

PARENT-REPORT MANIA RATING SCALES IN AN ADHD POPULATION

By

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Rates of diagnosed bipolar disorder in children and adolescents have significantly increased over the past decade. It has been argued that pediatric bipolar disorder is currently being overdiagnosed. It is speculated that symptom overlap between childhood bipolar disorder to conditions such as Attention-Deficit/Hyperactivity Disorder (ADHD), oppositional defiant disorder (ODD), and depression may be one cause for this rise in pediatric bipolar disorder diagnoses. Given the increased rate of bipolar disorder diagnoses, research has focused on developing mania rating scales to serve as screeners for this disorder. The present study sought to examine five parent-report mania rating scales with four groups; a control group, ADHD-only group, ADHD with Oppositional Defiant Disorder (ODD) group, and ADHD with depression group. The purpose of the study was to examine the mania rating scales' diagnostic utilities in clinical groups where ADHD with comorbid ODD and depression are common.

Results of the study indicate that children with both ADHD and ODD tend to score much higher on mania rating scales than children with ADHD only or ADHD with depression. There was almost no difference between published means for bipolar disorder and means for the three ADHD groups in the current study. This suggests that these scales may not discriminate very well between children with bipolar disorder and children with ADHD, particularly ADHD with

ODD. Additionally, a significant proportion of participants, especially children with both ADHD and ODD, met established cutoff criteria for probable bipolar disorder diagnoses. No scale appeared to significantly outperform any other scale in terms of its ability to discriminate between groups. There also did not appear to be a significant difference between children with ADHD only and ADHD with depression on their scores on the mania rating scales.

Given the results of this study, these scales should be cautiously used as screeners only to identify individuals for whom further assessment of bipolar disorder is warranted. Future research should replicate the present study with a larger sample in order to bolster the generalizability of the findings and perform analyses based on age, ADHD subtype, and depression diagnoses.

CHAPTER 1 INTRODUCTION

Clinical investigator Emil Kraepelin observed the onset of manic depression in childhood and adolescence in 1921. Additionally, case reports of pediatric mania have been documented as far back as the 1800s. In the past 30 years, sporadic case reports of pediatric bipolar disorder have been published. Despite these accounts, the conventional wisdom was that Bipolar Disorder is primarily a disorder with adult onset, occurring only rarely during late adolescence. (Youngstrom et al., 2006). However, there has been a recent increase in the rate of diagnoses of Bipolar Disorder in children and adolescents. Drug company marketing research in 2001 indicated that 95,000 children and adolescents in the United States were being treated for bipolar disorder (Youngstrom et al., 2006). Other reports have shown that the diagnosis of Bipolar Disorder in youths has increased 40-fold in the last 10 years (Moreno et al., 2007). Additionally, epidemiological studies estimate that at least 1% of youth may be affected with bipolar disorder (Lewinsohn et al., 1995), and clinical studies suggest that 20% of psychiatrically referred children and adolescents satisfy criteria for bipolar spectrum disorders (Meyer et al., 2004).

Two hypotheses have been posited to explain the increasing rate of diagnoses; 1) Pediatric Bipolar Disorder was being previously under-diagnosed and 2) the disorder is now being over-diagnosed. There is evidence to support the argument that the disorder was previously under-diagnosed. The median age of onset of Bipolar Disorder has been located at 19-23 years of age, indicating that for 50% of individuals, the onset is earlier. Long delays in treatment seeking have been documented when the onset occurs in childhood (possibly due to problems in recognizing the disorder). Adults with Bipolar Disorder have reported that as many as 60% experienced the onset of the disorder before 20 years of age, and 10-20% reported the onset before age 10 (Moreno et al., 2007). Another study found that half of its 494 adult patients with Bipolar

Disorder experienced some symptoms before age 19, and 5% recalled symptoms before age 5 (Kowatch & DelBello, 2003).

The second theory in response to the increased diagnostic pattern is that Pediatric Bipolar Disorder is being over-diagnosed. It is possible that the lack of age-specific diagnostic criteria may be promoting misdiagnosis of other conditions under the label of Bipolar Disorder. Also, subthreshold manic symptoms appear to be somewhat common (6-13.3%) in adolescent community samples, and have been reported in 3.3% of pediatric samples; however, only small proportions of these children meet full criteria for Bipolar Disorder. It is possible that these children meeting only subthreshold manic symptoms are being given the diagnosis, thus inflating the diagnostic rates. Finally, there is significant symptomatic overlap between Bipolar Disorder and ADHD, which may complicate accurate diagnostic rates in children and adolescents (Moreno et al., 2007).

Bipolar Disorder Diagnostic Criteria

Clinicians frequently refer to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR; American Psychiatric Association, 2000) for diagnostic guidelines for Bipolar Disorder. The types of Bipolar Disorder are characterized by manic, hypomanic, and mixed episodes. The DSM-IV criterion for a manic episode requires a distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least one week (or any duration if hospitalization is necessary). During the period of mood disturbance, three or more of the following must have persisted: (four if the mood is only irritable): a) inflated self-esteem or grandiosity b) decreased need for sleep c) more talkative than usual or pressure to keep talking d) flight of ideas or subjective experience that thoughts are racing e) distractibility f) increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation g) excessive involvement in pleasurable activities that have a high potential for painful

consequences (like engaging in buying sprees, sexual indiscretions, or foolish business investments). The symptoms cannot meet criteria for a mixed episode, and the mood disturbance must be sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or psychotic features must be present. Finally, the symptoms cannot be due to the direct physiological effects of a substance or general medical condition.

A hypomanic episode differs from a manic episode in that the episode must last at least 4 days, instead of a week, and the episode must not be severe enough to cause marked impairment or hospitalization, and there may be no psychotic features present. A mixed episode is characterized by criteria being met (except for duration) for a manic episode and a Major Depressive Episode, nearly every day for a week.

A Major Depressive Episode requires a distinct period lasting two or more weeks, with five or more of the following symptoms being present; a) depressed mood b) anhedonia c) significant weight change or change in appetite d) insomnia or hypersomnia, e) psychomotor agitation or retardation f) fatigue or loss of energy g) feelings of worthlessness or excessive and inappropriate guilt h) problems concentrating or thinking i) recurrent thoughts of death, suicidal ideation, intent, or attempt. Either depressed mood or anhedonia must be present for a diagnosis. The DSM-IV notes that depressed mood may present as irritable mood in children. Additionally, the DSM-IV diagnostic criteria indicate that weight and appetite changes may result in failure to make expected weight gain in children.

