parents sur la colère/dépression de l'adolescent. Dans les analyses multivariées, le TUS était associé au trouble panique et au du trouble oppositionnel avec provocation. **Conclusion:** Le TUS est hautement prévalent chez les adolescents canadiens souffrant de TB et est associé aux troubles anxieux, aux troubles du comportement, et à l'impulsivité. Cibler ces caractéristiques cliniques peut aider à guider l'élaboration de stratégies préventives et de traitement pour cette population.

Mots clés: *trouble bipolaire, trouble d'utilisation de substances, adolescents, drogue, alcool, prédicteur*

Introduction

Comorbid substance use disorders (SUD; i.e. alcohol or drug abuse or dependence) are highly prevalent among adults with bipolar disorder (BP), even compared to other psychiatric illnesses, with lifetime rates in excess of 50% (Bizzarri et al., 2007; Cerullo & Strakowski, 2007; Goldstein & Levitt, 2007; Regier et al, 1990; Swann, 2010). Comorbid SUD among adults with BP is associated with numerous proxies for increased salient clinical and demographic characteristics including anxiety disorders (Goldstein & Levitt, 2007), suicidality (Dalton, Cate-Carter, Mundo, Parikh, & Kennedy, 2003), and physical (Richardson, 2011) and sexual abuse (Kolodziej et al., 2005).

Over the past decade, there has been increasing evidence that rates of SUD are also excessive among adolescents with BP (Geller & Luby, 1997; Goldstein et al. 2008; Merikangas & McClair, 2012; Wilens et al., 2004). Similarly, SUD among adolescents with BP are associated with legal problems (Goldstein et al. 2008), suicidality (Goldstein et al. 2008; Goldstein et al., 2012), anxiety disorders (Wilens et al., 2004), post-traumatic stress disorder (PTSD; Goldstein et al. 2008; Steinbuchel et al., 2009), conduct disorder (Wilens et al., 2008), physical and sexual abuse (Goldstein et al., 2008), and pregnancy and abortion (Goldstein et al., 2008; Heffner et al., 2012). Importantly, the prevalence of SUD among youth with BP appears to be similar across BP subtypes (Goldstein et al., 2008; Goldstein et al., 2013). A study by Duffy and colleagues (Duffy, Alda, Crawford, Milin, & Grof, 2007) found that SUDs appeared to be a complication of a pre-existing mood disorder among offspring of individuals with BP.

Most previous studies examining SUD among adolescents with BP have included samples from the U.S. Canadian epidemiologic data confirm increased rates of SUD among adolescents with BP (Kozloff et al., 2010), however no previous clinical study has examined this topic among Canadian adolescents with BP, nor have any studies examined for correlates of SUD among Canadian adolescents with BP. Moreover, findings from offspring of parents with BP (Duffy, Grof, Grof, Zvolsky, & Alda, 1998; Duffy et al., 2007; Duffy et al., 2012) demonstrate the peak hazard of SUD was between 14-20 years of age, and that in addition to having a mood disorder, male sex, parental SUD, and psychosis were significantly associated with SUD. Similar to other findings among adolescents with BP, mood disorders among BP offspring most commonly predated SUD (Goldstein & Bukstein, 2010). However, only 11-33% of the high-risk offspring in these studies had BP. As such, no previous clinical study has examined the prevalence and correlates of SUD among Canadian adolescents with BP.

Findings from adults with BP suggest that there may be cross-national differences in comorbidities in general, and SUD specifically. Whereas a cross-national comparison of epidemiologic studies did not find differences in SUD prevalence (Merikangas et al., 2011), there do appear to be cross-national differences in SUD prevalence in clinically-derived samples (Post et al., 2011). These differing findings may be due to the worse course of illness and increased comorbidities among clinical samples, which result in the individuals seeking treatment. Post and colleagues compared BP characteristics and comorbidities in clinical BP samples from the U.S. and Europe (Post et al., 2011). Compared with Germany and the Netherlands, participants in the U.S. reported greater rates of SUD, and this difference appeared to be explained in part by higher rates of anxiety disorders and a history of physical or sexual abuse in the U.S. (Post et al., 2011).

