Comorbidity Between ADHD and Symptoms of Bipolar Disorder in a Community Sample of Children and Adolescents

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The prevalence and frequency of comorbidity of possible bipolar disorder was examined with attention-deficit hyperactivity disorder (ADHD) in a nonreferred population of twins. Children and adolescents aged 7 to 18 years with a history of manic symptoms were identified from a population-based twin sample obtained from state birth records (n = 1610). The sample was enriched for ADHD; however, there was also a random control sample (n = 466), which allowed a look at the population prevalence of the disorder. Juveniles with threshold or below threshold manic episodes were further assessed for comorbidity with *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; DSM-IV; American Psychiatric Association, 1994) and population-defined ADHD subtypes (from latent class analysis) using Fisher's exact test. Nine juveniles who exhibited DSM-IV manic (n = 1), hypomanic (n = 2) or below threshold episodes (n = 6) were identified. The population prevalence of broadly defined mania in the random sample was 0.2%. The possible manic episodes showed significant comorbidity with population-defined severe combined and talkative ADHD subtypes. It can be concluded that there is a significant association of bipolar symptoms with two population-defined subtypes of ADHD. Episodes of possible bipolar disorders as defined by DSM-IV are uncommon in this nonreferred sample. Children and adolescents with ADHD appear to be only modestly at increased risk for bipolar disorders.

Recent studies have found features of bipolar disorder in children and young adolescents that have an earlier onset than adult bipolar disorder and differ in many ways from the form seen in adults (Biederman et al., 1996; Geller & Luby, 1997; Wozniak et al., 1995). For example, pediatric bipolar disorder is reported to be chronic rather than episodic. (Faraone et al., 2003; Geller & Luby, 1997; Geller et al., 1995; Geller et al., 2002). Biederman et al. (2003) and Faraone et al. (2003) describe juvenile bipolar disorder as presenting with irritability, severe affective dysregulation and high levels of agitation and aggression. Geller and Luby (1997) describe mood disturbances such as elation and grandiosity that are found in adults but suggest that these symptoms might be hard to recognize in children. They also describe rapid cycling, including ultradian cycling, in which the youths cycle between mania and depression every day.

What is particularly pertinent to our work on the genetics of attention-deficit hyperactivity disorder (ADHD) is that many studies of prepubescent and early adolescent bipolar disorder describe frequent comorbidity with ADHD (Biederman et al., 1996; Biederman et al., 1998; Tramontina et al., 2003; Wozniak et al., 1995). Tramontina et al. (2003) reports that more than 75% of children with early-onset bipolar disorder can also be diagnosed with ADHD. Faraone et al. (1997) cite evidence of rates of ADHD ranging from 57% to 98% in their bipolar subjects. A review of the literature by Kim and Miklowitz (2002) report similar numbers. Faraone et al. (1997) found the highest rates of comorbidity between ADHD and juvenile bipolar disorder in prepubertal children with lower rates for the young adolescents. He suggests that the co-occurrence of pediatric bipolar disorder and ADHD may constitute a separate subtype of ADHD or bipolar disorder that is strongly influenced by genetic factors and may be useful in molecular genetic studies.

A potential limitation of these studies of bipolar disorder and of ADHD is that they have been performed on clinical populations. This may confound the results, as children receiving medical attention are likely to have a more severe illness and higher rates of comorbidity.

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Epidemiologic studies have examined *Diagnostic and Statistical Manual of Mental Disorders* (DSM)–defined bipolar disorders and symptoms of bipolar disorders in adolescents (Carlson & Kashani, 1988; Costello et al., 1996; Lewinsohn et al., 1995; Lewinsohn et al., 2003b). Carlson and Kashani report rates of 1.5% of bipolar II or cyclothymia. Lewinsohn et al. (1995) found 1% that could be described as having a bipolar disorder, although out of 1709, they found only two adolescents who they felt could be classified as bipolar I. Costello et al. (1996) found no cases of bipolar disorder, and a rate of only 0.1% for hypomania. Kim-Cohen et al. (2003) using data from the Dunedin study present higher rates of manic episodes; however, these are children who developed psychiatric disorders as adults.

