

# Bipolar Symptoms in Adult Attention-Deficit/Hyperactivity Disorder: A Cross-Sectional Study of 510 Clinically Diagnosed Patients and 417 Population-Based Controls

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**Objective:** Bipolar spectrum disorders (BSD) have several symptoms and features in common with attention-deficit/hyperactivity disorder (ADHD). Here we explored the prevalence of BSD and the relationship between symptoms of BSD and ADHD in adult ADHD patients.

**Method:** Norwegian adults diagnosed with DSM-IV ADHD during 1997 through 2007 (n = 510) and a random sample of 417 controls from the general population (aged 18–40 years) were recruited and responded to 85 questions rating symptoms of ADHD, lifetime symptoms of mood disorders, other comorbid conditions, and sociodemographic data.

**Results:** According to the Mood Disorder Questionnaire (MDQ), 50.6% of the ADHD patients screened positive for BSD, compared to 8.3% of the controls. In comparison, the prevalence of BSD according to DSM-IV in a subsample of interviewed patients (n = 50) was 32%. In the whole study sample (N = 927), an ADHD diagnosis was the strongest predictor for screening positive on the MDQ (OR = 5.0,  $P < .001$ ), but the correlation between dimensional symptom levels of ADHD and of BSD was strongest in the control group (Pearson correlation  $r = 0.7$ ,  $P < .001$  vs  $r = 0.3$ ,  $P < .001$ ). Patients screening positive on the MDQ had significantly more drug problems, higher ADHD symptom scores, and lower educational and occupational levels.

**Conclusions:** Our findings illustrate the close relationship between some symptoms of BSD and ADHD in adults. In clinical and research settings, patients screening positive for BSD should be assessed for a possible underlying or coexisting ADHD condition and vice versa.

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Attention-deficit/hyperactivity disorder (ADHD) is a common condition during childhood, adolescence, and adulthood, with recent worldwide prevalence estimates of 2% to 12% in children<sup>1,2</sup> and 3% to 4% in adults.<sup>3,4</sup> Adult ADHD is associated with significant lifetime psychiatric comorbidity.<sup>5,6</sup> There has been a special interest in the relationship between ADHD and bipolar disorder for several reasons. First, the rates of coexistence between ADHD and bipolar disorder are often reported to be higher than expected from the rates of each disorder in the general population, in childhood, in adolescence, and in adulthood.<sup>7,8</sup> Second, according to current diagnostic criteria, both disorders are characterized by symptoms involving dysregulation of energy, activity, affect, and impulsivity (DSM-IV). Third, both conditions are considered to be highly heritable with typical heritability estimates around 0.7 to 0.8.<sup>9–11</sup>

Whereas ADHD is one of the most commonly diagnosed conditions in child psychiatry, bipolar disorder in children is less frequent and is even considered controversial.<sup>12,13</sup> Until a few years ago, the opposite was true in adult psychiatry; bipolar disorder is a well-established clinical condition, but ADHD has only recently been accepted as a valid diagnosis in adulthood.<sup>14</sup> This is reflected by the fact that current formal diagnostic criteria for ADHD are based on child behavior, whereas the diagnostic criteria for bipolar disorder are mainly based on the clinical picture in adults. Some genetic studies have indicated a shared vulnerability for these conditions<sup>15–18</sup> and that, as suggested by some authors, comorbid ADHD and bipolar disorder may represent a distinct subtype of ADHD.<sup>15,18</sup> Possibly, bipolar disorder and ADHD may even represent different developmental manifestations of some shared biologic vulnerability.

Bipolar disorder may be underdiagnosed in the general population, often being misdiagnosed as unipolar depression.<sup>19</sup> This is especially true for bipolar disorders without a history of full mania, ie, the bipolar II disorder, bipolar disorder not otherwise specified (NOS), and cyclothymia<sup>20</sup> diagnoses from the DSM-IV-TR. It is also true for subthreshold variants of bipolar disorder, which are also included in the concept of bipolar spectrum disorders (BSD) by some authors.<sup>21–23</sup> General population studies have

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## FOR CLINICAL USE

- ◆ Adult patients with ADHD frequently suffer from comorbid symptoms of bipolar spectrum disorder, and this comorbidity is associated with a poorer outcome.
- ◆ Adults diagnosed with ADHD should be assessed for possible coexistent bipolar disorder, and vice versa.
- ◆ As mood instability appears to be an important clinical feature of ADHD in adults, diagnostic criteria may need to be revised to account for bipolar-like symptoms.

shown that bipolar II disorder and subthreshold variants of bipolar disorder, although less symptomatic than bipolar I disorder, are still significantly impairing conditions for both individuals and society.<sup>24,25</sup> Although having not been unanimously defined, the bipolar spectrum beyond bipolar I disorder includes disorders characterized by more frequent fluctuations of mood and energy, shorter duration of each episode, and a more mixed, chronic, and comorbid clinical picture.<sup>26,27</sup> This makes its distinction from ADHD and personality disorders more challenging than it is for classic bipolar I disorder.

The aims of this study were to (1) investigate the prevalence of BSD among clinically diagnosed adults with ADHD, (2) explore the relationship between symptoms of ADHD and symptoms of BSD in the same patients, and (3) examine the clinical characteristics of ADHD patients who had co-occurring symptoms of BSD. We have applied 2 commonly used diagnostic self-rating instruments for adults, the World Health Organization's (WHO's) Adult ADHD Rating Scale (ASRS) and the Mood Disorder Questionnaire (MDQ), in a sample of 510 clinically diagnosed adult ADHD patients and 417 adult comparison cases from the general population. Based on the above considerations, we hypothesized that (1) there is a higher frequency of bipolar symptoms and bipolar disorder among ADHD patients than among comparison cases, (2) there is an overlap of symptoms and syndromes between ADHD and BSD in adults with ADHD, (3) hyperactivity and impulsivity traits in ADHD are more associated with positive scores on the MDQ than inattentive traits because of the similarities of these symptoms with symptoms of hypomania and mania, and (4) ADHD patients with high scores on bipolar symptoms differ clinically from ADHD patients with low scores on bipolar symptoms.