Dimensional measures of psychopathology in relation to comorbid SUD among adults with BP have also been receiving increased attention in recent years. For example, trait impulsivity has been shown to be prominent in both SUD and BP (Swann, Dougherty, Pazzaglia, Pham, & Moeller, 2004). Indeed, a recent meta-analysis found that BP individuals with SUD were more impulsive than those without SUD (Richardson, 2011). Similarly, SUD among adults with BP has also been associated with greater levels of trait aggression (Grunebaum et al., 2006).

Due to marked international differences in clinical characteristics observed among adults with BP, and meaningful differences in the healthcare systems in Canada and the U.S. (Vasiliadis, Lesage, Adair, Wang, & Kessler, 2007), we sought to examine this topic in a Canadian sample of

BP adolescents. The differing healthcare systems in Canada and the U.S. may contribute to the willingness of adolescents to seek treatment, as well as the type of treatment they are provided, thus impacting their disorder progression. In addition, we sought to investigate dimensional measures of psychopathology, with an emphasis on mood dysregulation/lability, in relation to comorbid SUD among adolescents with BP.

Method

Sample

The present study includes 100 participants, ages 13-19, with BP I, II, or not otherwise specified (NOS). Participants were seeking assessment and/or treatment at a sub-specialty clinic in a tertiary academic health sciences centre. At least one parent/guardian for each adolescent also participated. Prior to study commencement, all participants and their parent/s provided written informed consent. Participants were a consent-giving subgroup of consecutive admissions. Research Ethics Board approval was obtained.

Procedure

Diagnoses (current and lifetime) were determined via the Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (KSADS-PL; Kaufman et al., 1997), which incorporates information from adolescents and their parent/s. All interviewers have a bachelor's or master's degree in the health sciences field and completed KSADS training under the supervision of the senior author (B.G). The mood sections of the KSADS-PL were replaced with extended mood sections, the KSADS Depression Rating Scale (DRS; Chambers et al., 1985) and KSADS Mania Rating Scale (MRS; Axelson et al., 2003). Diagnoses were determined with the consideration of all available information, with clinical judgment used when conflicting information was provided. Diagnoses were confirmed by a consensus meeting with a child psychiatrist following completion of the KSADS-PL interview (B.G).

As BP-NOS criteria are not specified in DSM-IV, our study operationalized BP-NOS using the following criteria from the Course and Outcome of Bipolar Youth (COBY) study (Birmaher et al., 2006): elevated and ⁄or irritable mood, plus: (i) two DSM-IV manic symptoms (three if only irritable mood is reported), (ii) change in functioning, (iii) mood and symptom duration of at least 4 h during a 24-h period, and (iv) at least four cumulative 24-h periods of episodes over the participant's lifetime that meet the mood, symptom, and functional change criteria. Participants were considered to have lifetime SUD if they met DSM-IV criteria for abuse of or dependence on alcohol or any drug other than nicotine.

The age of onset of BP was considered to be when the participant first met DSM-IV criteria for a manic, mixed, or hypomanic, or when he ⁄she first met study criteria for BP-NOS. The age of onset of an individual's SUD was considered to be when the participant first met DSM-IV criteria for alcohol or substance abuse or dependence.

History of physical and sexual abuse was obtained with an interviewer-administered medical history questionnaire and from the PTSD screen within the KSADS-PL. An interviewer-administered Safety Assessment Form was used to determine lifetime aggression and suicidality that may have occurred outside of the context of a depressive episode, with information on suicide attempts also obtained via the KSADS DRS.

The self-report Life Problems Inventory (LPI) was used to identify dimensional impulsivity, emotional dysregulation, identity confusion, and interpersonal problems (Rathus & Miller, 1995). The self-reported Children's Affective Lability Scale (CALS) was completed by the participant, and one parent completed the measure regarding the adolescent (Gerson et al., 1996). This self-report has two subscales, including angry/depressed and disinhibited/persistent.