Based on these diagnostic guidelines, the DSM-IV recognizes diagnoses of bipolar I Disorder, bipolar II disorder, cyclothymic disorder, and bipolar disorder not otherwise specified (NOS). For a diagnosis of bipolar I disorder, there must have been one or more manic or mixed

episodes. For diagnosis of bipolar II disorder, there must have been one or more major depressive episodes and one or more hypomanic episodes (there must never have been a mixed or manic episode). Cyclothymic disorder is characterized by a period of two or more years with hypomanic symptoms and depressive symptoms that don't meet criteria for a major depressive episode. Finally, bipolar disorder NOS can be used to characterize a disorder with bipolar features that does not meet criteria for any of the disorders aforementioned (American Psychiatric Association, 2000).

Bipolar Disorder in Children and Adolescents

Despite the specific diagnostic criteria outlined in the DSM-IV-TR, the clinical presentation of the disorder in children and adolescents varies. The Institute of Mental Health Research Roundtable on pre-pubertal bipolar disorder reached an agreement that pediatric bipolar disorder can present as “narrow” or “broad” phenotypes. The narrow phenotype fits the bipolar I and bipolar II diagnostic criteria. The broad phenotype is what constitutes the majority of referrals to clinicians; those children who present with severe irritability, “affective storms,” mood lability, severe temper outbursts, and symptoms of depression, anxiety, hyperactivity, poor concentration, and impulsivity with or without clear episodicity (Pavuluri et al., 2005).

With the majority of referrals representing the broad phenotype, there is considerable disagreement about whether the DSM-IV-TR diagnostic criteria that were created for adults are applicable to the pediatric presentation of bipolar disorder. For example, most children presenting with symptoms of bipolar disorder do not meet the criteria of seven or four days for manic/hypomanic episodes. Indeed, a rapid cycling phenomenon has been documented (Geller et al., 2001). In one study of pediatric patients with DSM-IV bipolar disorder symptomatology, 83.3% of participants were identified as having “any rapid cycling,” defined as a) rapid: four or more episodes per year, b) ultra-rapid: episodes lasting a few days to a few weeks, or c)

ultradian: cycling within a 24-hour period. Given the preponderance of rapid cycling in youth with symptoms of bipolar disorder, most would not meet criteria for a diagnosis of Bipolar I or Bipolar II disorder. Additionally, it may be difficult for clinicians to apply the DSM-IV criteria to children, as they may be unaware of how elated mood, grandiosity, and other manic symptoms present in children. Geller's research (2002) has shown that several of the DSM-IV mania criteria also present in children, and she has given elaborate examples of how these diagnostic criteria present in children with bipolar disorder versus controls.

For the diagnostic criterion of elated mood, a normal child would be expected to be extremely giddy if their grandparents were visiting or they were going to Disney World. However, a child with bipolar disorder may be extremely giddy in a situation where no one else is, and may have to be removed from the situation. For the criterion of grandiose behaviors, a normal child may pretend to be a firefighter after school and direct the other children to put out the fire. However, an example of grandiosity in a child with bipolar disorder is a young girl who opened a paper flower store in class and was annoyed when the teacher asked her to do work, and then refused to do this work.

For the criterion of decreased need for sleep, normal children need 8-10 hours of sleep. If they are unable to get that amount of sleep, they are tired the next day. However, children with bipolar disorder need decreased sleep, but subsequently are not tired the next day. Age-appropriate sexual behaviors may include a young child playing "doctor." However, hypersexuality in pediatric bipolar disorder may result in calling 1-900 lines and soliciting sexual acts from others. Finally, normal children do not generally have racing thoughts. However, children with bipolar disorder describe their racing thoughts in very concrete terms, such as "too much stuff is in my head" (Geller et al., 2002).

Although recommendations have been made to change diagnostic criteria for bipolar disorder to more accurately fit the presentation of the disorder's symptoms in children, current practice parameters by the American Academy of Child and Adolescent Psychiatry (2007) require that DSM-IV-TR diagnostic criteria for mania and hypomania, including the duration criteria, be followed when making these diagnoses in children and adolescents. Additionally, they have stated that the diagnostic validity of the disorder has not yet been documented in young children, therefore caution should be taken when making this diagnosis with preschoolers.

Bipolar Disorder: Overlap with ADHD

One of the major difficulties in diagnosing pediatric bipolar disorder is the overlap between manic episode criteria and diagnostic criteria for other disorders seen in childhood. There is significant symptomatic overlap between mania and Attention-Deficit Hyperactivity Disorder (ADHD), which may complicate arriving at accurate diagnostic rates in children and adolescents (Moreno et al., 2007).

According to the DSM-IV, there are three subtypes of ADHD: the predominantly inattentive type, the predominantly hyperactive/impulsive type and the combined type. The inattentive type of ADHD is characterized by difficulty sustaining attention in tasks or play activities, forgetfulness, losing necessary things, making careless mistakes, difficulty organizing tasks and activities, being easily distracted, not listening, and failing to finish schoolwork, chores, or work duties. The hyperactive/impulsive type of ADHD is characterized by symptoms of hyperactivity (fidgeting, inability to remain seated, restlessness, excessive talking, difficulty engaging in quiet activities, and often being "on the go") as well as symptoms of impulsivity (blurting out answers, difficulty awaiting turn, and often interrupting/intruding on others). The combined type of ADHD is characterized by symptoms of both inattention and hyperactivity/impulsivity.

In order to establish a diagnosis of ADHD, the clinician must ensure that the child displays developmentally inappropriate levels of inattention and/or hyperactivity/impulsivity along with associated impairment that are observed across situations, that the onset of symptoms was before seven years of age, and that the symptoms have occurred apart from other mental disorders such as pervasive developmental disorder, schizophrenia, or psychotic disorder. To diagnose the predominately inattentive type of ADHD, six or more symptoms of inattention must have been present for at least six months. For the predominantly hyperactive/impulsive type of ADHD, six or more symptoms of hyperactivity/impulsivity must have been present. Finally, for a diagnosis of the combined type of ADHD, both six or more symptoms of inattentions and six or more symptoms of hyperactivity/impulsivity must have been present for at least six months. It is also the case that when an individual's symptoms do not meet the criteria for one of the subtypes of ADHD, and it is unclear whether these criteria have previously been met, a diagnosis of Attention-Deficit/Hyperactivity Disorder Not Otherwise Specified can be made.

Some of the symptomatic overlap between mania and ADHD include shared symptoms of distractibility, psychomotor agitation, and talkativeness. In addition to overlapping symptoms between these disorders, bipolar disorder is highly comorbid with ADHD. Indeed, 75-87% of children with bipolar disorder meet diagnostic criteria for ADHD (Tillman et al., 2003). However, there is significant debate over whether the high comorbidity rate between these two disorders is reflective of two separate disorders, or of the overlap in DSM-IV diagnostic criteria. Several studies have examined this issue, using methods to correct for the overlapping diagnostic criteria. Using the subtraction method to remove shared symptomatology, or the proportion method to remove shared symptomatology but require a modified proportion of symptoms, 48%-69% of children with mania continued to meet the mania criteria (Kim & Miklowitz, 2002).

