Attention-Deficit/Hyperactivity Disorder in Adults With Bipolar Disorder or Major Depressive Disorder: Results From the International Mood Disorders Collaborative Project

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Objective: Relatively few studies have evaluated the clinical implications of lifetime attention-deficit/hyperactivity disorder (ADHD) in adults with bipolar disorder or major depressive disorder (MDD). Herein, we sought to determine the prevalence as well as the demographic and clinical correlates of lifetime ADHD in persons with a mood disorder.

Method: The first 399 patients enrolled in the International Mood Disorders Collaborative Project (IMDCP) were evaluated for lifetime ADHD using the Mini-International Neuropsychiatric Interview-Plus (MINI-Plus) as the primary instrument to derive current and lifetime *DSM-IV* diagnoses. All analyses of variables of interest were conducted utilizing the MINI-Plus, the Adult ADHD Self-Report Scale-v1.1, and the Wender Utah Rating Scale-Short Form. The effect of ADHD on clinical presentation, course of illness variables, comorbidity, anamnesis, treatment, and outcome are reported. The IMDCP is a joint initiative of the Mood Disorders Psychopharmacology Unit at the University Health Network, University of Toronto, Toronto, Ontario, Canada, and the Cleveland Clinic Center for Mood Disorders Treatment and Research at Lutheran Hospital, Cleveland, Ohio. All data for this study were procured between January 2008 and January 2009.

Results: The percentages of subjects with MDD or bipolar disorder meeting the *DSM-IV* criteria for lifetime adult ADHD were 5.4% and 17.6% ($P < .001$), respectively. Lifetime comorbid ADHD in both mood disorder populations was associated with earlier age at illness onset (MDD, $P = .049$; bipolar disorder, $P = .005$), a higher number of psychiatric comorbidities (eg, MDD and current panic disorder with agoraphobia [$P = .002$]; bipolar disorder and social phobia [$P = .012$]), and decreased quality of life (MDD, $P = .018$).

Conclusions: The overarching findings herein are that the adult ADHD phenotype is commonly reported by individuals with MDD or bipolar disorder and is associated with a greater illness burden and complexity.

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During the past decade, a similar composite has emerged for mood disorders and adult attention-deficit/hyperactivity disorder (ADHD).[1–4] Both conditions have a relatively high prevalence, low case detection, protracted illness course, high rate of comorbidity, multifactorial etiology, substantial heritability of liability, substantial illness burden and economic cost, and significant interpersonal and vocational maladjustment. Moreover, results from neuroimaging investigations implicate common regions and neural circuits subserving essential features for both conditions.[5–7]

Several epidemiologic and clinical studies have documented a high rate of lifetime ADHD in pediatric bipolar samples.[8–11] Comorbid ADHD is associated with a more complex illness presentation and decreased response to lithium in young populations with bipolar disorder.[12] Features of ADHD often persist into adulthood, implying homotypic continuity with the pediatric phenotype.[13] Nevertheless, relatively few systematic studies of adults have evaluated the diagnostic and clinical implications of lifetime ADHD comorbidity in adults with bipolar disorder.[14] Moreover, managing ADHD in the bipolar disorder population with conventional treatment (eg, psychostimulants) poses a hazard for destabilization of bipolar disorder.

To our knowledge, the only large systematic evaluation of the bipolar disorder–ADHD phenotype was conducted by the National Institute of Mental Health's Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).[14] The overall lifetime prevalence of comorbid ADHD in their cohort (N = 1,000) was 9.5% (14.7% for men; 5.8% for women). Individuals with comorbid bipolar disorder and ADHD had an earlier

Clinical Points

- Attention-deficit/hyperactivity disorder (ADHD) is a common comorbidity in adults with mood disorders, with a higher prevalence in bipolar disorder compared to major depressive disorder.
- ADHD in the adult mood disorder population is associated with a more severe mood disorder course and presentation.
- All adults with mood disorder should be screened for features suggestive of ADHD.

age at onset, shorter "well" intervals, a greater burden of depression, and higher rates of psychiatric comorbidity.

The primary aims of this initiative were to report on the prevalence and clinical implications of lifetime comorbid ADHD in individuals with either bipolar disorder or major depressive disorder (MDD). Our sample comprised the first consecutive 399 patients enrolled in the International Mood Disorders Collaborative Project (IMDCP) between the Mood Disorders Psychopharmacology Unit at the University Health Network, University of Toronto, Toronto, Ontario, Canada, and the Cleveland Clinic, Cleveland, Ohio.