The Carlson and Kashani and the Lewinsohn studies show higher rates of what can be referred to as subthreshold levels of manic episodes. Carlson and Kashani (1988) report that 13.3% of the adolescents in their sample had periods of at least 2 days in which they exhibited four or more manic symptoms. However, none of these subjects showed enough impairment to meet diagnostic criteria. Lewinsohn et al. (1995) found that 5.7% of adolescents in the sample reported having exhibited a distinct period of elevated, expansive or irritable mood and other manic symptoms but did not meet criteria for bipolar I or bipolar II disorder, or cyclothymia. Both Carlson and Kashani (1988) and Lewinsohn et al. suggest that manic features in community samples may represent milder forms of bipolar disorder and thus fewer symptoms might be detected. Lewinsohn et al. (1995) postulate that symptoms such as elation and grandiosity alone may signal affective problems. Reporting on a later phase of the study, Lewinsohn et al. (2003b) defined subthreshold episodes as having the presence of a core manic symptom (elevated mood or irritability) and at least one other manic symptom and never having met criteria for bipolar disorders. Thus, in our nonreferred population we might be more likely to find subthreshold cases of bipolar disorder than if we were studying a clinical population.

Although there is evidence of subclinical bipolar disorder in children and adolescents in epidemiologic populations, to our knowledge there are no studies aimed at examining the relationship between bipolar disorder and ADHD in nonreferred populations. The goal of the current study is to examine the relationship between possible bipolar disorder and ADHD in a nonreferred sample of children and adolescents of ages 7 to 18 years. More specifically, we ask whether subthreshold or full criteria cases of mania are significantly associated with either DSM-IV (4th ed.; American Psychiatric Association, 1994) or population-derived subtypes of ADHD. If a relationship between child and adolescent bipolar symptoms and these subtypes were to be found, it would be relevant to the findings of Faraone et al. (1997) by postulating the association of discrete genetic subtypes of ADHD with possible bipolar disorder. This study also gives us the opportunity to determine rates of possible bipolar disorder in a community sample.

This study compares ADHD and bipolar disorder in two ways. The first uses DSM-IV subtypes and the second uses latent class analysis (LCA). Recent population-based twin studies of ADHD have demonstrated the presence of multiple genetically independent ADHD subtypes that only partially overlap with DSM-IV ADHD subtypes (Rasmussen et al., 2004; Todd et al., 2001; Volk et al., 2005). These studies used LCA (McCutcheon, 1987) to identify naturally occurring clusters of the 18 DSM-IV ADHD symptoms in population-based samples of male and female twins. LCA is a widely used categorical clustering technique that assigns individuals to discrete homogeneous groups. Comparing concordance rates for identical (monozygotic [MZ]) and fraternal (dizygotic [DZ]) twins, there was strong evidence for independent heritability of the latent class-derived, population-based ADHD subtypes in all three samples. No studies of the relationship of these population-based ADHD subtypes with bipolar disorder have appeared.

In order to explore the relationship between ADHD and possible bipolar illness, we examined data from a large-scale birth records–based community study of ADHD in children aged 7 to 18 in which children may or may not have come to clinical attention. The high incidence of ADHD in this population should help us define the relationship between possible bipolar disorder and ADHD and its subtypes.

Methods

Subjects comprised MZ and DZ twin pairs aged 7 to 18 years drawn from birth records in the state of Missouri. This ongoing study aims to investigate the genetic basis of ADHD. After twins were identified, one parent (usually the mother) was administered a screening interview to determine if either of the twins were at risk of ADHD by virtue of their endorsing three or more inattentive ADHD symptoms on a 6-item ADHD screener for at least one twin. Twins who were at risk for ADHD as determined by the screener were oversampled. Twins from families who were randomly identified from birth records were also included. The family-wise completion rate of screening interviews was 92.5% and of diagnostic interviews was 65.1%. The current analyses are based on 1610 child and adolescent twins (37.5% female, 13.7% African American, approximately 2.3% other minorities). The sample was 46% child (ages 7 to 12 years) and 54% adolescent (13 to 18 years). Participants did not differ from nonparticipants on a wide range of socioeconomic and demographic factors (Neuman et al., in press).

Twins were interviewed about their own psychiatric and health history as well as psychosocial information

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using the Missouri Assessment for Genetics Interview of Children (MAGIC; Todd et al., 2003), an instrument based on the Diagnostic Interview for Children and Adolescents (DICA; Reich, 2000). One parent (usually the mother) was asked to report the same information on the parent version of the MAGIC. Parents were interviewed separately about each twin. Further details of the assessment can be found in Todd et al. (2003).

The reports for diagnoses of ADHD and possible juvenile bipolar disorder (both mania and depression) were taken from the parent report only. ADHD has traditionally been found to be reported better by the parent. Parent reports of mania were also used, as we wanted to ensure that these symptoms were severe enough to be noticed by others, as is described in DSM-IV.