## METHOD

This is a cross-sectional study of 510 Norwegian patients diagnosed with adult ADHD and a comparison group of 417 persons from the general population.

### Participants

**Patients.** The patients were recruited as part of a genetic study using a national registry of adults diagnosed with

ADHD in Norway during 1997 through 2005. The diagnostic assessment of the patients in the registry was made by 1 of 3 national expert committees for ADHD/hyperkinetic disorder and was based on thorough information records (including information from informants) provided by the referring clinicians, mainly psychiatrists. The diagnosis of ADHD was made according to the *ICD-10* research criteria,<sup>28</sup> with 2 modifications: allowance was made for the inattentive subtype in *DSM-IV* to be sufficient for the diagnosis and for the presence of comorbid psychiatric disorders if the criteria for ADHD were present before the appearance of the comorbid disorder. This diagnostic assessment strategy was chosen as a compromise; the *ICD-10* is the official diagnostic system used in Norway, yet the assessment must be comparable with the *DSM-IV*. The referral and diagnostic assessments by the committees were, until May 2005, mandatory for adult patients in Norway who were to be considered for treatment with stimulant drugs. In addition, to increase recruitment and to also include patients diagnosed later than May 2005, clinicians nationwide were asked to recruit formally diagnosed adult patients with ADHD. These patients were assessed by specialists in clinical psychiatry or psychology according to national guidelines based on the criteria described above, though without the mandatory evaluation of the committees. The inclusion criteria were a diagnosis of ADHD according to the criteria described above and age over 18 years. There were no formal exclusion criteria. The intention behind this strategy was to recruit a clinically representative sample of adult ADHD patients from the entire country.

A total of 1,700 invitation letters were sent to adult ADHD patients from 2005 to 2007. Most of the invitations were sent during autumn 2006, mainly targeting patients who were referred after year 2000. By December 2007, three hundred thirty-eight (19.9%) of the invited patients had returned completed questionnaires. An additional 172 patients recruited directly from clinicians were also included, yielding a final sample of 510 adults with persistent ADHD diagnosis. The age distribution of the included patients was quite similar to the national cohort (64% vs ~67% between 20–39 years old), but the proportion of women was higher among responders than for the whole cohort of the national registry (42% vs ~28%).

For further details about the recruitment strategy and the patient sample, we refer to Johansson et al,<sup>29</sup> Halleland et al,<sup>30</sup> and Halmøy et al.<sup>31</sup>

**Controls.** A control group was recruited using the database of The Medical Birth Registry of Norway (MBRN). The MBRN includes all people born in Norway after January 1, 1967. A total of 2,163 invitation letters were sent out to a randomly selected sample of persons between 18 and 40 years old from all over Norway, during January and March 2007. The control group in this study is composed of the 417 people (19.2%) who had responded with completed questionnaires by December 2007.<sup>31</sup> The proportion of women was 56.7% among responders compared to 49.0% for the entire invited sample, and the mean age was 31.0 and 30.3 years for the invited versus included controls, respectively.

## Design

The prevalence of bipolar disorder was ascertained using a combination of 3 different approaches: (1) all participants were asked whether they had been diagnosed with bipolar disorder; (2) all participants filled in a screening questionnaire for BSD, the MDQ; and (3) a random sample of patients ( $n = 50$ ) was further invited to diagnostic semistructured interviews to obtain more information. In addition, all included patients and controls filled in questionnaires rating current ADHD symptoms, co-occurring disorders, and sociodemographic data, including educational level and occupational activity. An informed consent based on detailed written information about the project was obtained from all patients and controls. The study was approved by the Regional Committee for Medical Research Ethics of Western Norway.

## Reported Measures

Two self-report questionnaires were used in this study: the Adult ADHD Self-Report Scale (ASRS), which measures the presence and frequency of current symptoms of ADHD,<sup>32,33</sup> and the Mood Disorder Questionnaire (MDQ), a screening questionnaire for BSD.<sup>34</sup>

The ASRS is the WHO's rating scale for adult ADHD designed to measure current ADHD symptoms. It consists of 18 items based on *DSM-IV* symptoms/criteria for ADHD that are measured on a 5-point scale (0 = never/seldom and 4 = very often), yielding a possible total score range from 0 to 72. Items 1 through 9 cover the symptoms of inattention and items 10 through 18, the symptoms of hyperactivity and impulsivity. In this study, we used both a continuous and a categorical scoring method (21 or more on each subscale for defining subtypes). Both methods have recently been validated by Kessler et al.<sup>33</sup>

The MDQ is a 15-item screening instrument for BSD that has been validated for use in the general population and in psychiatric patient populations.<sup>34,35</sup> The first 13 questions concern periods of lifetime symptoms of mania and hypomania, and the last 2 ask about co-occurrence of

symptoms and ranking of functional impairment caused by the symptoms. A standard MDQ positive score is defined as 7 or more answers of "yes" on the first 13 items, "yes" on question 14 (co-occurrence of symptoms), and "level 3 or more" on question 15 (moderate to severe impairment). A modified scoring method, in which the impairment criterion is omitted (MDQ7), has shown higher sensitivity for detecting BSD beyond bipolar I disorder than the standard MDQ score.<sup>36-38</sup> Both standard MDQ and MDQ7 scores were analyzed in this study.