Participants completed the self-report Stressful Life Events Schedule (SLES) to identify the occurrences of various stressful events (e.g. ran away from home, broke up with boyfriend/girlfriend) and the perceived impact of each event (Williamson et al., 2003). Parents also completed the SLES about their adolescent. Psychiatric history of first- and second-degree relatives was obtained through an interview with parents and the adolescent, using the Family History Screen (Weissman et al., 2000).

Analyses

Chi square analyses and Fisher's Exact test were used for categorical variables and independent samples t-tests were used for dimensional measures. The threshold for statistical significance was set at $p<0.05$. The clinical characteristics and comorbidities that were at least marginally associated with SUD ($p<0.1$) in the univariate analyses were included in the regression analyses, with SUD as the dependent variable. False discovery rate (FDR) was utilized to control for multiple comparisons. Statistical analyses were conducted with SPSS version 21.

Results

SUD Prevalence

The lifetime prevalence of SUD was 33% (33/100). Nineteen percent of all adolescents reported a lifetime alcohol use disorder (11% abuse, 8% dependence) and 25% reported a lifetime drug use disorder (4% abuse, 21% dependence). Eight percent of the sample reported only a lifetime alcohol use disorder, 14% reported only a lifetime drug use disorder, and 11% reported both a lifetime alcohol use disorder and a lifetime drug use disorder. Cannabis abuse or

dependence was reported by all participants who reported a lifetime drug use disorder. SUD onset preceded BP onset for 61% of the sample, BP preceded SUD for 18% of the sample, and SUD and BP onset were concurrent for 21% of the sample.

Univariate Analyses

Univariate analyses are presented in Table 1. Participants with SUD, as compared to those without SUD, reported significantly greater lifetime prevalence of conduct disorder (24.2% vs. 3%; p = 0.02) and oppositional defiant disorder (ODD) (63.6% vs. 22.4%; p = 0.01). As compared to participants without SUD, those with SUD reported greater assault of others (50% vs. 20%; p = 0.03) and a greater number of stressful life events (p = 0.01). SUD was significantly associated with greater self-reported impulsivity (p = 0.01).

Multivariable Analyses

In multivariable analyses, the following variables were significantly associated with SUD: panic disorder ([odds ratio (OR) = 8.45, 95% confidence interval (CI): 1.64-43.43, p = 0.01] and ODD (OR = 4.97, 95% CI = 1.22-20.27, p = 0.02).

Discussion

The present study of Canadian adolescents with BP found SUD to be associated with higher rates of multiple comorbidities including conduct disorder, ODD, and panic disorder, as well as violence, impulsivity, and stressful life events. Specifically, SUD was associated with greater rates of assault, as well as greater mood lability, as reported by their parents. In the present sample, one third of adolescents had an SUD. In multivariable analyses, SUD was independently significantly associated with comorbid panic disorder and ODD. These findings, from a clinical sample of Canadian adolescents with BP, largely converge with previous findings from U.S. clinical samples, and expand the literature regarding dimensional phenotypes associated with comorbid SUD among adolescents with BP.

The limitations of the current study must be considered in interpreting these results. First, a cross-sectional methodology was utilized, thus precluding any inferences regarding causation. Second, urine toxicology was not used. Although it would only confirm current SUD, as opposed to lifetime SUD, urine toxicology may have optimized diagnostic accuracy. Third, the majority of cases of SUD had cannabis or alcohol use disorders. Correlates of SUDs related to less commonly used substances such as cocaine may differ from those reported here (Services US, 2012). Fourth, the present sample was drawn from a tertiary clinical setting and therefore may not be representative of other samples such as untreated community samples. Fifth, although the present sample is among the larger ones in the current literature in adolescent BP, the sample size was not adequate to detect small effect sizes as significant. Lastly, the present study is based on a treatment seeking sample at a tertiary centre, and may therefore not generalize to the general population. However, the high SUD rates found in the present study are similar to the rates reported among adolescents in the general population (Kozloff et al., 2010).