METHOD

The IMDCP is a joint initiative of the Mood Disorders Psychopharmacology Unit at the University Health Network, University of Toronto, Toronto, Ontario, Canada, and the Cleveland Clinic Center for Mood Disorders Treatment and Research at Lutheran Hospital, Cleveland, Ohio. Both the Mood Disorders Psychopharmacology Unit and the Cleveland Clinic Center for Mood Disorders Treatment and Research are academic specialty research programs providing clinical service to adults (aged 18–65 years at the Toronto site and ≥ 18 years at the Cleveland site) seeking evaluation and treatment for MDD or bipolar disorder. The Mood Disorders Psychopharmacology Unit is exclusively an outpatient program while the Cleveland Clinic Center for Mood Disorders Treatment and Research offers both outpatient and inpatient services.

Both the Mood Disorders Psychopharmacology Unit and the Cleveland Clinic Center for Mood Disorders Treatment and Research have an established research platform in order to foster a structured approach to patient evaluation and initiation of standardized treatment protocols. Both centers share a battery of common assessments listed in Table 1. Exclusion criteria for entry into the IMDCP are unwillingness or inability to provide informed consent or to comply with study assessment.

The Mini-International Neuropsychiatric Interview-Plus (MINI-Plus) was the primary instrument used to derive *DSM-IV* diagnoses (current and lifetime). In the case of ADHD, this instrument does not differentiate between inattentive and hyperactive subtypes. The MINI-Plus–derived lifetime ADHD diagnosis is established if, prior to the age of 7, a subject meets 6 of 10 criteria for ADHD and, during adult years, a subject meets 9 of 14 criteria. The Adult ADHD Self-Report Scale (ASRS-v1.1) and the Wender Utah Rating Scale-Short Form (WURS-25) screen for adult and childhood ADHD, respectively. All analyses of variables of interest were conducted utilizing the MINI-Plus, the ASRS-v1.1, and the WURS-25. Our primary data analysis was based on the MINI-Plus lifetime ADHD diagnosis and provides data for ASRS-v1.1 and WURS-25 only when the respective results are discrepant from the MINI-Plus. Statistical correction for multiple comparisons was conducted.

The data for this analysis were procured from patients assessed at the mood disorder clinics located at the University Health Network and Lutheran Hospital between January 2008 and January 2009. All data were initially captured with paper versions of all scales and then either manually entered or scanned with automated capture software (TeleForm, Version 8; Syscom Services, Inc; Silver Spring, Maryland) prior to statistical analysis. Statistical analysis was conducted using SPSS for Windows, Versions 13.0 and 16.0 (SPSS Inc, Chicago, Illinois). The χ^2 statistic was utilized for prevalence rates of nominal and ordinal variables. Independent-samples *t* tests were utilized for continuous dependent variables and dichotomous variables. All tests were 2-tailed, with statistical significance set at $P < .05$.

The Mood Disorders Psychopharmacology Unit research platforms at both centers were approved by the Research Ethics Board of the University Health Network, University of Toronto, and the Institutional Review Board of the Cleveland Clinic Foundation at Lutheran Hospital, respectively, and written informed consent was obtained from all subjects enrolled in the IMDCP.

RESULTS

Demographic and clinical characteristics are presented in Table 2. The mean (SD) age of the cohort presenting with MDD or bipolar disorder with comorbid ADHD was 38.0 (13.2) years and 36.7 (10.5) years, respectively. The number (%) of subjects diagnosed with MDD, bipolar I, and bipolar II were 203 (50.9), 119 (29.8), and 56 (14.0), respectively. The predominant symptomatic presentation at entry and during assessment was depression. To

Table 1. Scales Utilized in the International Mood Disorders Collaborative Project