The MAGIC is a relatively new instrument that was developed for a study on the genetics of ADHD. However, the DICA, of which the MAGIC is a revision, has been used in two studies of children from bipolar families. Several children in those studies were diagnosed with possible bipolar disorder (Todd et al., 1996; Todd et al., 1994).

All of the mania questions are carefully crafted so as to assess manic symptoms in the specific age groups (child and adolescent). All contain age-appropriate examples of what a manic symptom might be. Impairment questions are asked specifically for the manic symptoms. Further, the validity of possible bipolar disorder was established by best-estimate diagnosis by two senior investigators (Wendy Reich and Richard D. Todd). These included the nine children presented in this article and another nine children matched for age and sex. Complete agreement was achieved on all cases of possible bipolar disorder, including cases in which the mood was hypomanic. Complete agreement was also achieved on cases in which bipolar or possible bipolar disorder were not present.

There were no 'skip-outs' in the mood disorder and ADHD sections of the interview, so subsyndromal clustering of symptoms could be assessed. Both current and lifetime symptom information were queried. Interrater reliability for manic, depressive and ADHD symptoms (including clustering, impairment and age of onset) as asked in the MAGIC are excellent, with kappas ranging from 0.79 to 1.0 (Todd et al., 2003).

In addition, possible mania, ADHD and control subjects from the MAGIC were compared from the Child Behavior Checklist (CBCL; Achenbach, 1991) scores. Both ADHD and possible mania subjects were rated considerably higher on all scales than were the controls. These scores were then compared with scores derived by Biederman et al. (1995). ADHD subscale score profiles were virtually identical to Biederman et al.'s (1995), while possible bipolar disorder individuals showed the same elevations on the withdrawal, somatization, thought disorder, attention problems, delinquency and aggression subscales. Our scores on CBCL subscales were not as high as the Biederman et al. (1995) scores, but they were of a similar pattern. For these reasons, the MAGIC is a useful instrument for diagnosing mania in children and adolescents.

In order to determine if possible bipolar illness and ADHD were comorbid, we first attempted to identify children and adolescents with symptoms of mania. We also assessed the 'manic' children for a lifetime depressive episode or symptoms of depression for further evidence of bipolarity.

Comorbidity of DSM-IV ADHD and bipolar and possible bipolar disorder cases were measured in two ways. Once we assessed the number of children with possible bipolar disorder we looked to see if these juveniles also met criteria for DSM-IV ADHD and any of the DSM-IV subtypes: predominately inattentive, predominately hyperactive and combined. Comorbidity was also assessed in population-defined ADHD subtypes based on LCA. As noted above, these classes are more phenotypically homogeneous and may represent more biologically similar groups (Rasmussen et al., 2004; Todd et al., 2001).

LCA is a parametric variant of cluster analysis used to identify subtypes of related individuals based on their response profiles to individual sets of items. These response profiles can then be used to assign individuals to their most likely latent class (McCutcheon, 1987). In the current study, individuals were assigned to latent classes created from 18 ADHD symptoms based on criteria from the best fitting latent class model of Rasmussen et al. (2004). This includes data on over 7000 individuals and has demonstrated the presence of similar classes in males and females (both children and adolescents) across two large population-based twin studies. In all cases the assignment to a particular class was at least twice as probable as assignment to any other class. Of particular relevance to this study was that individuals in the severe combined latent class averaged about eight inattentive and seven hyperactive DSM-IV ADHD symptoms (prevalence about 3% for girls and 5.6% for boys). Individuals in the talkative latent class averaged about 0.7 inattentive and 2.7 hyperactive/impulsive symptoms (prevalence about 9% for boys and girls). Individuals in this class frequently endorse the 'talkative' ADHD symptom and impulsive symptoms. Individuals in the few symptoms latent class averaged less than 0.2 ADHD symptoms (prevalence about 60% for females and 56% for males).

All statistical analyses used the Fisher's exact test to compare proportions in different cells of 2×2 tables.