The prevalence of SUD in the current samples is consistent with rates reported in U.S. clinical samples (32-34%) (Goldstein et al., 2013; Wilens et al., 2008) and in a Canadian epidemiologic sample (32%) (Kozloff et al., 2010). Moreover, the prevalence of SUD of the current sample is similar to rates reported by some U.S. studies of adolescents with BP (Goldstein et al., 2008).

The association of panic disorder with SUD in the current study converges with numerous previous studies of adults with BP, (Chen & Dilsaver, 1995; Simon et al., 2004) as well as previous studies of adolescents with BP (Goldstein et al., 2013; Wilens et al., 2008). Panic disorder has been found to be strongly associated with SUD among BP adolescents and adults even more so than anxiety disorders in general (Goldstein & Levitt, 2008; Goldstein et al., 2013; Goodwin & Hoven, 2002).

There have been mixed findings regarding the association of ODD and SUD among BP youth. Some past studies have not found ODD to be associated with SUD among BP adolescents or adults (Goldstein et al., 2008; Kenneson, Funderburk, & Maisto, 2013). However, a recent study found ODD to be a strong predictor of first-onset SUD among BP adolescents (Goldstein et al., 2013). Data from the National Comorbidity Survey Replication study found ODD to be associated with SUD among adults with early-onset BP (Kenneson et al., 2013). The association of CD with SUD did not remain significant after controlling for other variables, likely due in part to the relatively low prevalence of CD as compared to ODD.

This study's finding of a strong and independent association between impulsivity and SUD substantiates and expands upon the previous findings from adults with BP (Grunebaum et al. 2006; Swann, 2010; Swann et al., 2004). Increased rates of police contact among BP adolescents with SUD in the current study converge with previous findings in adults (Quanbeck et al., 2004) and adolescents (Goldstein et al., 2008) in the U.S, although there are also discrepant findings (Barzman, DelBello, Fleck, Lehmkuhl, & Strakowski, 2007).

Contrary to the literature (Goldstein & Bukstein, 2010) SUD onset preceded BP onset for 61% of the sample, SUD and BP onset were concurrent for 21%, and BP preceded SUD for 18% of the sample. Although this finding may reflect true cross-national differences, replication in other samples is warranted.

Consistent with past findings, psychiatric hospitalizations were not found to be significantly associated with SUD

Table 1. Demographics and clinical characteristics of adolescents with bipolar disorder (BP) with versus without substance use disorders (SUD)