In addition, the patients answered 31 questions concerning sociodemographic and clinical factors, including educational and occupational levels and comorbid symptoms and problems, in particular those related to mood disorders. The questions related to comorbidity were scored as "yes" or "no," ie, "Have you ever experienced significant anxiety and/or depression?" and "Have you ever had problems with alcohol?" Information regarding formal diagnosis and medical treatment history was also provided by the patients' doctors (mainly psychiatrists) on a separate form.

The ASRS and MDQ have not yet been subject to official validations in Norway. However, translated versions exist and are currently being used in clinical practice, official evaluation projects, and research. The versions of questionnaires used in this study have been used in earlier publications.<sup>30,31</sup>

To certify the validity of the self-reported data regarding co-occurring disorders, 10% (50) of the patients were subjected to psychiatric interviews. Self-reported problems were then compared to formal diagnostic assessment from the interviews. The interviews were performed at the outpatient section of the Department of Biological and Medical Psychology at the University of Bergen. For feasibility reasons, invitations to psychiatric interviewing were primarily addressed to patients living in the area of Bergen. The psychiatric interview was based on the Mini-International Neuropsychiatric Interview (MINI), MINI Plus, version 5.0.0., a module-based semistructured diagnostic interview for *DSM-IV* and *ICD-10* Axis I diagnoses in adults.<sup>39</sup> The interviews were carried out by 2 experienced clinical psychiatrists (A.H. and M.D.), who were blinded regarding both the ADHD diagnostic status and the results from the self-report questionnaires of the persons interviewed.

## Statistical Analyses

The data were initially analyzed by descriptive methods using  $\chi^2$  tables and  $t$  tests for independent samples. Logistic regression analyses were used to study predictors for positive screen on the MDQ, with standard MDQ positive score as the dependent variable and age, gender, self-reported depression and/or anxiety, alcohol or drug problems, and presence of ADHD and bipolar disorder in first-degree family members as independent variables. Scatter plot and correlation statistics for dimensional scores were used in order to study the relationship between symptoms of ADHD

**Table 1. Sociodemographic and Clinical Characteristics of Patients With Attention-Deficit/Hyperactivity Disorder (ADHD) and Controls**

Characteristic	Patients			Controls			P Value, Patients vs Controls
	Total (n = 472–510) <sup>a</sup>	Women (n = 241) <sup>b</sup>	Men (n = 269) <sup>b</sup>	Total (n = 417) <sup>a</sup>	Women (n = 241) <sup>b</sup>	Men (n = 176) <sup>b</sup>	
%							.001
Age, mean (SD), y	34.4 (10.3)	47.3	52.7	29.9 (6.1)	57.8	42.2	<.001
Educational level, % (n)							<.001
Junior high school	27.5 (119)	34.7	34.1	5.6 (22)	29.5	30.5	
Senior high school	49.7 (215)	24.4	30.0	6.1*	4.8		
College/university	22.9 (99)	52.1	47.3	35.5 (140)	29.7	43.1	
Occupational level, % (n)		23.5	22.7	59.1 (234)	64.2	52.1	<.001
Employed	27.2 (126)	24.3	30.1	79.2 (297)	77.3	81.9	
Sick leave, temporary	6.0 (28)	5.0	6.9	2.7 (10)	3.3	1.9	
Disabled	30.2 (140)	33.9	26.8	2.1 (8)	2.8	1.3	
Rehabilitation	20.3 (94)	20.2	20.3	2.9 (11)	3.3	2.5	
Unemployed	4.5 (21)	2.8	6.1	1.9 (7)	0.9	3.1	
Other	11.9 (55)	13.8	9.8	11.2 (42)	12.6	9.4	
Self-reported comorbidity, % (n)							
Depression/anxiety	69.2 (343)	71.3	66.8	16.2 (67)	17.6	14.4	<.001
Bipolar disorder	12.3 (58)	12.9	11.7	1.7 (7)	1.7	1.7	<.001
Dyslexia	53.3 (264)	47.9*	58.2	13.5 (56)	11.3	16.6	<.001
Alcohol problems	25.2 (125)	16.6**	32.6	2.6 (11)	2.1	3.4	<.001
Problems with other drugs	26.6 (132)	16.9**	34.9	2.4 (10)	1.3	4.0	<.001
Treatment for psychiatric disorder other than ADHD	42.1 (208)	51.3**	33.3	7.0 (29)	7.5	6.3	<.001
ASRS score, mean (SD)	45.8 (12.1)	47.7*	44.0	22.7 (9.8)	22.0	23.7	<.001
MDQ sum score, mean (SD)	8.1 (3.9)	7.5*	8.6	3.0 (3.3)	2.6*	3.4	<.001
MDQ positive, % (n)	50.6 (244)	43.7*	56.9	8.3 (34)	6.3	10.9	<.001
MDQ7 positive, % (n)	71.1 (347)	67.7	74.3	18.4 (76)	12.6	26.1	<.001
ADHD in family (first-degree relatives), % (n) <sup>c</sup>	39.1 (194)	46.6**	32.2	3.9 (16)	4.6	2.8	<.001
Bipolar disorder in family (first-degree relatives), % (n) <sup>c</sup>	11.3 (56)	11.8	10.8	2.7 (11)	1.7	4.0	<.001

<sup>a</sup>The total number of patients in each subanalysis is varying according to the number of persons with missing items for each variable.