Scale Abbreviation	Scale, Full Name	Description
MINI-Plus 5.0.0[15]	Mini-International Neuropsychiatric Interview-Plus (clinician-rated)	Interview capturing general Axis I psychiatric disorders
HDRS-17[16]	Hamilton Depression Rating Scale, 17-item	Questionnaire for assessment of depression severity
MADRS[17]	Montgomery-Asberg Depression Rating Scale	Questionnaire for assessment of depression severity
YMRS[18]	Young Mania Rating Scale	Questionnaire for assessment of hypomania/mania severity
CGI-S[19]	Clinical Global Impressions-Severity of Illness scale (investigator's judgment)	Overall impression of illness severity as assessed by clinician
UKU[20]	Udvalg for Kliniske Undersøgelser Side Effect Rating Scale	Questionnaire designed to capture side effects experienced within the past 7 days as a result of psychotropic agents
SEX FX[21]	Sex Effects Scale (men/women version)	Questionnaire evaluating overall sexual desire, functioning, and satisfaction
Klein Trauma[22]	Klein Trauma and Abuse-Neglect Questionnaire (developmental traumas)	Used in assessment of childhood trauma, abuse, and neglect before the age of 15
PDSQ[23]	Psychiatric Diagnostic Screening Questionnaire (patient-rated)	Self-report scale capturing general Axis I psychiatric disorders
NEO-FFI[24]	NEO Five-Factor Inventory	Self-report scale exploring personality and possible personality disorders
Q-LES-Q[25]	Quality of Life Enjoyment and Satisfaction Questionnaire	Self-report scale evaluating patient's quality of life enjoyment and satisfaction
SDS[26]	Sheehan Disability Scale	Self-report scale evaluating disability as a direct result of mood disorder symptoms
EWPS[27]	Endicott Work Productivity Scale	Self-report scale evaluating patient's productivity in the workplace during the past week
TAQ[28]	Trimodal Anxiety Questionnaire	Self-report scale utilized in assessment of anxiety
RSES[29]	Rosenberg Self-Esteem Scale	Self-report scale evaluating patient's self-esteem
ASRS-v1.1[30]	Adult ADHD Self-Report Scale	Self-report scale capturing adult attention-deficit/hyperactivity disorder
WURS-25[31]	Wender Utah Rating Scale-Short Form	Self-report scale capturing childhood attention-deficit/hyperactivity disorder
MDQ[32]	Mood Disorder Questionnaire	Self-report screen for bipolar disorder

Table 2. Sociodemographic Characteristics for Individuals With Major Depressive Disorder or Bipolar Disorder by the Presence of *DSM-IV*–Defined Adult ADHD[a]

	Major Depressive Disorder				Bipolar Disorder			
Sociodemographic Characteristics	No ADHD (N = 192), Mean (SD)	Adult ADHD (N = 11), Mean (SD)	*t* Test	*P* Value	No ADHD (N = 145), Mean (SD)	Adult ADHD (N = 31), Mean (SD)	*t* Test	*P* Value
Age, y	45.94 (14.94)	38.00 (13.18)	1.724	.086	39.13 (12.97)	36.68 (10.54)	0.979	.329
	n (%)	n (%)	χ^2	*P* Value	n (%)	n (%)	χ^2	*P* Value
	n = 188	n = 11			n = 138	n = 31		
Sex			2.149	.143			0.422	.516
Male	62 (32.98)	6 (54.55)			45 (32.16)	12 (38.71)		
Female	126 (67.02)	5 (45.45)			93 (67.39)	19 (61.29)		
	n = 64	n = 8			n = 83	n = 24		
Employment status			0.144	.930			5.988	.050
Employed full-time/part-time	28 (43.75)	3 (37.50)			44 (53.01)[b]	11 (45.83)		
Disabled or unemployed	23 (35.94)	3 (37.50)			27 (32.53)	13 (54.17)[b]		
Student, homemaker, or retired	13 (20.31)	2 (25.00)			12 (14.46)[b]	0 (0)		
	n = 64	n = 7			n = 81	n = 24		
Marital status			0.205	.903			3.813	.149
Single	24 (37.50)	3 (42.86)			36 (44.44)	12 (50.00)		
Married or cohabiting	33 (51.56)	3 (42.86)			28 (34.57)	11 (45.83)		
Divorced, separated, or widowed	7 (10.94)	1 (14.29)			17 (20.99)	1 (4.17)		
	n = 64	n = 8			n = 80	n = 24		
Education			3.376	.497			4.114	.391
No high school or some high school	4 (6.25)	1 (12.50)			4 (5.00)	3 (12.50)		
High school diploma	5 (7.81)	1 (12.50)			12 (15.00)	5 (20.83)		
Some college or college diploma	19 (29.69)	4 (50.00)			29 (36.25)	9 (37.50)		
Undergraduate degree	23 (35.94)	2 (25.00)			16 (20.00)	5 (20.83)		
Postgraduate degree	13 (20.31)	0 (0)			19 (23.75)	2 (8.33)		
	n = 42	n = 5			n = 42	n = 13		
Ethnicity			0.381	.537			0.997	.318
White	39 (92.86)	5 (100)			37 (88.10)	10 (76.92)		
Nonwhite	3 (7.14)	0 (0)			5 (11.90)	3 (23.08)		