	Overall sample n = 100 n (%)	SUD n = 33 n (%)	No SUD n = 67 n (%)	Statistic	p-value	p-value (FDR corrected)
Demographics						
Age[a]	16.2 ± 1.5	16.5 ± 1.4	16.0 ± 1.5	t = -1.70	0.09	0.29
Gender (Female)	67 (67%)	24 (63.6%)	46 (68.7%)	X^2= 0.25	0.62	0.86
Race (White)	85 (86%)	26 (81.8%)	59 (88.1%)	X^2 = 0.71	0.34	0.72
Living with Both Biological Parents	56 (56%)	18 (54.5%)	38 (56.7%)	X^2= 0.04	0.84	0.92
Clinical Characteristics						
BP subtype						
BP-I	26 (26%)	8 (24.2%)	18 (26.9%)	X^2= 0.13	0.71	0.88
BP-II	40 (40%)	25 (45.5%)	15 (37.3%)	X^2= 0.52	0.47	0.82
BP-NOS	34 (34%)	10 (30.3%)	24 (36.4%)	X^2= 0.36	0.55	0.86
BP onset age	14.3 ± 2.5	14.6 ± 2.7	14.2 ± 2.5	t = -0.70	0.48	0.82
SUD onset age	14.1 ± 1.7	13.9 ± 1.8	-	-	-	-
Baseline depression (current episode)	18.5 ± 12.7	19.1 ± 12.2	18.2 ± 3.0	t = -0.46	0.64	0.86
Baseline mania (current episode)	15.93 ± 11.6	15.2 ± 11.3	16.3 ± 11.8	t = 0.43	0.67	0.86
Lifetime CGAS (most severe past episode)	41.1 ± 7.4	40.0 ± 6.3	41.5 ± 7.9	t = 0.90	0.37	0.72
CALS (adolescent)						
Disinhibited/persistant	11.6 ± 6.5	11.1 ± 6.7	11.8 ± 6.4	t = 0.44	0.66	0.86
Angry/depressed	18.5 ± 11.8	20.5 ± 12.9	17.5 ± 11.2	t = -1.10	0.27	0.69
CALS (parent)						
Disinhibited/persistant	11.6 ± 6.5	7.9 ± 5.8	7.0 ± 6.1	t = -0.59	0.55	0.86
Angry/depressed	16.9 ± 12.1	21.9 ± 11.8	15.4 ± 11.8	t = -2.6	0.009	0.07
LPI (total score)	148.67 ± 63.66	164.03 ± 70.83	140.87 ± 58.77	t = -1.67	0.10	0.31
Impulsivity	33.1 ± 17.1	40.4 ± 17.3	29.3 ± 14.1	t = -3.29	0.001	0.01
Emotional Dysregulation	38.0 ± 17.9	40.5 ± 19.4	36.7 ± 17.1	t = -0.98	0.33	0.72
Identity Confusion	40.7 ± 17.9	41.8 ± 19.2	40.1 ± 17.4	t = -0.42	0.67	0.86
Interpersonal Problems	36.9 ± 17.1	41.2 ± 18.0	34.7 ± 16.3	t = -1.74	0.08	0.28
Number of stressful life events	8.5 ± 5.4	10.9 ± 6.1	7.2 ± 4.5	t = -3.30	0.001	0.01
Wong-Baker score (pain past month)	1.5 ± 1.6	1.4 ± 1.5	1.5 ± 1.6	t = 0.28	0.77	0.92
Psychiatric hospitalizations (yes)	50 (50%)	20 (60.6%)	30 (44.8%)	X2= 2.20	0.14	0.40
Suicidal Ideation	61 (61%)	19 (57.6%)	42 (62.7%)	X2= 0.24	0.62	0.86
Suicide attempt	25 (25%)	10 (30.3%)	15 (22.4%)	X2= 0.74	0.39	0.72
Physical abuse[b]	9 (9%)	6 (18.2%)	3 (4.5%)	FET2	0.06	0.23
Sexual abuse	12 (12%)	7 (21.2%)	5 (7.5%)	FET2	0.06	0.23

[a]Values for all continuous variables are written as mean ± SD.
[b]Fishers Exact Test
FDR = false discovery rate

Table 2. Comorbidities and clinical characteristics of adolescents with bipolar disorder (BP) with versus without substance use disorders (SUD)