<sup>b</sup>Mean values or percentages, as applicable, are shown.

<sup>c</sup>Proportion of "yes" responses (the alternative responses here were yes/no/not sure).

\* $P < .05$ , \*\* $P < .001$ , 2-tailed significance for difference between gender.

Abbreviations: ASRS = Adult ADHD Self-Report Scale, MDQ = Mood Disorder Questionnaire.

and of bipolar disorder. A 2-tailed level of .05 was chosen for statistical significance. All analyses were performed using the Statistical Package for Social Sciences version 15.0.1 (SPSS Inc, Chicago, Illinois).

## RESULTS

### Sociodemographic and Clinical Characteristics of Patients and Controls

The gender distribution and mean age of the studied patient and control groups were slightly different, with a lower proportion of women (47.3% vs 57.8%) and a higher mean age (34.4 vs 29.9 years) in the patient group compared to the control group (Table 1). The educational and occupational levels were significantly lower among patients than controls. Significantly more patients than controls reported a lifetime history of depression and/or anxiety, bipolar disorder, and alcohol and drug problems. In particular, a known bipolar disorder was reported by 12.3% of patients and by 1.7% of controls. Half of the ADHD patients (50.6%) screened positive on the MDQ versus 8.3% of the control group when the standard cutoff score described in the Method was used; 71.1% of the patients had a mean score of 7 or more on the MDQ, compared to 18.4% in the control group. Patients reported significantly higher frequencies

of both ADHD and bipolar disorder in their first-degree family members than controls.

### Clinical Diagnoses and Correlation Between Self-Reported Data and MDQ Scores

The interviewed subsample of patients (n = 50) did not differ statistically from the noninterviewed sample of patients (n = 460) regarding gender, age, educational or occupational outcome, proportion of MDQ positive scores, self-reported levels of anxiety and/or depression, or alcohol or drug problems (eTable 1, available at <http://www.psychiatrist.com>). Of the interviewed patients, 80.0% (n = 40) fulfilled *DSM-IV* criteria for lifetime depression and/or anxiety disorder, ie, generalized anxiety disorder, panic disorder, social phobia, agoraphobia, obsessive-compulsive disorder, and/or posttraumatic stress disorder, of whom 67.5% (n = 27) reported a lifetime anxiety and/or depression on the questionnaire. Twenty-six percent (n = 13) reported lifetime alcohol problems and 28% (n = 14), lifetime problems with other substances.

Two of the interviewed patients reported having or having had bipolar disorder on the questionnaire, whereas the interview identified 4 patients fulfilling criteria for bipolar I disorder, 9 patients with bipolar II disorder, and 3 patients with bipolar disorder NOS, yielding a total of 32% fulfilling



criteria for a BSD. Two of the 4 patients diagnosed with bipolar I disorder were MDQ positive (but all 4 were MDQ7 positive), 6 of the 9 patients with bipolar II disorder were MDQ positive (8 MDQ7 positive), and 10 of the 16 patients with a BSD were MDQ positive (15 MDQ7 positive). The correlation was weakest between standard MDQ score and bipolar I disorder ( $r=0.06$ ,  $P=.67$ ) and strongest between MDQ7 score and broadly defined BSD ( $r=0.46$ ,  $P=.001$ ). The sensitivity and specificity of the MDQ for identifying a BSD were 0.63 and 0.72, respectively, when using the standard cutoff score (MDQ positive), and 0.94 and 0.50, respectively, when using a mean score of 7 or more without the impairment criteria (MDQ7). The sensitivity and specificity of the MDQ for detecting bipolar I disorder were 0.50 and 0.61 (1.0 and 0.39 using MDQ7) and for bipolar II disorder, 0.67 and 0.67, respectively (0.89 and 0.42 for MDQ7).

There were moderate to strong correlations between self-reported problems and formal diagnoses for alcohol and drug problems and for anxiety and/or depression among the interviewed patients but moderate to weak correlations between self-reported and interview-diagnosed bipolar disorder. In general, patients seemed to underreport co-occurring disorders and problems on the questionnaires, mood disorders in particular (see eTable 1: interviewed sample of ADHD patients ( $n=50$ ) versus noninterviewed patients ( $n=460$ ), with correlations between self-report data and diagnoses obtained from interview).

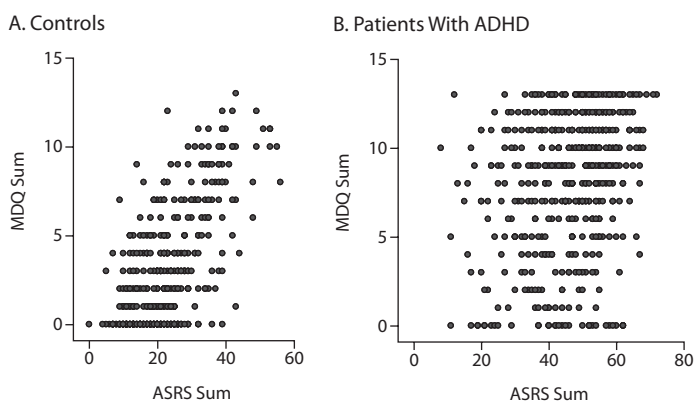
### Correlation Between Symptoms of ADHD and Symptoms of BSD

Scatter plot and correlation analyses of ASRS scores versus MDQ scores showed a significant linear relationship between current symptoms of ADHD (ASRS) and lifetime symptoms of bipolar disorder (MDQ) in the whole sample of patients and controls (ASRS vs MDQ;  $r=0.65$ ,  $P<.001$ ). The correlation between ASRS and MDQ scores was stronger among controls ( $r=0.65$ ,  $P<.001$ ) than among patients ( $r=0.27$ ,  $P<.001$ ), (Figure 1A and 1B). The ADHD patients tended to disperse into 2 groups on the scatter plot, 1 group with high scores on the MDQ and 1 smaller group with low scores on the MDQ (Figure 1B).