[a]Sample size for each analysis varied according to available/missing data.
[b]Observed count was greater than expected count.
Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

Table 3. Severity of ADHD Symptoms in Individuals With Major Depressive Disorder or Bipolar Disorder

Measure of ADHD Severity	Major Depressive Disorder (N = 203), Mean (SD)	Bipolar Disorder[a] (N = 176), Mean (SD)	*t* Test	*P* Value	Bipolar I Disorder (N = 119), Mean (SD)	Bipolar II Disorder (N = 56), Mean (SD)	*t* Test	*P* Value
ASRS total score (adult)	33.73 (12.72)	38.46 (12.97)	−3.070	.002	37.47 (13.94)	39.33 (10.83)	−0.817	.415
WURS total score (childhood)	28.43 (19.83)	43.48 (12.13)	−6.223	< .001	44.65 (20.75)	38.29 (17.73)	1.773	.078

[a]One subject with bipolar disorder could not be ascertained as bipolar I or bipolar II.
Abbreviations: ADHD = attention-deficit /hyperactivity disorder, ASRS = Adult ADHD Self-Report Scale, WURS = Wender Utah Rating Scale.

Table 4. Markers of Illness Severity in Individuals With Major Depressive Disorder or Bipolar Disorder by the Presence of *DSM-IV*–Defined Adult ADHD

	Major Depressive Disorder				Bipolar Disorder			
Severity Marker	No ADHD (N = 192), Mean (SD)	Adult ADHD (N = 11), Mean (SD)	*t* Test	*P* Value	No ADHD (N = 145), Mean (SD)	Adult ADHD (N = 31), Mean (SD)	*t* Test	*P* Value
HDRS-17 score	18.01 (7.53)	19.36 (8.95)	−0.574	.567	16.20 (8.43)	14.52 (8.89)	0.966	.335
MADRS score	26.11 (10.87)	25.20 (11.59)	0.257	.798	23.09 (12.88)	20.77 (11.00)	0.926	.356
CGI-S score	4.72 (1.38)	4.56 (1.42)	0.354	.724	3.92 (1.47)	3.93 (1.51)	−0.043	.966
YMRS score	3.63 (3.40)	7.00 (5.55)	−2.643	.009	5.01 (5.58)	5.29 (6.15)	−0.250	.803
Q-LES-Q score	35.99 (13.84)	24.78 (9.86)	2.387	.018	32.32 (12.38)	31.70 (11.17)	0.182	.856
RSES score	24.49 (4.44)	28.00 (6.82)	−2.220	.028	25.02 (5.57)	25.70 (6.22)	−0.585	.560
SDS score	19.24 (8.83)	14.25 (6.04)	1.576	.117	17.44 (8.29)	15.60 (9.25)	1.059	.292
TAQ score	122.38 (57.16)	145.22 (51.26)	−1.168	.245	129.00 (46.16)	136.27 (37.39)	−0.796	.427
Behavioral	33.12 (16.89)	41.11 (15.46)	−1.381	.170	34.02 (14.98)	35.23 (14.28)	−0.400	.690
Cognitive	46.99 (22.01)	58.56 (15.58)	−1.550	.123	52.73 (18.85)	54.10 (17.08)	−0.361	.719
Somatic	42.28 (26.76)	45.56 (26.75)	−0.356	.722	42.25 (20.93)	46.93 (19.83)	−1.102	.272
EWPS score	30.62 (18.39)	50.75 (25.62)	−1.943	.062	38.58 (18.12)	23.56 (16.22)	2.473	.017
MDQ score	3.67 (2.99)	5.89 (3.02)	−2.159	.032	9.87 (3.04)	10.97 (2.20)	−1.828	.070
Age at depression onset, y	25.99 (15.49)	16.10 (12.44)	1.981	.049	19.32 (9.76)	13.52 (6.79)	2.833	.005
No. of lifetime depressive episodes	12.46 (46.30)	9.33 (9.45)	0.117	.907	18.32 (27.04)	27.25 (32.53)	−0.872	.386
Age at hypomania/mania onset, y	NA	NA	NA	NA	24.86 (11.33)	21.32 (13.78)	1.483	.140
No. of lifetime hypomanic/manic episodes	NA	NA	NA	NA	15.92 (35.44)	37.76 (56.41)	−2.029	.045