	Overall sample n = 100 n (%)	SUD n = 33 n (%)	No SUD n = 67 n (%)	Statistic	p-value	p-value (FDR corrected)
Co-Morbidity						
Any anxiety	72(72%)	24(72.7%)	48(71.6%)	X2= 0.01	0.91	0.95
ADHD	41(41%)	18(54.5%)	23(34.3%)	X2= 3.7	0.053	0.23
Conduct disorder	10(10%)	8(24.2%)	2(3%)	FET2	0.002	0.02
ODD	36(36%)	21(63.6%)	15(22.4%)	X2= 16.3	<0.001	0.01
Panic disorder	17(17%)	10(30.3%)	7(10.4%)	X2= 6.2	0.013	0.07
PTSD	4(4%)	2(6.1%)	2(3%)	FET2	0.60	0.86
Bulimia nervosa	9(9%)	6(18.2)	3(4.5%)	FET2	0.06	0.23
Psychosis	24(24%)	6(18.2%)	18(26.9%)	X2= 0.91	0.34	0.72
Legal Problems						
Police contact or arrest	43(43%)	20(60.6%)	23(34.3%)	X2= 6.2	0.013	0.07
Assault of others	27(30%)	15(50%)	12(20%)	X2= 8.6	0.003	0.03
Lifetime Medication						
Second generation antipsychotic	53(53%)	18(54.5%)	35(52.2%)	X2= 0.05	0.83	0.92
Lithium	20(20%)	5(15.2%)	15(22.4%)	X2= 0.72	0.39	0.72
Antimanic	59(59 %)	19(57.6%)	40(59.7%)	FET2	1.00	1.00
Lamotrigine	6(6%)	2(6.1%)	4(6%)	FET2	1.00	1.00
SSRI antidepressants	32(32%)	11(33.3%)	21(31.3%)	X2= 0.04	0.84	0.92
Stimulants	16(16%)	5(15.2%)	11(16.4%)	X2= 0.03	0.87	0.93
Family Psychiatric History						
Family history of mood disorder (MDE)	78(78%)	28(84.8%)	50(74.6%)	X2= 1.35	0.25	0.68
Family history of mood disorder (hypomania/ mania)	53(53%)	18(54.5%)	35(52.2%)	X2= 0.05	0.83	0.92
Family history of SUD	45(45%)	17(51.5%)	28(41.8%)	X2= 0.84	0.36	0.72

[a]Values for all continuous variables are written as mean ± SD.
[b]Fishers Exact Test
FDR = false discovery rate

in the present study, although mixed findings have been found in past studies. In a youth BP sample (Goldstein et al., 2008), psychiatric hospitalizations were not associated with SUD, whereas in adult samples (Cassidy, Ahearn, & Carroll, 2001; Sonne, Brady, & Morton, 1994), those with SUD had more psychiatric hospitalizations. Reasons for this discrepancy are uncertain given the cross-sectional methodology and lack of information about the timing of hospitalization in relation to SUD. It is plausible that hospitalization may lead to after-care that helps prevent SUD in some cases, whereas in other cases SUD may precipitate behaviors that lead to hospitalization, yielding a null finding across the entire group. Future longitudinal studies are warranted to address this topic.

Conclusions

The findings of the current study suggest that interventions treating comorbid disorders and dimensional lability may be beneficial among those with SUD. Family focused treatment is efficacious for BP adolescents without SUD, and a pilot study of adolescents with comorbid BP and SUD found that family focused treatment modified for use in this population led to improved depressive and manic symptoms (Goldstein et al., 2015). However, to our knowledge, no psychosocial treatment study to date has yielded significant reductions of substance use among adolescents with BP. Further research examining early interventions among BP adolescents with or at risk for SUD is warranted.

The results of the current study suggest some potential clinical implications for youth with BP. Early interventions

targeting comorbid disorders and dimensional liability traits associated with SUD may improve BP course of illness. More specifically, ameliorating panic disorder, disruptive behavior disorders, and impulsivity may prevent or delay SUD onset. It is important to acknowledge that while impulsivity may have predisposed those with BP to SUD, the cross-sectional methodology does not allow us to rule out the reverse association. Replication utilizing a larger sample and longitudinal methodology is necessary to better understand factors associated with the development of SUD as well as the impact of SUD on the course of BP among Canadian adolescents. As has previously been done with adults (Baethge et al., 2008) future prospective studies are warranted to determine the bidirectional associations between mood and substance use in BP. Utilizing neuroimaging and biomarkers to further examine the association between mood and substance use among adolescents with BP is also warranted, to better parse the biological underpinning of the association. Given the pernicious effect of SUD on the course of BP among adults, strategies that effectively reduce the incidence and burden of SUD among youth have the potential to mitigate the symptomatic, functional, and risk-related burden of BP.

Acknowledgments / Conflict of Interest

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