Results

Of the 1610 children and adolescents included in this study, 1006 were male and 604 were female. Seven hundred and forty-one were children and 869 were adolescents. Three hundred and fifty-nine met criteria for DSM-IV ADHD. Three met full criteria for DSM-IV mania or hypomania although one of the hypomanic

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children did not exhibit a depressed episode. Of the remaining two, one could be confidently diagnosed as bipolar I and the other as bipolar II. Six additional children showed multiple manic symptoms but did not meet DSM-IV diagnostic criteria. Characteristics of these youth are summarized in Table 1. Seven of these nine youth met full DSM-IV criteria for at least one DSM-IV depressed episode further indicating the possibility of bipolar disorder. Two individuals experienced manic symptoms with no lifetime depression symptoms. Of the seven cases, mania either had an earlier onset than depression (n = 3) or occurred at the same age (n = 2). Five of nine cases had prepubertal onset of manic symptoms, while three exhibited manic symptoms in early adolescence and one not until age 17 years. Seven of these juveniles showed significant impairment from manic symptoms. The two with 'impairment reported' by the parent met DSM-IV criteria for hypomania. According to DSM-IV criteria, hypomanic episodes are not severe enough to cause marked impairment. Eight of the nine had been referred for treatment of the manic symptoms as well as the depression, though only two had been prescribed a mood stabilizer.

For the total sample, five possible bipolar individuals were male (frequency = 0.003) and four were female (frequency = 0.003, no significant sex differences). Two were children (frequency = 0.001) and seven were adolescents (frequency = 0.004, difference not significant). Of these nine individuals, one was from a random control family (1 of 466 offspring) giving a community cross-sectional population prevalence of 0.2%. This boy met all but the duration criteria for DSM-IV mania and had a history of a major depressive episode.

Of the 359 children in our sample diagnosed with DSM-IV ADHD, only three showed comorbidity with possible bipolar disorder (0.84%) differing from the comorbidity results presented in the clinical studies. On the other hand, the possible bipolar children show frequent comorbidity with ADHD (33%). Distributions of possible mania with population-defined ADHD subtypes are shown in Table 2.

Table 3 presents tests for significant comorbidity of possible juvenile mania with DSM-IV and population-based subtypes of ADHD. There are no significant associations of possible bipolar disorder for any of the DSM-IV ADHD subtypes. In contrast, the population-derived ADHD subtypes show significant associations with the few or no symptoms of ADHD subtype (one case) as well as the severe combined subtype (two cases) and the talkative subtype (one case). These significant associations comprise four of the nine possible cases of mania. The other five are found in the mild inattentive subtype (one case), the mild combined subtype (three cases) and the severe inattentive subtype (one case). When the cases of possible bipolar disorder are divided by DSM-IV ADHD subtypes, there are six cases with no ADHD, one in the predominately inattentive subtype, and two in the combined subtype.

Discussion

The prevalence of possible bipolar disorder among our children and adolescents is low compared with the clinical studies and lower than the community estimates of Carlson and Kashani (1988) and Lewinsohn et al. (1995). Our rate was approximately 0.2% for youth from randomly identified families and 0.84% for youth with DSM-IV defined ADHD. However, this may be in part because of our criteria, which required that the symptoms be severe enough to be noticed by others, in this case the parents. Furthermore, our population of 466 individuals is much smaller than that of the epidemiological studies. It is encouraging, however, that the epidemiological studies showed what can also be referred to as 'possible' cases.

We did not find any significant association of possible mania with DSM-IV ADHD subtypes. Analyses of population-derived ADHD subtypes showed a significant association between the severe combined subtype and the talkative subtype and possible juvenile bipolar illness. Of the nine possible mania cases only one was associated with the few or no ADHD symptoms class, although that association was significant. The association between the severe combined and the talkative ADHD subtypes and possible bipolar disorder indicates that possible bipolar disorder found in children and adolescents may be associated with the ADHD symptoms found in these classes. Our results also indicate that in nonreferred samples, children with symptoms of bipolar illness are relatively rare. The children we diagnosed as possible bipolar showed a good correspondence with the adult definition of mania as well as having coexisting depressive symptoms. The positive association of possible bipolar disorder with the population-defined severe combined and talkative subtypes of ADHD is consistent with a possible genetic connection between the two disorders.

We did not find symptoms specific to pediatric bipolar disorder, such as the affective storms or the ultradian cycling states, but again this may be because our population was nonreferred and because we did not specifically ask about them. However, it is worth noting that the three children significantly correlated with the population-based ADHD subtypes had prepubertal onset of the manic and depressed symptoms.