Therefore, although there may be some cases where overlapping diagnostic criteria between the disorders causes incorrect diagnoses, there is also evidence that the two disorders frequently present together.

Bipolar Disorder: Overlap with Depression and ODD

In addition to the diagnostic overlap as it is complicated by the relationship between bipolar disorder and ADHD, several other disorders are important to consider in making a diagnosis of bipolar disorder. Given the fact that depressive symptoms are necessary for the diagnosis of bipolar II disorder and cyclothymia, and can be used to diagnose bipolar I disorder, it is imperative to carefully consider presenting symptoms in this light. Additionally, the depressive symptoms of irritability, insomnia, psychomotor agitation, and problems concentrating can mimic manic symptoms.

Finally, although oppositional defiant disorder (ODD) does not share specific diagnostic criteria with bipolar disorder, the explosive, volatile outbursts seen in some children with bipolar disorder may also reflect diagnostic criteria for ODD. Indeed, 46-79% of children with bipolar disorder also meet diagnostic criteria for ODD (Tillman et al., 2003). The high comorbidity rates and symptomatic overlap between bipolar disorder and these other disorders place additional concern on how pediatric bipolar disorder is being diagnosed.

Diagnostic Instruments and Screening Measures

Given the diagnostic complications and symptomatic overlap between bipolar disorder and other disorders, more research is turning to the development of diagnostic instruments for assessing pediatric bipolar disorder. Many measures are used to assist in the diagnosis of pediatric bipolar disorder, including structured and semi-structured interviews, parent-completed questionnaires, teacher-completed questionnaires, and child-completed questionnaires.

Structured and Semistructured Diagnostic Interviews

Structured interviews include the Diagnostic Interview for Children and Adolescents Revised (DICA-R; Reich & Welner, 1988) and the Diagnostic Interview Schedule for Children Version IV (DISC-IV; Shaffer, Fisher, & Lucas, 2000). Semistructured interviews include the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) and the Child and Adolescent Psychiatric Assessment (CAPA; Angold & Costello, 2000).

Given the debate about whether DSM-IV bipolar disorder diagnostic criteria are appropriate for children, the WASH-U-KSADS ((Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia; Geller, Zimmerman, & Williams, 2001) was developed. It was revised from the original K-SADS to expand the mania section to include more extensive areas to assess each manic symptom. There is also a section to document rapid cycling phenomenon (Geller, Zimmerman, & Williams, 2001). The WASH-U-KSADS has demonstrated high inter-rater reliability and six-month stability. Despite its usefulness, clinicians are turning to shorter forms to assist them in examining and screening for child/adolescent bipolar disorder, including parent-report, child/adolescent self-report, and clinician-report checklists.

Parent, Teacher, and Self-Report Rating Scales

The Mood Disorder Questionnaire (MDQ) was designed as a screening instrument for bipolar disorder, and was validated in an adult population. The wording was modified so the measure could be used with an adolescent population, but the parent version appears to outperform the adolescent version. The parent version of the Mood Disorder Questionnaire (P-MDQ) for adolescents contains 13 yes/no items reflective of a diagnosis of manic symptoms and bipolar disorder, and is administered to parents of adolescents between 12 and 17 years of age

(Wagner et al., 2006). It has demonstrated good internal consistency and discriminative validity (Youngstrom et al., 2006).

The General Behavior Inventory (GBI) is a 73-item self-report questionnaire that measures depressive, hypomanic, manic, and mixed mood symptoms used with respondents as young as age 11. It yields two scale scores; depressive and hypomanic/biphasic scales. The GBI has been shown to have good discriminative validity and excellent reliability. The Parent General Behavior Inventory (P-GBI) was adapted from the GBI so that parents can rate their children between the ages of 5 and 17. Given the lengthy nature of the P-GBI (73 items), Youngstrom et al (2008a) created the Parent General Behavior Inventory Short Form 10 (PGBI-SF-10). It contains 10 items and allows parents to rate the manic symptoms of children between ages 5 and 17. It was developed to preserve diagnostic efficiency while allowing a shorter completion time and easier reading level. Preliminary analyses have shown that the short form discriminates between cases with bipolar disorder, ADHD/disruptive behavior disorders, and unipolar depression. There is also a 28-item Adolescent General Behavior Inventory (AGBI). A teacher version was also developed from this scale (T-GBI), but research suggests it does not discriminate well between children with bipolar disorder and controls.

The Parent Young Mania Rating Scale (P-YMRS) is a parent-completed measure that contains 11 items used to assess the severity of mania in children and adolescents between ages 5 and 17 (Gracious et al., 2002). It was developed from the Young Mania Rating Scale (YMRS,) a similar 11-item measure which is completed by the clinician after interviewing the patient. Although the P-YMRS has demonstrated adequate internal consistency and discriminative validity, the YMRS appears to perform better. There is also a version of the YMRS that is self-report and completed by adolescents (A-YMRS). Additionally, a teacher version (T-YMRS) was

most recently developed from this scale. However, preliminary studies of the T-YMRS has not shown good discriminative validity for the measure between children with bipolar disorder and controls.

The Child Bipolar Questionnaire (CBQ) is a 65-item behavioral assessment tool that examines several different childhood psychiatric disorders in addition to bipolar disorder. The Core Index Subscale of the larger Child Bipolar Questionnaire contains 22 items identified as representing prominent symptom dimensions of pediatric bipolar disorder, including manic symptoms. Research has shown the subscale to demonstrate excellent reliability, and preliminary discriminative validity between children with bipolar disorder and those with ADHD only (Papalos et al., 2006).

The Child Mania Rating Scale (CMRS) is a parent-completed, 21-item-scale. Items reflect the DSM-IV criteria for a manic episode. Parents are instructed to endorse a problem only if it is causing problems and is beyond developmentally typical behavior. This scale is unique in that it was initially developed for children, rather than being modified from an existing rating scale for adults. Research has shown the scale to have excellent internal consistency and test-retest reliability, and adequate construct validity (Pavuluri et al., 2006). A teacher version of this scale (CMRS-T) was also recently developed, but does not discriminate well between controls and children with bipolar disorder.

Although research discusses the increasing rates of bipolar disorder in children and adolescents, issues in diagnosis appear related to the difficulty in identifying symptoms of mania in this population. Clinicians appear much more confident in their ability to identify depressive symptomatology in children and adolescents in comparison to their comfort in identifying mania in pediatric populations. Indeed, multiple rating scales have been developed to identify

depression in children and adolescents. However, given that mania is the core feature in bipolar disorder, research is focusing more on developing rating scales to specifically identify mania in children and adolescents, rather than developing scales to measure both mania and depression. Such measures as the PGBI-SF-10 and CBQ core index subscale reflect the emphasis of screening for these manic symptoms, as these rating scales were derived from much longer scales measuring mania, depression, and other comorbidities.