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, CGI-S = Clinical Global Impressions-Severity of Illness scale, EWPS = Endicott Work Productivity Scale, HDRS-17 = 17-item Hamilton Depression Rating Scale, MADRS = Montgomery-Asberg Depression Rating Scale, MDQ = Mood Disorder Questionnaire, NA = not applicable, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, RSES = Rosenberg Self-Esteem Scale, SDS = Sheehan Disability Scale, TAQ = Trimodal Anxiety Questionnaire, YMRS = Young Mania Rating Scale.

our knowledge, no patients in the cohort were being actively treated for ADHD. Of the 399 patients, 20 were excluded from the analysis because of incomplete diagnostic data, resulting in a sample size of 379.

The percentages of subjects with MDD or bipolar disorder meeting criteria for a lifetime diagnosis of comorbid ADHD were 5.4% and 17.6% ($P < .001$), respectively. The prevalence of ADHD was significantly higher in bipolar disorder than in MDD, as evaluated using the MINI-Plus and the WURS-25, but not the ASRS-v1.1. We did not find a significant difference between the mood disorder groups in the rate of lifetime ADHD as a function of sex. Moreover, we did not find a significant difference between subpopulations with bipolar I or bipolar II disorder in the rate of lifetime ADHD.

Baseline depression severity, as measured by the total Montgomery-Asberg Depression Rating Scale (MADRS) score, as well as the Clinical Global Impressions-Severity of Illness score, was not significantly different between groups. Individuals with MDD meeting ASRS-v1.1 criteria for ADHD had higher levels of depression severity as evaluated by both the MADRS and the Hamilton Depression Rating Scale, a difference not observed in the bipolar sample (Tables 3 and 4). Individuals meeting criteria for MDD and lifetime ADHD had lower quality of life ratings, as measured by the Quality of Life Enjoyment and Satisfaction Questionnaire, when compared to those with MDD but without ADHD. Quality of life ratings in individuals with bipolar disorder did not differ as a function of ADHD comorbidity.

The mean (SD) age at onset for the initial affective episode was earlier in individuals with MDD with comorbid ADHD (16.10 [12.44] years vs 25.99 [15.49] years) and in bipolar individuals with comorbid ADHD (13.52 [6.79] years vs 19.32 [9.76] years) compared to those without lifetime ADHD. The mean (SD) age at hypomania/mania onset in the bipolar population was also earlier in the comorbid subgroup (21.32 [13.78] years) than in those without lifetime ADHD comorbidity (24.86 [11.33] years).

There were no differences in the frequency of affective episodes in either the MDD or bipolar disorder groups as a function of lifetime ADHD (Table 5). Moreover, individuals with lifetime comorbid

Table 5. Psychiatric Comorbidity for Individuals With Major Depressive Disorder or Bipolar Disorder by the Presence of *DSM-IV*–Defined Adult ADHD