### Predictors of MDQ Positive Screen

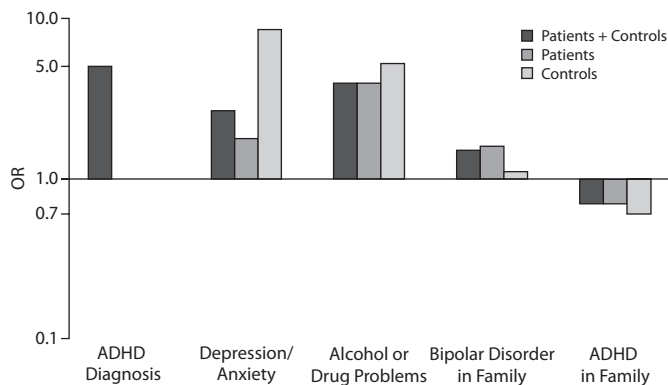
In a logistic regression analysis of the whole sample of patients and controls (as described in the Method), a diagnosis of ADHD, ie, patient versus control status, was the strongest predictor for screening positive on the MDQ, with a 5-fold increased risk of being MDQ positive for patients with ADHD compared to controls (OR = 5.0,  $P<.001$ ) (Figure 2). Histories of alcohol or substance abuse (OR = 4.0,  $P<.001$ ) and of self-reported depression and/or anxiety

Figure 1. Relationship Between Symptom Scores of Attention-Deficit/Hyperactivity Disorder (ADHD) (Adult ADHD Self-Report Scale [ASRS]) and Bipolar Spectrum Disorder (Mood Disorder Questionnaire [MDQ]) in (A) 417 Controls and (B) 510 Patients With ADHD<sup>a</sup>



<sup>a</sup>A single symbol may represent several individuals.

Figure 2. Predictors of a Positive Screen on the MDQ for Patients ( $n=510$ ), Controls ( $n=417$ ), and Whole Sample ( $N=927$ ): Results From the Logistic Regression Analyses (OR shown on a logarithmic scale)<sup>a</sup>



<sup>a</sup> $P$  value  $<.001$  for all shown ORs except those for bipolar disorder and ADHD in family, which had  $P$  values  $>.05$ .

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, MDQ = Mood Disorder Questionnaire, OR = odds ratio.

(OR = 2.7,  $P<.001$ ) were also positively associated with a positive MDQ screen. Substance abuse was the strongest predictor for screening positive on the MDQ among patients (OR = 4.0,  $P<.001$ ), whereas depression/anxiety was the strongest predictor among controls (OR = 8.5,  $P<.001$ ). Age and gender were not significantly associated with MDQ status in this model, except for a slightly positive correlation with age in the control sample (OR = 1.08,  $P=.03$ ). Presence of bipolar disorder and ADHD in first-degree family members, although not statistically significant, showed opposite trends of association to a positive MDQ score in the patient

**Table 2. Sociodemographic and Clinical Characteristics of Mood Disorder Questionnaire (MDQ)-Positive Versus MDQ-Negative Patients With Attention-Deficit/Hyperactivity Disorder (ADHD)**

Characteristic	MDQ-Positive Patients (n = 244) <sup>a</sup>	MDQ-Negative Patients (n = 239)	P
Women, %	41.4	54.2	.005
Age, mean (SD), y	34.2 (11.1)	34.3 (9.3)	.890
Education, % (n)			<.001
Junior high school	34.1 (71)	19.1 (40)	
University	15.4 (32)	31.1 (65)	
Occupational status, % (n)			.005
Employed	19.7 (45)	34.8 (77)	
ASRS score, mean (SD)	49.0 (10.8)	42.3 (12.8)	<.001
ADHD subtype according to ASRS, % (n)			<.001
Inattentive	12.8 (31)	20.6 (49)	
Hyperactive/impulsive	7.0 (17)	5.1 (12)	
Combined	65.4 (159)	42.6 (101)	
Subthreshold (<20 on each subscale)	14.8 (36)	20.6 (75)	
Self-reported conditions, lifetime, % (n)			
Depression/anxiety	78.6 (191)	59.7 (141)	<.001
Bipolar disorder	16.9 (39)	7.9 (18)	.004
Treatment for psychiatric disorder other than ADHD	46.0 (110)	36.3 (86)	.031
Problems with alcohol	35.8 (87)	14.9 (35)	<.001
Problems with other drugs	41.6 (101)	10.2 (24)	<.001
Self-reported conditions in first-degree family members, % (n)			
ADHD in family	34.0 (82)	44.5 (106)	.050
Depression/anxiety in family	45.2 (109)	41.6 (99)	.132
Bipolar disorder in family	14.5 (35)	8.0 (19)	.041

<sup>a</sup>The total number of patients in each subanalysis is varying according to the number of persons with missing items for each variable.  
Abbreviation: ASRS = Adult ADHD Self-Report Scale.

group: reported bipolar disorder in the family showed a positive trend ( $OR = 1.6$ ,  $P = .15$ ) and ADHD in the family, a negative trend of association with a positive MDQ score ( $OR = 0.7$ ,  $P = .07$ ).