Although rating scales are not meant as final diagnostic instruments, they can serve as good screening instruments for cases for which further evaluation is necessary. However, given the number of mania rating scales that have been created in the past few years, it is helpful to know which measures best discriminate bipolar disorder from other disorders. Unfortunately, there have been few studies that have examined several mania rating scales together. One study compared six mania rating scales, including parent-completed measures and child/adolescent self-report measures (Youngstrom et al., 2005). The scales included in this study were the P-MDQ, adolescent self-report MDQ, the PGBI-SF-10, the A-GBI, the P-YMRS, and the A-YMRS, and they were administered to diverse samples in both academic and community mental health settings. Results indicated that the PGBI-SF-10, P-MDQ, and P-YMRS (in decreasing order of efficiency) significantly discriminated bipolar from non-bipolar cases. Additionally, the parent measures significantly outperformed the adolescent self-report measures, and the A-YMRS performed no better than chance. The three teacher-report mania rating scales, the T-GBI, T-YMRS, and CMRS-T, were administered together in a study with different clinical groups. However, teacher ratings on these scales could not discriminate children with bipolar disorder from children with ADHD or controls (Youngstrom et al., 2008b).

Despite the usefulness of this study, there were some important limitations which need to be addressed in future research. When examining the discriminative validity for the parent-report measures, the bipolar group was compared to a non-bipolar group which included children and adolescents with diagnoses of ADHD, depression, disruptive behavior disorders, and controls. Grouping these other children together makes it difficult to ascertain how these measures would discriminate between children with bipolar disorder only versus children with only ADHD. Additionally, it is questionable whether children with ADHD plus comorbidities would score differently on these measures. It is likely that a pure ADHD group and ADHD groups with other comorbidities (such as depressive symptomatology and ODD) would score higher on these measures. If this is indeed the case, this could decrease the utility of these measures as screening instruments in clinical settings where clinicians typically do not have large pediatric bipolar disorder populations with which to make comparisons. Additionally, the CBQ and CMRS have not been included in studies which compare multiple mania rating scales, and so research is needed to compare these measures to the three mania rating scales in the Youngstrom study.

Screening measures are extremely useful in settings where a quick, time-efficient instrument can highlight those children for whom further assessment is needed. Although these measures should not be used as final diagnostic instruments, it is important that they accurately reflect the construct being measured. Given the increasing rate of bipolar disorder diagnoses in children and adolescents, a disorder for which treatment may include powerful medications, understanding the accuracy of screening measures is imperative. Given the significant overlap and diagnostic confusions between mania and ADHD, and the high comorbidity rates between ADHD and other disorders, more research is needed on mania rating scales. Specifically, given

the research supporting the use of parent mania rating scales over scales from other informants such as children or teachers, research on parent rating scales is needed.

Therefore, the current study aims to fill this research void by examining the usefulness of parent-completed mania rating scales with 4 groups; controls, children with ADHD only, children with both ADHD and ODD, and children with both ADHD and depressive symptomatology. The five mania rating scales to be compared are the Parent Mood Disorder Questionnaire (P-MDQ), Parent Young Mania Rating Scale (P-YMRS), Child Bipolar Questionnaire (CBQ), Child Mania Rating Scale (CMRS) and Parent General Behavior Inventory Short Form 10 (PGBI-SF-10). These are the only parent-completed mania rating scales currently available to screen for mania symptoms in a pediatric population.

The first aim of this study was to compare these four groups on these five rating scales. It was hypothesized that all three ADHD groups would score higher on the mania rating scales than the control group. Additionally, it was hypothesized that both the ADHD with ODD group, and the ADHD with depressive symptomatology group, would demonstrate significantly higher scores on the mania rating scales than the ADHD only group. The second aim of this study was to compare the four groups' mean scores on the mania rating scales to previously published means for these scales in pediatric bipolar populations. Although it is likely that the published means for children with Bipolar Disorder would be higher than the means for any of the groups in the current study, it was hypothesized that they would not be significantly higher than the means for the ADHD groups with ODD and depressive symptomatology. The third aim of this study was to compare the relationship between degree of ADHD symptom severity for the three ADHD groups, and scores on the mania rating scales. It was hypothesized that higher scores on the mania rating scales would be correlated with more severe ADHD symptomatology.

Subsequent analyses of interest also involved determining the percentage of participants in each group that met cutoff criteria on each mania rating scale for probable bipolar disorder diagnoses. It was hypothesized that the ADHD with ODD and ADHD with depression groups would have a higher percentage of participants meeting cutoff criteria than the ADHD only group or controls.

CHAPTER 2 METHODS

Procedures

Approval to conduct the study was first obtained from the Institutional Review Board (IRB). Upon approval, parents of children with ADHD and clinical controls were recruited from several locations; the University of Florida Psychology Clinic, the ADHD Interdisciplinary Program, and the Lake City Project CATCh program. Additionally, fliers were posted in the Health Science Center and on community bulletin boards.

Parents recruited from the Psychology Clinic and the ADHD Interdisciplinary Program were being seen at the clinics for scheduled ADHD evaluations for their children based on referral to the clinic by physicians or parents. Parents recruited from the Project CATCh program in Lake City, Florida were attending regularly scheduled clinic sessions for their children. This is an extension clinic of the University of Florida Psychology Clinic. Parents of children with ADHD and controls at each of these locations were contacted by their therapist, physician, or psychologist to determine their interest in hearing about the research study. If they expressed interest in learning more about the research study, the principal investigator provided them with that information.

If a parent had more than one child that fit the study criteria, they were asked to select one child on which to make responses. They were informed about the confidentiality of their responses, as well as their ability to receive feedback about the results of the study upon its completion, if so desired.

Parents of children with ADHD who qualified for the study were given an informed consent, a demographic information sheet, and an ADHD screening measure (Conners' Parent Rating Scale- Revised: Long Form; CPRS-R:L). For the purposes of this study, the informed

consent incorporated permission from the parent to use data from their child's clinical assessment, where applicable, including the Conners' Parent Rating Scale and information related to diagnoses. The demographic sheet asked parents for general information (such as name, address, phone numbers, child's date of birth and gender, family income, and parental education level), as well as the child's diagnoses (if known).

After the parent completed the ADHD screening measure, the CPRS, the measure was scored to confirm that the child qualified for the study. The following indices of the CPRS-R:L were used; ADHD Index, DSM-IV Inattentive, and DSM-IV Hyperactive-Impulsive indices. In order to qualify for the study, T-scores of 65 or above must have been received on the ADHD Index plus the DSM-IV Inattentive and/or DSM-IV Hyperactive-Impulsive scales. Elevations on these indices provide strong evidence for ADHD. Even if a child had a prior diagnosis of ADHD, T-scores of 65 or above must have been received on the selected scales of the CPRS in order to qualify for the study.