	Major Depressive Disorder				Bipolar Disorder			
Psychiatric Comorbidity	No ADHD (N = 192), n (%)	Adult ADHD (N = 11), n (%)	χ^2	*P* Value	No ADHD (N = 145), n (%)	Adult ADHD (N = 31), n (%)	χ^2	*P* Value
Panic disorder, lifetime	41 (21.35)	5 (45.45)	3.403	.065	57 (39.31)	17 (54.84)	2.154	.142
Panic disorder, current	29 (15.10)	5 (45.45)[a]	8.124	.004	25 (17.24)	8 (25.81)	1.069	.301
Limited symptoms of panic attacks, lifetime	21 (10.94)	0 (0)	1.228	.268	13 (8.97)	1 (3.23)	1.221	.269
Agoraphobia, lifetime	42 (21.88)	4 (36.36)	1.198	.274	45 (31.03)	13 (41.94)	1.142	.285
Agoraphobia, current	30 (15.63)	4 (36.36)[a]	3.990	.046	34 (23.45)	8 (25.81)	0.039	.843
Panic disorder, current, without agoraphobia	10 (5.21)	1 (9.09)	0.410	.522	10 (6.90)	5 (16.13)	2.561	.110
Panic disorder, current, with agoraphobia	17 (8.85)	4 (36.36)[a]	9.748	.002	15 (10.34)	2 (6.45)	0.515	.473
Agoraphobia, current, without history of panic disorder	10 (5.21)	0 (0)	0.554	.457	9 (6.21)	1 (3.23)	0.463	.496
Agoraphobia, current, without current panic disorder but with a past history of panic disorder	1 (0.52)	0 (0)	0.053	.818	12 (8.28)	3 (9.68)	0.043	.835
Agoraphobia, current, without history of limited-symptom panic attacks	3 (1.56)	0 (0)	0.161	.688	3 (2.07)	3 (9.68)[a]	4.256	.039
Social phobia (social anxiety disorder), current	22 (11.46)	4 (36.36)[a]	5.725	.017	34 (23.45)	12 (38.71)	2.685	.101
Specific phobia, current	9 (4.69)	1 (9.09)	0.424	.515	8 (5.52)	6 (19.35)[a]	6.362	.012
Obsessive-compulsive disorder, current	18 (9.38)	1 (9.09)	0.001	.971	21 (14.48)	10 (32.26)[a]	5.093	.024
Posttraumatic stress disorder, current	25 (13.02)	2 (18.18)	0.240	.624	28 (19.31)	7 (22.58)	0.116	.733
Alcohol dependence, current	25 (13.02)	1 (9.09)	0.077	.781	12 (8.28)	5 (16.13)	1.656	.198
Alcohol abuse, current	9 (4.69)	1 (9.09)	0.599	.741	9 (6.21)	7 (22.58)[a]	8.142	.017
Alcohol dependence, lifetime	33 (17.19)	1 (9.09)	0.489	.484	33 (22.76)	13 (41.94)[a]	4.454	.035
Alcohol abuse, lifetime	27 (14.06)	2 (18.18)	0.509	.775	32 (22.07)	7 (22.58)	3.748	.154
Substance dependence, lifetime	22 (11.46)	3 (27.27)	2.410	.121	29 (20.00)	11 (35.48)	3.578	.059
Substance dependence, current	9 (4.69)	3 (27.27)[a]	9.474	.002	16 (11.03)	7 (22.58)	3.053	.081
Substance abuse, current	5 (2.60)	2 (18.18)[a]	7.480	.006	10 (6.90)	4 (12.90)	1.398	.237
Anorexia nervosa, current	0 (0)	1 (9.09)[a]	17.541	.000	1 (0.69)	0 (0)	0.221	.638
Bulimia nervosa, current	4 (2.08)	1 (9.09)	2.127	.145	11 (7.59)	2 (6.45)	0.066	.797
Generalized anxiety disorder, current	98 (51.04)	8 (72.73)	1.961	.161	69 (47.59)	17 (54.84)	0.354	.552
Antisocial personality disorder, lifetime	3 (1.56)	2 (18.18)[a]	11.961	.001	14 (9.66)	7 (22.58)	3.795	.051
Somatization disorder, lifetime	4 (2.08)	0 (0)	0.234	.629	4 (2.76)	1 (3.23)	0.014	.907
Somatization disorder, current	3 (1.56)	0 (0)	0.174	.676	1 (0.69)	1 (3.23)	1.400	.237
Hypochondriasis, current	6 (3.13)	1 (9.09)	1.112	.292	4 (2.76)	1 (3.23)	0.014	.907
Premenstrual dysphoric disorder probable, current	7 (3.65)	1 (9.09)	1.009	.315	7 (4.83)	3 (9.68)	1.031	.310
Suicide risk, current	143 (74.48)	10 (90.91)	1.513	.219	100 (68.97)	23 (74.19)	0.275	.600
Suicide risk severity			2.154	.341			1.476	.478
Low (1–5)	37 (19.27)	5 (45.45)			28 (19.31)	8 (25.81)		
Moderate (6–9)	28 (14.58)	1 (9.09)			19 (13.10)	2 (6.45)		
High (≥ 10)	77 (40.10)	5 (45.45)			55 (37.93)	13 (41.94)		

[a]Significant at $P < .05$.
Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

ADHD were similar to those without comorbid ADHD in their MINI-Plus suicide risk severity score and current suicide risk. Lifetime ADHD was associated with a higher rate of antisocial personality disorder in both MDD and bipolar disorder.

Individuals with MDD and lifetime comorbid ADHD had a significantly higher rate for panic disorder–current, agoraphobia-current, social anxiety disorder–current, substance abuse and dependence–current, and antisocial personality disorder–lifetime. Individuals with bipolar disorder meeting criteria for ADHD were also more likely to meet criteria for agoraphobia-current, alcohol abuse–current, alcohol dependence–lifetime, and antisocial personality disorder–lifetime (Table 5).