Limitations

A limitation of this study is that pediatric bipolar disorder was not diagnosed in the same way as is articulated in some studies that focus on juvenile bipolar disorder in clinical populations. As stated above, we were not able to assess the affective storms described in many studies, nor were we able to assess rapid (ultradian) cycling states. Our cases are representative of narrow-spectrum adult bipolar disorder. However, these criteria have identified candidates for bipolar diagnoses and subthreshold bipolar disorder in adolescents in other nonreferred samples, as do the

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Table 1
Characteristics of Youth With Manic Symptoms

Sex	Age	Depression/ mania	Age of onset	Treatment	Medication	Irritable mood	Elevated mood	Expansive mood	Other diagnoses	Sample of mania symptoms
F	18	Depression Manic symptoms	11 14	Psychiatrist Counsellor Psychiatrist	fluoxetine bupropion lithium	Yes	Yes	No	ODD CD	'Talks fast, making out plans, gets excited, hyper, manicky.' Goes for nights without sleeping — not tired. When 'manicky' talks nonstop — gets flooded with different plans. Mom says she is bipolar. Significant impairment.
F	18	Depression Hypomania	16 15	Psychologist Psychologist	None	Yes	Yes	No	ODD	'Super-happy, social, increased activity, talked a lot.' Gave away all tapes and CDs that were not Christian — became very religious — not like that now. Impairment reported.
F	17	Depression Manic	17 17	MD None	prednisone for lupus	Yes	No	No	No	'Flight of ideas, words just fly out of her mouth — not connected with what she just said. Talked on telephone nonstop — unusual for her. Overinvolved in activities, social life.' Significant impairment.
M	16	Manic symptoms	9	None	None	Yes	No	Yes	No	'Saved hair so mother could sell it after he became famous baseball player.' Gave his autograph to people. Significant impairment.
M	13	Depression Mania	5 10	Hospitalisation MD	paroxetine	Yes	No	No	ODD OCD	'Five episodes, periods of not sleeping for two nights without being tired; "not-sleeping marathons".' Gave away clothes, CD player, other people's things. Possible psychotic symptoms. Seeing and hearing things that other people could not see or hear. Thinks he is better than everyone else. During one period, signed up for every school play, started several new sports, began going to church. Significant impairment.
M	9	Depression Manic symptoms	8 8	Doctor Counsellor Priest Doctor Counsellor Priest	None	Yes	No	No	DSM-IV ADHD ODD	'Cycles, irritable mood lasts few days. Everyone noticed cycling.' Started to write a book; finished two chapters. Planned to get married this year. Significant impairment.
F	14	Hypomania	13	None	None	No	Yes	Yes	No	Elated — strangely excited and happy. On the phone to friends all the time. Planned her wardrobe for an entire month. Planned on being an Olympic star with no apparent athletic ability. Most over-confident person mom had ever seen — a lot different from way she usually is — noticed by husband and aunts. Gathered names for a petition to keep pedophiles locked up. Impairment reported.
M	7	Depression Manic symptoms	6 5	MD MD	methylphenidate	Yes	No	Yes	DSM-IV ADHD	Flight of ideas, racing thoughts, talking constantly, words slurred, wanted to give away all his race cars (mom wouldn't let him). Tried to wire his tree house for cable. Planned on being a millionaire any day now. Significant impairment.
M	14	Depression Manic symptoms	7 5	MD Counsellor MD	bupropion lithium methylphenidate	Yes	No	Yes	DSM-IV ADHD ODD CD	During each 'spell' talked too fast, paced like a panther, grandiosity. Felt he was the strongest person in the world. Planned creating Nintendo games. Tried to call the President (mom wouldn't let him). Not sleeping without being tired. Many episodes. Significant impairment.

Table 2

Number of Manic/Hypomanic Individuals by Age and Sex for Population-Defined ADHD Subtypes