If the child qualified for the study after scoring the CPRS-R:L, parents then completed the five pediatric mania screening measures (P-YMRS, P-MDQ, CBQ Core Index Subscale, CMRS, and P-GBI-SF10). Parents were advised of the repetitive nature of the questions and were encouraged to put forth equal effort on each rating scale. The measures were also collated in such a way to equally distribute potential response bias due to the repetitive nature of the questions. Finally, the parents were administered select portions of the Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS: Geller et al, 1998). Specifically, the mood disorders, Oppositional Defiant Disorder, and Attention-Deficit Hyperactivity Disorders sections were administered. Administration of these sections of the WASH-U-KSADS helped ensure children did not meet criteria for a bipolar spectrum

disorder, and that they did meet criteria for ADHD, with or without depressive symptomatology or oppositional defiant disorder. Parents of children with ADHD who completed all portions of the study were compensated 10 dollars for their participation.

Inter-rater reliability for diagnoses was established with 25% of the participants. The WASH-U-KSADS diagnostic interviews were taped for 25% of the participants. A graduate student who was trained to administer and score the diagnostic interview then scored the interviews. An interrater reliability analysis using the Kappa statistic was performed to determine consistency among raters for diagnoses. The interrater reliability for the raters was found to be $Kappa = 0.86$ ($p < 0.001$), which is considered an outstanding kappa level (Landis & Koch, 1977).

Parents of controls who qualified for the study were given an informed consent, a demographic information sheet, and the Parent Rating Scale of the Behavior Assessment System for Children- Second Edition (BASC-2 PRS, Reynolds & Kamphaus 2004). The BASC was then scored. T-scores above 60 on the Internalizing Problems, Externalizing Problems, and Behavioral Symptoms Indices, and their subscales, resulted in exclusion from the study. Once it was determined that parents qualified for the study, they were given the five pediatric mania screening measures to complete (P-YMRS, P-MDQ, CBQ Core Index Subscale, CMRS, and P-GBI-SF10). Parents of controls who completed all portions of the study were compensated five dollars for their participation.

Participants

This study recruited parents of children with ADHD only, ADHD plus depressive disorders, and ADHD plus oppositional defiant disorder, between the ages of 5 and 17. Additionally, this study recruited controls who did not meet criteria for a diagnosis of ADHD, ODD, or a mood disorder. Children could have any of the three ADHD subtypes; predominantly

inattentive type, predominantly hyperactive/impulsive type, or combined type. Three groups of children with ADHD were recruited; ADHD only, ADHD plus depressive symptomatology, or ADHD plus oppositional defiant disorder. Exclusionary criteria for the study included presence of bipolar disorder, pervasive developmental disorder or psychotic disorder for the ADHD groups, and presence of pervasive developmental disorder, psychotic disorder, ADHD, ODD, bipolar disorder, or depression in the control group.

Power analyses were initially conducted to assess the sample size needed to find significant effects in the current study. Data used were taken from the Youngstrom et al study (2005) as it was one of the few studies which provided means and standard deviation scores for multiple mania rating scales. Effect sizes ranged from .30 for the P-YMRS to .56 for the P-MDQ. Results of power analyses varied from a total sample of 40 participants to 128 depending on the rating scale. However, the average sample size needed at a power of .8 was 72. This suggested needing 18 participants in each of the four groups for the present investigation.

In order to qualify for a diagnosis of ADHD, children were required to meet the diagnostic criteria set forth by the DSM-IV. To determine diagnoses, parents first completed the Conners' Parent Rating Scale. In order to qualify for the study, T-scores of 65 or above must have been received on the ADHD Index plus the DSM-IV Inattentive and/or DSM-IV Hyperactive-Impulsive indices. Additionally, the principal investigator administered the ADHD portion of the WASH-U-KSADS to confirm the ADHD diagnosis. For the ADHD group with depressive symptomatology, children were included with research diagnoses of major depressive disorder, dysthymic disorder, or depressive disorder not otherwise specified. These diagnoses were determined from the mood disorders section of the WASH-U-KSADS. Finally, diagnoses of

oppositional defiant disorder were also determined through the corresponding section of the WASH-U-KSADS.

In order to qualify to be in the control group, parents completed the corresponding age-appropriate Parent Rating Scale of the Behavior Assessment System for Children- Second Edition (BASC-2 PRS, Reynolds & Kamphaus 2004). T-scores above 60 for the Internalizing Problems, Externalizing Problems, and Behavioral Symptoms Indices, and their subscales, resulted in exclusion from the study. Additionally, children were excluded from the control group if a parent reported a prior exclusionary diagnosis on the demographic form.

A sample of 80 subjects was initially recruited for the study. However, eight subjects who consented to the study were disqualified. Two potential control group subjects were disqualified based on high scores on the BASC, five parents of children with ADHD were disqualified due to low scores on the CPRS, and one parent was disqualified after administering the WASH-U-KSADS as their child met diagnostic criteria for bipolar disorder. A final sample of 72 participants was retained for the study.

The final sample consisted of 18 controls without evidence of psychopathology, 21 children with ADHD only, 18 children with ADHD plus ODD, and 15 children with ADHD plus depressive disorder. In the three ADHD clinical groups, two children had diagnoses of ADHD Inattentive-Type, one child had a diagnosis of ADHD Hyperactive-Impulsive Type, and the rest of the sample had diagnoses of ADHD Combined-Type. Of the 15 children in the ADHD plus depression group, three had diagnoses of major depressive disorder, one had a diagnosis of dysthymic disorder, and the other 11 children in this group had diagnoses of depression NOS. Ethnicity breakdowns in the sample consisted of 52 (72.2% of sample) Caucasian children, 14 African-American (19.4%) children, two Hispanic (2.8%) children, three Mixed-Ethnicity

(4.2%) children, and one American-Indian (1.4%) child. Table 2-1 contains a breakdown of gender and age demographic data for each of the four groups in the study.

Measures

The Conners Parent Rating Scale – Revised: Long Form (CPRS-R:L; Conners, 1997)

This measure contains 80 items and assesses behaviors related to hyperactivity, impulsivity, attention problems, oppositional behaviors, cognitive problems, anxiety problems and social problems. The directions request parents to consider the child's behavior during the past month, and responses are given on a Likert scale, ranging from 0, not at all true, to 3, very true. The ADHD Index is considered to be the most useful score for discriminating children with ADHD from a non-clinical sample (Conners, 1997), and DSM-IV Symptoms subscales (DSM-IV Inattentive Scale; DSM-IV Hyperactive-Impulsive Scale) correspond with the DSM-IV ADHD symptoms. Research has provided considerable psychometric support for the CPRS-R, including excellent internal consistency, high test-retest reliability, and good discriminative power between clinical and non-clinical children (Conners et al., 1998).