### Characteristics of ADHD Patients Screening Positive for BSD

Of the 510 patients, 244 screened positive and 239 negative on the MDQ (27 patients had 2 or more missing items and were not included in the analyses). The mean age did not differ between the MDQ-positive and the MDQ-negative patients, but there were significantly more men in the MDQ-positive group (58.6% vs 45.8%, Table 2). The MDQ-positive patients with ADHD had significantly lower educational level, and only 19.7% reported being employed at the time of inclusion into the study compared to 34.8% of the MDQ-negative patients. Current symptoms of ADHD (according to ASRS) were significantly higher among the MDQ-positive patients. The higher scores on the ASRS for the MDQ-positive patients were more pronounced on the hyperactivity/impulsivity subscale than on the inattentive subscale (mean difference, 3.9 vs 2.8, respectively), and the MDQ positive patients compared to the MDQ negative patients were more often of the hyperactive/impulsive or combined subtypes and less often classified as inattentive subtype or subthreshold cases according to the ASRS. In general, the MDQ-positive patients reported higher rates of comorbid symptoms and problems than the MDQ-negative patients, with significant differences for mood disorders and alcohol and substance abuse. They also reported having

been treated more often for psychiatric disorders other than ADHD. Interestingly, although the percentage was twice as much as it was in the MDQ-negative group, only 16.9% of the MDQ-positive patients with ADHD reported a known bipolar disorder. The MDQ-positive patients with ADHD reported significantly more bipolar disorder in first-degree family members, whereas ADHD was more often present in family members of the MDQ-negative group.

## DISCUSSION

The main findings of this study are as follows: (1) Of the adult ADHD patients, 50.6% screened positive for bipolar disorder on the MDQ. (2) We found an overall strong linear correlation between symptoms of ADHD and symptoms of bipolar disorder in the whole sample of patients and controls, but the strongest correlation was in the control group. (3) Patients seemed to diverge into 2 groups: 1 major group with high affective symptom load and 1 with more "pure" ADHD symptoms. The affective group had more hyperactive and impulsive symptoms, lower educational level and occupational outcome, and higher rates of substance abuse. Here we discuss the clinical significance and implications of these findings.

### Diagnostic and Psychometric Issues

The proportion of patients screening positive on the MDQ was much higher than the proportion of patients self-reporting a lifetime history of bipolar disorder and higher than the proportion of bipolar disorder identified by the

DSM-based interview. One explanation for this gap could be misdiagnosed or unrecognized bipolar disorder among ADHD patients. Before being diagnosed with ADHD, the patients in this study had been subject to thorough clinical evaluations with emphasis on differential diagnostic assessment. There is reason to believe that the clinical awareness of bipolar disorder among adult psychiatrists was at least as high as for ADHD at the time of the diagnostic evaluation. However, because the MDQ does not question the duration of the manic/hypomanic periods, does not ask about depressive episodes, and does not explicitly exclude drug or substance-related episodes, it comprises a broader definition of bipolar disorder than the *ICD-10* and *DSM-IV* used in clinical assessment. The mentioned higher awareness for bipolar disorder than for ADHD in adult psychiatry may not necessarily apply to such an expanded concept of BSD.

Another main finding in our study was the strong linear relationship found between lifetime symptoms of bipolar disorder and current symptoms of ADHD. This correlation may simply reflect that symptoms of bipolar disorder and ADHD are highly overlapping. However, our finding that the correlation was weakest in the patient group, where the symptom load of both ADHD and bipolar disorder were highest, contradicts explanation by simple overlap of common symptoms. Rather, it may support the hypothesis that affective symptoms are an inherent part of a syndrome shared by a subgroup of adult ADHD patients. The emotional aspect of ADHD has been recognized for many years in children<sup>40</sup> and is still an observable, clinical reality, both in children and adults.<sup>41,42</sup> Several decades ago, Wender initiated studies on ADHD in adults, and he later proposed affective symptoms as part of the ADHD diagnosis<sup>43</sup>; however, subsequent use of the Wender Utah criteria has been limited because they fail to identify the inattentive subtype of ADHD and because they do not clearly delineate ADHD from affective and conduct disorders.<sup>44</sup> Still, because emotional symptoms are not part of present diagnostic criteria, it may be confusing as to whether the emotional dysregulation recognizable in some ADHD patients should be considered a correlated personality trait, a defined subtype of ADHD, a comorbid affective disorder, or just secondary symptoms of a primary nonaffective disorder. The episodic (state) versus the chronic (trait) nature of bipolar disorder and ADHD, respectively, has so far been considered a main factor in differentiating affective symptoms related to ADHD from bipolar disorder. With the ongoing expansion of bipolar disorder to comprise a broader spectrum of disorders,<sup>24,45</sup> in which requirements for duration and consequences of hypomanic episodes are less restrictive, this distinction may become less obvious. In child psychiatry, the term *severe mood dysregulation* is used by some authors to describe the clinical phenomenon of chronic, impairing irritability with hyperarousal symptoms seen in some children in an effort to maintain the term *bipolar disorder* as a more narrowly

defined phenotype, more easily distinguishable from other overlapping disorders.<sup>46,47</sup>

Rates of bipolar disorder and of reported comorbidity between ADHD and bipolar disorder depend on the diagnostic criteria used for bipolar disorder. This may be one explanation of the diverging rates of bipolar disorder found in both clinical and epidemiologic studies of adult ADHD patients. They vary from rates of bipolar disorder similar to the general population (~1%) or only slightly elevated<sup>5,48,49</sup> to rates of bipolar disorder from 19% to 47%.<sup>4,50,51</sup> The debate regarding the phenomenology of pediatric bipolar disorder,<sup>48,52–54</sup> the increasing rates of diagnoses of bipolar disorder in child psychiatry,<sup>55,56</sup> and the recent focus on bipolar disorder as an underrecognized condition in adult psychiatry<sup>21,22,24</sup> may largely be explained by the expansion of the definition of bipolar disorder toward a spectrum of disorders. In adult psychiatry, this may also challenge the differential diagnosis between the syndromes of BSD and ADHD with some of the personality disorders.<sup>57–59</sup>