Patients meeting criteria for both bipolar disorder and lifetime ADHD, but not patients with comorbid MDD and ADHD, had lower work productivity scores as measured by the Endicott Work Productivity Scale. Also, individuals with comorbid bipolar disorder and ADHD were relatively more likely to be currently unemployed or receiving disability.

DISCUSSION

The overarching findings of our analysis are that the ADHD phenotype is commonly reported in adult individuals with a mood disorder. Individuals with bipolar disorder are approximately 3 to 4 times more likely to receive a comorbid ADHD diagnosis than are those individuals with MDD. Notwithstanding the fact that our sample was numerically modest when compared to the STEP-BD cohort, the rate of comorbid ADHD in our bipolar subsample was similar to their observations. Moreover, a separate Turkish study with a bipolar sample (N = 159) similar to ours reported a 16.3% prevalence rate of adult ADHD.[33,34]

The STEP-BD group[14] reported that individuals with bipolar I disorder were differentially affected by lifetime comorbid ADHD when compared to individuals with bipolar II disorder. We also observed a higher percentage of bipolar I individuals versus bipolar II individuals affected by lifetime ADHD. Admittedly, the population sample in our group of individuals with bipolar disorder in general, and more specifically, bipolar II disorder, was considerably smaller than in the STEP-BD group.

Among individuals with MDD, the presence of comorbid lifetime ADHD was associated with an age at mood disorder onset approximately 10 years earlier when compared to those without ADHD. For individuals with bipolar disorder, those with lifetime ADHD had a mood disorder age at onset approximately 6 years earlier than those without ADHD. The STEP-BD group[14] reported that the age at bipolar disorder onset in individuals with ADHD was approximately 5 years earlier than in those without ADHD. The pertinacity of these collective observations relates to the question of whether or not the "comorbidity" of ADHD and bipolar disorder in younger populations reflects distinct comorbidity, overlapping syndromes, or heterotypic continuity.[35]

Converging with results from both epidemiologic and clinical studies, individuals in the IMDCP with MDD or bipolar disorder *and* lifetime comorbid ADHD were differentially affected by anxiety disorder as well as substance use disorders.[4] Moreover, the subjects with comorbid ADHD were more likely to meet criteria for antisocial personality disorder. The STEP-BD group[14] reported that individuals with bipolar disorder and ADHD had a greater frequency and earlier age at onset of violence and legal problems.

There are several methodological limitations that affect inferences and interpretation of our results. Most subjects were experiencing symptoms related to a mood disorder; as such, there is no definitive mechanism to assure that overdiagnosis (or underreporting) of ADHD did not occur.[14] A second limitation relates to the representativeness of individuals utilizing university-based mood clinics, as well as Berkson's bias.[36] Third, our attempt to look at both MDD and bipolar disorder subpopulations as a function of ADHD comorbidity resulted in a relatively small sample size. A separate limitation relates to interrater reliability between sites. Both the Toronto and Cleveland sites have demonstrated interrater reliability at each respective center; at the time of data-capture analysis herein, both centers had not demonstrated interrater concordance with respect to MINI-Plus–derived diagnosis. Notwithstanding this latter limitation, both centers have extensive experience in clinical trials utilizing the MINI-Plus as well as other diagnostic and rating instruments.

In addition, our dataset was missing a significant number of data points across several variables. The primary reason for missing data relates to the time-consuming nature of the data-gathering process (eg, up to 2 hours in duration) that was unacceptable to many individuals utilizing services at both centers. Moreover, although we corrected for multiple comparisons, we conducted a large number of statistical tests on a relatively small subsample size, thereby introducing a risk for type 1 error. Finally, most individuals with comorbid ADHD were not receiving guideline-concordant care for that condition, raising the possibility that the increased severity in the mood disorder–ADHD group was in part due to insufficient treatment of ADHD.

Taken together, the IMDCP results represent a partial replication of several findings previously reported by the STEP-BD group.[14] Our results extend the observations further by separately reporting on similar variables in individuals with MDD. The greater burden associated with the ADHD phenotype in mood disorder populations invites the need for adequately designed clinical trials aiming to establish safe and effective pharmacologic and psychosocial approaches in individuals meeting criteria for both conditions.

Drug name: lithium (Lithobid and others).

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