Behavior Assessment System for Children- Second Edition Parent Rating Scales (BASC-2 PRS; Reynolds & Kamphus, 2004)

The parent report version of the BASC yields ratings across externalizing behavioral domains, internalizing behavioral domains, additional clinical behavioral scales, as well as adaptive skills. Domains include subscales such as depression, anxiety, attention problems, hyperactivity, aggression, and conduct problems. The parent rating scales contain between 134 and 160 items depending on the child's age, and responses are given on a 4-choice response format. When scored, the BASC provides validity and response set indices. The BASC has demonstrated high internal consistency reliability, high test-retest reliability, and good inter-rater reliability (Reynolds & Kamphus, 2004).

The Child Bipolar Questionnaire (CBQ) Core Index Subscale (Papalos et al., 2006)

This subscale, part of the larger Child Bipolar Questionnaire, contains 22 items identified as representing prominent manic symptoms of pediatric bipolar disorder. Each of the items is rated on a 4-point likert scale. Research has shown the subscale to demonstrate excellent reliability, and preliminary discriminative validity between children with bipolar disorder and those with ADHD only. The score derived from the subscale is the number of 22 core symptoms and features rated "3" or "4." The Core Index score was found to distinguish between children with bipolar disorder and those with ADHD and no mood disorder. It has been noted that a score of 4 or higher is suggestive of bipolar disorder. As this is a relatively new scale, research is currently being collected to gain more psychometric support for the measure. Cronbach's coefficient alpha, a measure of the reliability and consistency of the scale, was calculated for each of the mania rating scales in the current study. Cronbach's coefficient alpha for the CBQ core index subscale, calculated from 72 completed measures, was .92, indicating good reliability for this measure.

The Child Mania Rating Scale (CMRS; Pavuluri et al., 2006):

This scale contains 21 items reflecting the DSM-IV criteria for a manic episode. Each item is answered on a 4 point likert-type scale. Parents are instructed to endorse a problem only if it is causing problems and is beyond developmentally typical behavior. Research has shown the scale to have excellent internal consistency and test-retest reliability, and adequate construct validity. A cut score of 20 on the scale resulted in specificity of .94 and sensitivity of .82 for differentiating bipolar disorder from ADHD and controls. Cronbach's coefficient alpha for the CMRS in the current study, calculated from 72 measures, was .90, also indicating good reliability.

The Parent Mood Disorder Questionnaire- Adolescent Version (P-MDQ; Wagner et al., 2006)

This scale contains 13 yes/no items reflective of manic symptoms, and is administered to parents of adolescents between 12 and 17 years of age. This scale also included a question asking whether several of the symptoms have occurred at the same time, and whether these symptoms caused a problem. Additionally, there is a checklist that asks whether blood relatives have experienced different types of psychopathology, as well as whether a health professional has ever diagnosed the person completing the questionnaire with bipolar disorder. It has demonstrated good internal consistency and discriminative validity (Youngstrom et al., 2006). Research has shown that a score of 5 or more items on the parent version resulted in a specificity of .81 and sensitivity of .72 (Wagner et al., 2006). Although this measure has been validated with adolescents, it was administered to children ages 5-17 in this study. Cronbach's coefficient alpha for the P-MDQ in the current study, calculated from 72 completed measures, was .84, which is considered good reliability.

Parent Young Mania Rating Scale (P-YMRS; Gracious et al., 2002)

This scale contains 11 items used to assess the severity of mania in children and adolescents between ages 5 and 17. Each of the items is rated on a 5-point scale; 7 of the items are scored from 0-4, while 4 of the items are given double weight and scored from 0-8, to weight them for their clinical importance and the likelihood of underreporting. The P-YMRS has demonstrated adequate internal consistency and discriminative validity (Youngstrom et al., 2005). Cronbach's coefficient alpha for the P-YMRS in the current study, calculated from 72 completed measures, was .79, which falls in the acceptable range for reliability.

Parent General Behavior Inventory Short Form 10 (P-GBI-SF-10; Youngstrom et al., 2008)

This scale contains 10 items and allows parents to rate the manic symptoms of children between ages 5 and 17. The P-GBI-SF-10 was developed from the 73-item Parent General Behavior Inventory, to preserve diagnostic efficiency while allowing a shorter completion time and easier reading level. Preliminary analyses have shown that the short form discriminates between cases with bipolar disorder, ADHD/disruptive behavior disorders, and unipolar depression. Scores between 5 and 9.9 resulted in a sensitivity of 94% and specificity of 54%, while scores between 10 and 14.9 resulted in a sensitivity of 78% and specificity of 78%. Cronbach's coefficient alpha for the P-GBI-SF-10 in the current study, calculated from 72 completed measures, was .92, indicating good reliability for this measure.

The Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia (WASH-U-KSADS; Geller et al., 1998)

This is a semi-structured, clinician administered interview that is used to yield DSM-IV diagnoses, and is the most widely-used instrument in studies of pediatric mania funded by the National Institute of Mental Health. The 1986 version of the KSADS was expanded and modified, to include expanded prepubertal mania and rapid cycling sections. The WASH-U-KSADS has demonstrated excellent reliability for mania symptoms, mood diagnoses, rapid cycling patterns, and time frames. Research has shown the mania and rapid cycling sections to have acceptable reliability (Geller et al., 2001).

Statistical Analyses

The first aim of this study was to compare the four participant groups on the five parent-completed mania measures. It was hypothesized that all three ADHD groups would score higher on the mania rating scales than the control group. Additionally, it was hypothesized that the ADHD with ODD and ADHD with depression groups would score higher on the mania rating

scales than the ADHD only group. In order to assess if any demographic variables had a systematic relationship with the independent variables or dependent variables, Pearson product-moment correlations were conducted. Demographic variables assessed were child age, gender, ethnicity, and family income. Family income was the only variable to demonstrate a significant relationship to any of the outcome measures or group status, and it demonstrated a significant relationship to all of the outcome measures and group status. Given the significant relationship between family income and both group status and the mania rating scales, MANCOVAs were initially conducted using family income as a covariate.

However, results for the MANCOVA demonstrated that family income did not have a significant impact on variability of outcome scores. As multiple families declined to report family income, reducing the sample size by nine subjects, a MANOVA was conducted without the covariate. Results were functionally equivalent to those where the covariate was included. ADHD subtype analyses could not be conducted as only three children with ADHD in the study did not have a diagnosis of ADHD Combined-Type. Post-hoc univariate ANOVAs with Bonferroni corrections were conducted to determine the direction of effects for the group differences.