Among patients, the strongest predictor for screening positive on the MDQ was a history of alcohol or substance abuse. The prevalence of substance abuse is high in ADHD patients, and because the MDQ does not discriminate between substance-induced episodes and other hypomanic episodes, the high proportion of patients screening positive on the MDQ could represent false-positives explained by symptoms and behavior related mainly to substance abuse.<sup>60</sup> On the other hand, alcohol and substance problems are well-known and frequent features also of bipolar disorder<sup>61</sup> and may therefore not necessarily be considered an artifact but rather an extended characteristic of BSD, ie, bipolar III 1/2 disorder in Akiskal and Pinto's<sup>27</sup> definition of the bipolar spectrum. Again, this will depend on the definition of bipolar disorder being used, whether it allows or does not allow substance-induced mood disorders to be included.

With half of the patients screening positive for bipolar disorder according to the MDQ, it is relevant to ask how apt the MDQ is in detecting bipolar disorder. As discussed, the MDQ comprises a broader definition of bipolar disorder than the *ICD-10* and *DSM-IV*. In the general population, the MDQ has low sensitivity (0.28) but high specificity in detecting bipolar disorder (0.97).<sup>35</sup> In clinical samples, ie, mainly depressed patients or patients at mood clinics, the sensitivity is higher (0.58–0.73) and the specificity is as high as in the general population (0.9).<sup>34,62</sup> To our knowledge, no studies have applied the MDQ in a clinical sample of adults with ADHD. The sensitivity of the MDQ for detecting bipolar disorder, derived from the interviewed subsample of ADHD patients in our study, falls within the range obtained from other clinical populations. The specificity, however, was much lower, which probably explains the low correlations found between screening and interview diagnoses of bipolar disorder. This low specificity may reflect the problem of distinguishing between symptoms of adult ADHD and bipolar disorder.

### ADHD and Bipolar Symptoms: Overlapping Syndromes or Distinct Subgroup?

Regardless of categorical definitions and cutoffs for bipolar disorder, our study showed a strong correlation between symptoms of bipolar disorder and of ADHD. Importantly, this linear correlation was much weaker among patients, who seemed to diverge into 2 groups, a major group reporting lifetime occurrence of bipolar symptoms and a minor group with few or no such symptoms (29% MDQ7 negative). Further analyses showed that the MDQ-positive ADHD patients had more comorbid problems and were more functionally impaired than the MDQ-negative patients. Consistent with our *a priori* hypothesis, the MDQ-positive group was more often of the combined and hyperactive/impulsive subtype of ADHD compared to the MDQ-negative ADHD patients. These findings are also in line with the literature, showing that the combination of ADHD and bipolar disorder, or symptoms of bipolar disorder, yields a poorer outcome than ADHD without symptoms of bipolar disorder<sup>50,63</sup> and that the combined subtype of ADHD is more frequent in ADHD patients with comorbid bipolar disorder compared to ADHD patients without bipolar disorder.<sup>50</sup> The MDQ-negative group had a higher proportion of childhood-diagnosed ADHD and a higher frequency of reported ADHD in first-degree family members, whereas the MDQ high-scoring group had significantly higher rates of bipolar disorder in first-degree family members. These results may lend support to the hypothesis of a clinical subgroup of ADHD, possibly closer to the bipolar spectrum of disorders. Overlapping genetic findings in groups of ADHD and bipolar disorder patients are also consistent with this view.<sup>18</sup> Thus, some of the ADHD patients with bipolar-like symptoms may represent a valid clinical subgroup rather than just ADHD patients with comorbid bipolar disorder. Our data further suggest that this subgroup may be larger among patients formally diagnosed with ADHD in adulthood.

### Methodological Limitations

A major limitation of this study is that the results are obtained mainly by self-report questionnaires, with only 10% of the patients being more thoroughly examined for bipolar disorder. The ASRS and the MDQ are well-known and widely used autoquestionnaires, both in the clinic and in research, but still have not been subject to official validations in Norway. However, validation studies performed in various other countries have found them apt for use in both the United States and European populations. In addition, studies from countries that did not use nationally validated MDQ versions have yielded results comparable to other studies using the MDQ.<sup>64,65</sup> Another limitation is the relatively high nonresponse rates, with only 20% percent of the invited patients and 19% of the invited controls participating in the study. Caution is therefore necessary in generalizing the results of this study to the general

population or other samples of ADHD patients. Women had a higher response rate than men in both the patient and the control groups, resulting in a relatively higher proportion of women in the control group. In the population-based control group, 8.7% screened positive on the MDQ. This is higher than the 2.5% to 3.7% obtained by the MDQ in general population studies<sup>66,67</sup> but closer to recent epidemiologic prevalence estimates of 4.4% to 6.4% in BSD.<sup>21,24</sup> However, the nonclinical group in our study was relatively young and included more women than men. Hirschfeld et al<sup>67</sup> found in their large-scale community screening study that 9.3% of people aged between 18 and 24 years screened positive on the MDQ, which is comparable to the 8.3% in the population-based sample in our study. In addition, the reported levels of lifetime depression/anxiety (16.2%) and of known bipolar disorder (1.7%) in our control group, were quite similar to prevalence rates obtained in epidemiologic studies both from Norway and other countries.<sup>19,68</sup>

### CONCLUSIONS

A strong, positive correlation was found between symptom severities of ADHD and of bipolar disorder. Adults with ADHD had a 5-fold elevated risk of screening positive for BSD compared to a general population sample. Alcohol and/or substance abuse were the strongest predictors for screening positive for BSD among adults with ADHD. Adults with ADHD screening positive for BSD had a poorer outcome as adults and were less often diagnosed in childhood compared to ADHD patients with negative screens on the MDQ. Moreover, they had higher frequency of reported bipolar disorder and lower frequency of ADHD in first-degree family members. The nature of the relationship between ADHD and bipolar disorder, however, is still not clear. More studies are needed to compare ADHD and bipolar patients and, in particular, to explore the boundaries between ADHD and the broadly defined spectrum of bipolar disease.