		Hypomanic	Mania	Mania –1sx	Mania –2sx	Mania –d	Mania –d1	Mania –d2	Total
A. Severe combined									
Boys	Child	0	0	0	0	0	1	1	49
	Adolescent	0	0	0	0	1	2	2	49
Girls	Child	0	0	0	0	0	0	0	20
	Adolescent	0	0	0	0	0	0	0	7
B. Mild combined									
Boys	Child	0	0	0	0	0	0	0	62
	Adolescent	0	0	0	0	0	0	0	45
Girls	Child	0	0	0	0	0	0	0	23
	Adolescent	0	0	0	1	0	1	2	14
C. Few ADHD symptoms									
Boys	Child	0	0	0	0	0	0	0	167
	Adolescent	0	0	0	0	0	0	0	286
Girls	Child	0	0	0	0	0	0	0	194
	Adolescent	0	1	1	1	1	1	1	221
D. Severe inattentive									
Boys	Child	0	1	1	1	1	1	1	29
	Adolescent	0	0	0	0	0	0	0	54
Girls	Child	0	0	0	0	0	0	0	13
	Adolescent	0	0	0	0	0	0	0	5
E. Mild inattentive									
Boys	Child	0	0	0	0	0	0	0	68
	Adolescent	0	0	0	1	0	0	1	97
Girls	Child	0	0	0	0	0	0	0	33
	Adolescent	0	0	0	0	0	0	0	19
F. Mild hyperactive									
Boys	Child	0	0	0	0	0	0	0	15
	Adolescent	0	0	0	0	0	0	0	28
Girls	Child	0	0	0	0	0	0	0	11
	Adolescent	0	0	0	0	0	0	0	2
G. Severe hyperactive									
Boys	Child	0	0	0	0	0	0	0	15
	Adolescent	0	0	0	0	0	0	0	5
Girls	Child	0	0	0	0	0	0	0	3
	Adolescent	0	0	0	0	0	0	0	3
H. Talkative									
Boys	Child	0	0	0	0	0	0	0	23
	Adolescent	0	0	0	0	0	0	0	14
Girls	Child	0	0	0	0	0	0	0	16
	Adolescent	1	0	0	0	0	0	0	20
Total		**1**	**2**	**2**	**4**	**3**	**6**	**8**	

epidemiologies cited in this study (Lewinsohn et al., 2003a). Our work with a nonreferred population and with the population-derived ADHD subtypes suggests possible genetic relationships between specific subtypes of ADHD and possible bipolar disorder in children and adolescents as defined by DSM-IV.

Another limitation is the possible confound with medication in that antidepressants and methylphenidate have been known to trigger manic episodes. Other medications may trigger manic symptoms as well. For example, the manic symptoms for the female adolescent with lupus could have been caused by the

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Table 3A

Association of Various Definitions of Mania/Hypomanic With DSM-IV ADHD Subtypes

Diagnosis	No ADHD	Inattentive	Hyperactive	Combined
Hypomania	1.000	1.000	1.000	1.000
Mania	.396	.188	1.000	1.000
Mania minus 1 sx	.396	.188	1.000	1.000
Mania minus 2 sx	1.000	.341	1.000	1.000
Mania minus duration	.127	.268	1.000	.294
Mania minus duration 1 sx	.129	.465	1.000	.133
Mania minus duration 2 sx	.388	.566	1.000	.215

Note: sx = symptom.

Table 3B

Association of Various Definitions of Mania/Hypomania With Population-Derived ADHD Subtypes

Diagnosis	ADHD few symptoms LC1	Mild inattentive LC2	Talkative LC3	Mild combined LC4	Mild hyperactive LC5	High combined LC6	High inattentive LC7	High hyperactive LC8
Hypomania	.461	1.000	**.045**	1.000	1.000	1.000	1.000	1.000
Mania	1.000	1.000	1.000	1.000	1.000	1.000	.122	1.000
Mania minus 1 sx	1.000	1.000	1.000	1.000	1.000	1.000	.122	1.000
Mania minus 2 sx	.340	.440	1.000	.313	1.000	1.000	.229	1.000
Mania minus duration	.598	1.000	1.000	1.000	1.000	.215	.177	1.000
Mania minus duration 1 sx	.101	1.000	1.000	.431	1.000	**.008**	.323	1.000
Mania minus duration 2 sx	**.028**	1.000	1.000	.156	1.000	**.019**	.405	1.000

Note: *p* values are two-sided probability for Fisher's exact test.

medication Prednisone. It is also possible that the methylphenidate and antidepressants prescribed for some of the children may have triggered manic symptoms. However, this is always a confound when dealing with children, most of whom were treated for depression or ADHD. Four of the six possible mania children were not treated with any medication and the two others had been prescribed mood stabilizers.

Clinical and Public Health Implications

In this population-based sample, which was enriched for the presence of ADHD, mania was rare, frequently had onset prior to depression and was associated with ADHD less than 50% of the time. These findings suggest that screening for presence or history of ADHD and depression may not be helpful in increasing diagnostic confidence in cross-sectional evaluations of children or adolescents referred for possible mania. The low overall prevalence of possible mania in the random control population (0.2%) suggests that it may be prudent to have a low threshold for referral of mania patients for specialized evaluation in order to identify those children who may benefit from intervention. The high rate of referral of cases in the current sample to treatment for both depression and mania is encouraging in that it suggests that such referral patterns for this difficult population may be better than expected in the general population. The treatment of only two of the nine possibly manic individuals with mood stabilizers, however, suggests that use of possibly effective pharmacological treatments lags behind referral patterns for this disorder.

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