The second aim of this study was to compare the four groups' mean scores on the mania rating scales to previously published means for these scales in pediatric bipolar populations. For the purposes of these analyses, means from the Youngstrom et al. 2005 study were used for the P-YMRS, P-MDQ, and P-GBI-SF10. The published mean and standard deviation for the CMRS were taken from the Pavuluri et al. 2006 study. Means for the CBQ were unavailable for this analysis. Although it was likely that the published means for children with bipolar disorder would be higher than the means for any of the groups in the current study, it was hypothesized

that they would not be significantly higher than the means for the ADHD groups with ODD and depressive symptomatology. For this aim, z-scores were calculated for the four groups' mean scores to compare to previously published means for these scales. Z-scores are significant at plus or minus 1.96 at the .05 significance level.

The final aim was to document the relationship between indices of ADHD symptom severity and scores on the mania rating scales. Symptom severity indices were obtained from the following scales on the Conners' Parent Rating Scale; the ADHD Index, the DSM-IV Inattentive subscale, and the DSM-IV Hyperactive-Impulsive subscale. These subscales were chosen as they relate directly to current ADHD criteria in the DSM-IV, have been previously shown to discriminate ADHD from other populations, and are psychometrically established subscales (Conners, 2000). It was hypothesized that there would be a significant positive correlation between indices of ADHD symptom severity and scores on the mania rating scales. It was presumed that characteristics of hyperactivity and impulsivity are more likely to overlap with mania symptoms in comparison with inattentive symptoms. Therefore, it was hypothesized that the DSM-IV Hyperactive-Impulsive subscale would be more positively correlated with scores on the mania rating scales, as the ADHD Index and DSM-IV Inattentive subscale reflect more inattentive symptoms. A Pearson's Product Moment Correlation was run for these analyses.

In addition to these three aims, subsequent analyses of interest involved determining the degree to which children in these groups meet common cutoff scores for bipolar disorders when using these measures. While not a direct aim, these analyses provide descriptive data regarding the bipolar measures in an ADHD population. Using published cutoff scores for the bipolar measures, percentages of the children in each of the three clinical groups and the control group were categorized as "Yes" or "No" as to whether they exceeded cutoff score criteria, providing

qualitative data about the measures in ADHD and control groups. Chi-squares were then used to compare percentages of those surpassing the cutoff between the three ADHD groups to see if one group was significantly more likely than another group to surpass cutoff scores on the different rating scales. Bonferroni corrections were applied in order to control the overall Type 1 error rate as multiple significance tests were conducted.

Table 2-1. Demographic Data

	n	M	SD
Child Age			
Controls	18	10.94	3.78
ADHD only	21	9.00	2.43
ADHD + ODD	18	8.5	2.38
ADHD + Depression	15	12.27	2.05
Child Gender			
Controls			
Boys	10		
Girls	8		
ADHD only			
Boys	14		
Girls	7		
ADHD + ODD			
Boys	12		
Girls	6		
ADHD + Depression			
Boys	8		
Girls	7		

CHAPTER 3 RESULTS

Comparison of Group Scores on Mania Rating Scales

To address the first aim, a MANOVA was conducted to determine whether the four groups differed in their scores on the mania rating scales. The overall MANOVA was significant, $F(15,177) = 7.15, p < .001$, indicating that there were significant differences between groups for these measures.

There were significant differences between groups on the CMRS, $F(1,68) = 29.15, p < .001$, power = 1.00. Follow-up univariate ANOVAs with Bonferroni corrections were performed. The ADHD + ODD group ($M = 27.33, SD = 1.79$) yielded significantly higher scores than the other three groups. The ADHD only group ($M = 17.19, SD = 1.66$) and ADHD + depression group ($M = 16.60, SD = 1.96$) did not differ significantly in their scores on this measure, but their scores were significantly higher than the control group ($M = 3.72, SD = 1.79$). Means, standard deviations, and p-values for all scales are available in tables 3-1 and 3-2.

There were also significant differences between groups on the PGBI-SF-10, $F(1,68) = 22.16, p < .001$, power = 1.00. Post-hoc univariate ANOVAs with Bonferroni corrections were performed. The ADHD + ODD group ($M = 13.67, SD = 5.19$) had significantly higher scores on this measure than the other three groups. The ADHD only group ($M = 6.0, SD = 5.76$) and the ADHD + depression group ($M = 8.0, SD = 5.69$) did not differ significantly in their scores on this measure, but were significant higher than the control group's scores ($M = 0.67, SD = 1.03$).

There were significant differences between the four groups on the P-MDQ, $F(1,68) = 14.05, p < .001$, power = 1.00. Post-hoc univariate ANOVAs revealed that the control group's scores ($M = 1.78, SD = 2.29$) on the MDQ were significantly lower than the other three groups. However, the ADHD only group ($M = 6.00, SD = 2.76$), ADHD + ODD group ($M = 7.28, SD =$

2.44) and ADHD + depression group ($M = 5.47, SD = 3.23$) did not differ significantly from each other in their scores.

There were significant differences between the four groups on their scores on the P-YMRS, $F(1,68) = 21.09, p < .001, power = 1.00$. Post-hoc univariate ANOVAs with Bonferroni corrections were conducted to determine the direction of the effects. Analyses revealed that the ADHD + ODD group ($M = 19.83, SD = 8.64$) had significantly higher scores than the other three groups. The ADHD only group ($M = 8.26, SD = 5.76$) and the ADHD + depression group ($M = 11.67, SD = 8.80$) did not significantly differ in their scores on the YMRS, but were significantly higher than the control group's scores ($M = 2.11, SD = 3.05$).

Finally, there were significant differences between the four groups on the CBQ core index subscale, $F(1,68) = 26.45, p < .001, power = 1.00$. Post-hoc univariate ANOVAs with Bonferroni corrections revealed that the ADHD + ODD group ($M = 10.22, SD = 3.828$) had significantly higher scores on the measure than the other three groups. Although there were no significant differences in scores between the ADHD only group ($M = 5.90, SD = 4.27$) and the ADHD + Depression group ($M = 6.33, SD = 3.31$), both of these groups had significantly higher scores on this measure than the control group ($M = 0.28, SD = 0.67$).

Comparison of Group Scores to Previously Published Means for Bipolar Disorder

To address the second aim and compare the four groups' mean scores on the mania rating scales to previously published means for children with bipolar disorder on the same scales, z-scores were calculated. Tables 3-3 lists these z-scores. Table 3-4 lists the previously published means and standard deviations for each measure for children with bipolar disorder. For the control group, published means for bipolar disorder were significantly higher for the CMRS and PGBI-SF-10, and approached significance (z-score = 1.87, $p = .062$) for the P-MDQ. For the ADHD-only group (z-score = 1.95, $p = .051$) and the ADHD with depression group (z-score =

1.70, $p = .089$), published means for bipolar disorder also approached significance for the PGBI-SF-10. For the ADHD-only and ADHD with depression groups, none of the others scales' scores were close to being significantly different from scores of children with Bipolar Disorder.

Additionally, the ADHD + ADD group's scores did not significantly differ from the published means for bipolar disorder on any of the scales. In sum, there were no significant differences between the previously published means for children with bipolar disorder, and the ADHD with ODD or ADHD with depression groups on any of the mania rating scales.