### Implications

We suggest that in clinical practice, adult patients diagnosed with bipolar disorder should be assessed for possible underlying or comorbid ADHD, and vice versa. In future research, studies of bipolar patients, in particular patients with bipolar II disorder and bipolar disorder NOS, should include an evaluation of past and current ADHD symptoms to assess the prevalence and the role of ADHD in a broader concept of BSD. Further neurobiological and genetic research is also needed to explore the relationships of these conditions.

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**Supplementary material:** eTable 1 is available at <http://www.psychiatrist.com>.

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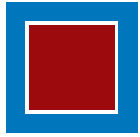
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For the CME Posttest for this article, see pages 96–97.

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# THE JOURNAL OF CLINICAL PSYCHIATRY

## **Supplementary Material**

**Article Title:** Bipolar Symptoms in Adult Attention-Deficit/Hyperactivity Disorder: A Cross-Sectional Study of 510 Clinically Diagnosed Patients and 417 Population-Based Controls

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### **List of Supplementary Material for the article**

1. [eTable 1](#) Interviewed (50) Versus Non-Interviewed ADHD Patients (460). Correlations Between Self-Reported Data and Diagnoses Obtained From Interview

### **Disclaimer**

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

**eTable 1. Interviewed (50) Versus Non-Interviewed ADHD Patients (460). Correlations Between Self-Reported Data and Diagnoses Obtained From Interview**

	Interviewed Patients		Non-Interviewed Patients	<i>P</i>
	Self-reported data	MINI plus-diagnoses <sup>1</sup>	Self-reported data	
N (% of all patients)	50 (9.8)		460 (90.1)	
Age in years, mean (SD)	33.9 (8.7)		34.4 (10.5)	.720
Gender % women	48.0 (24)		47.4 (218)	.935
Educational level % (n)	22.4 (11) junior high school		27.9 (107) junior high school	.551
Occupational level % (n)	24.5 (120) in work		27.7 (115) in work	.096
	42.8 (21) disabled/rehab		51.3 (213) disabled/rehabilitation	
	14.3 (7) other		11.3 (47) other	
ADHD diagnosis in childhood % (n)	12.0 (6)		18.9 (84)	.232
Treatment with stimulants in childhood % (n)	12.0 (6)		17.0 (76)	.363
ASRS score, mean (SD)	49.1 (8.5)		45.4	.008
Anxiety and /or depression % (n)	58.0 (29)	80.0 <sup>2</sup> (40) ( <i>r</i> = 0.39*).	70.2 (313)	.078
		74.0 <sup>3</sup> (37) ( <i>r</i> = 0.51**)		
Bipolar disorder % (n)	4.0 (2)	8.0 (4) bipolar 1 ( <i>r</i> = 0.24, NS)	13.2 (56)	.066
		18.0 (9) bipolar 2 ( <i>r</i> = 0.32*)		
		32.0 (16) BD broadly defined <sup>4</sup> ( <i>r</i> = 0.37*)		
MDQ positive % (n)	38.0 (19)	Bipolar 1 ( <i>r</i> = 0.06, NS)	52.3 (227)	.055
		Bipolar 2 ( <i>r</i> = 0.26, NS)		
		BD broadly defined <sup>4</sup> ( <i>r</i> = 0.32*)		
MDQ7 positive % (n)	60.0 (30)	Bipolar 1 ( <i>r</i> = 0.23, NS)	72.0 (317)	.234
		Bipolar 2 ( <i>r</i> = 0.26, NS)		
		BD broadly defined <sup>4</sup> ( <i>r</i> = 0.46**)		
Alcohol problems % (n)	26.0 (13)	36.0 (18) dependency (12) and/or abuse (16) ( <i>r</i> = .70**)	24.9 (111)	.863
Problems with other drugs % (n)	28.0 (14)	30.0 (15) dependency (15) and/or abuse (15) ( <i>r</i> = .66**)	26.4 (118)	.952

<sup>1</sup>Proportion of interviewed patients meeting *DSM-IV*-criteria by MINI plus interview.

<sup>2</sup>Anxiety and/ or depression by MINI plus here include current or past major depression and/or one of the following anxiety disorders: general anxiety disorder, panic disorder, social phobia, agoraphobia, obsessive compulsive disorder and/or post traumatic stress disorder.

<sup>3</sup>Anxiety and/or depression here include current or past major depression only.

<sup>4</sup>Includes BD I, BD II, BD NOS, ie, subthreshold criteria for mania or hypomania or possibly substance-induced mania or hypomania.

\**P* < .05.

\*\**P* ≤ .001, and NS = *P* > .05 for the two-tailed significance level of the bivariate correlation.

Abbreviations: *r* = Pearson's correlation between self-report data and diagnoses obtained by diagnostic interview, SD = standard deviation.