Relationship of Group Scores on Mania Rating Scales to ADHD Symptomatology

In order to address the third aim and examine the relationship between ADHD symptom severity indices and the five mania rating scales, Pearson Product-Moment Correlation coefficients were calculated. Scores on the PMDQ ($r = .279$, $p < .05$) correlated positively with the ADHD Index subscale. None of the other mania rating scales were significantly correlated with the ADHD Index subscale or the DSM-IV Inattentive subscale. However, the P-MDQ ($r = .331$, $p < .05$), CMRS ($r = .357$, $p < .01$), and CBQ ($r = .367$, $p < .01$) were positively correlated with the DSM-IV Hyperactive-Impulsive subscale. Additionally, each of the mania rating scales were positively correlated with each other, with correlation coefficients ranging from .462 to .803, $p < .001$. Table 3-5 lists the bivariate correlation coefficients and their associated p-values.

Participants Meeting Established Cutoff Criteria for Bipolar Disorder

Established cutoff scores for suggested bipolar disorder diagnoses were available for each of the measures. For the PGBI-SF-10, two separate cut scores, five and ten, were used in analyses, as these were both published in the literature. Table 3-6 lists the number and percentage of participants in each group meeting cutoff criteria for probable bipolar disorder diagnoses. Additionally, chi-squares were conducted to compare the three clinical groups on their percentages of meeting published cutoff scores for probable bipolar disorder diagnoses.

Bonferroni corrections were made on subtests within each measure such that the criterion for significance changed from .05 to .017.

For the CMRS at a cut score of 20, there was a significant association between group status and cutoff score status, $\chi^2(2) = 17.96, p < .001$. The ADHD + ODD (83.3%) group had a significantly higher percentage of participants meeting cutoff score criteria than the ADHD with Depression (13.3%) group ($\chi^2(1) = 16.05, p < .001$) and the ADHD only (33.3%) group ($\chi^2(1) = 9.85, p < .001$). There was no significant difference between the ADHD only and ADHD with Depression groups in percentages of cases meeting cutoff criteria, $\chi^2(1) = 1.87, p = .172$

For the PGBI-SF-10 at a cut score of 5, there was a significant association between group status and cutoff score status, $\chi^2(2) = 9.33, p = .009$. The ADHD + ODD (88.9%) group had a significantly higher percentage of participants meeting cutoff score criteria than the ADHD only (52.4%) group, $\chi^2(1) = 6.06, p = .014$. However, there were no significant differences between the ADHD + ODD and ADHD + Depression (66.7%) groups in percentages of cases meeting cutoff criteria, $\chi^2(1) = 2.42, p = .12$, or between the ADHD + Depression and ADHD only groups, $\chi^2(1) = 2.42, p = .12$.

For the PGBI-SF-10 at a cut score of 10, there was also a significant association between group status and cutoff score status, $\chi^2(2) = 17.25, p < .001$. The ADHD + ODD (88.9%) group had a significantly higher percentage of participants meeting cutoff score criteria than the ADHD only group (23.8%), $\chi^2(1) = 16.52, p < .001$. The ADHD + ODD group also had a significantly higher percentage of participants meeting cutoff score criteria than the ADHD + Depression (40%) group, $\chi^2(1) = 8.80, p = .003$. There were no significant differences between the ADHD only and ADHD + Depression groups in percentages of cases meeting cutoff criteria, $\chi^2(1) = 1.08, p = .298$.

For the P-MDQ at a cut score of 5, the overall model was not significant, $\chi^2(2) = 3.74, p = .154$. This indicates that there were not significant differences between the three clinical groups on percentage of participants meeting cutoff score criteria. For the CBQ core index subscale at a cut score of 4, the model was also not significant, indicating that there were no significant differences between the three clinical groups on percentage of participants meeting cutoff score criteria on this measure, $\chi^2(2) = 4.61, p = .10$.

For the P-YMRS at a cut score of 17, there was a significant association between group status and cutoff score status, $\chi^2(2) = 13.65, p = .001$. There was a significantly larger percentage of participants in the ADHD + ODD (66.7%) group meeting cutoff score criteria than the ADHD only (9.5%) group, $\chi^2(1) = 13.75, p = .001$. However, there was no significant difference between the ADHD + ODD and ADHD + Depression (40%) groups on percentage of participants meeting cutoff criteria, $\chi^2(1) = 2.35, p = .13$. Additionally, there was no significant difference between the ADHD + Depression and ADHD only groups on percentage of participants meeting cutoff criteria, $\chi^2(1) = 4.70, p = .03$.

Table 3-1. Comparison of Mean Scores between Groups on Mania Rating Scales

	Controls		ADHD only		ADHD + ODD		ADHD + Depression	
	M	SD	M	SD	M	SD	M	SD
CMRS	3.72	1.79	17.19	1.66	27.33	1.79	16.60	1.96
PGBI-SF-10	0.67	1.03	6.00	5.76	13.67	5.19	8.00	5.69
P-MDQ	1.78	2.29	6.00	2.76	7.28	2.44	5.47	3.23
P-YMRS	2.11	3.05	8.29	5.76	19.83	8.64	11.67	8.80
CBQ	0.28	0.67	5.90	4.27	10.22	3.83	6.33	3.31

Table 3-2. P-Values for Comparison of Mean Scores between Groups on Mania Rating Scales

	Controls		ADHD Only		ADHD + ODD	
CMRS	ADHD		p < .001*			
	ADHD + ODD		p < .001*	p = .001*		
	ADHD + Depression		p < .001*	p = 1.00	p = .001*	
PGBI-SF-10	ADHD		p = .006*			
	ADHD + ODD		p < .001*	p < .001*		
	ADHD + Depression		p < .001*	p = 1.00	p = .008*	
P-MDQ	ADHD		p < .001*			
	ADHD + ODD		p < .001*	p < .001*		
	ADHD + Depression		p = .001*	p = .889	p < .006*	
P-YMRS	ADHD		p = .039*			
	ADHD + ODD		p < .001*	p < .001*		
	ADHD + Depression		p = .001*	p = .889	p = .006*	
CBQ	ADHD		p < .001*			
	ADHD + ODD		p < .001*	p < .001*		
	ADHD + Depression		p < .001*	p = 1.00	p = .009*	

Table 3-3. Comparison of Group Means for the Mania Rating Scales to Previously Published Means for Bipolar Disorder via Z-Scores

	Controls	ADHD only	ADHD + ODD	ADHD + Depression
CMRS	4.58*	1.29	-1.18	1.44
PGBI-SF-10	2.60*	1.95	1.01	1.70
P-MDQ	1.87	0.63	0.26	0.79
P-YMRS	1.54	0.82	-0.51	0.43

* p < .05 level

Table 3-4. Previously Published Means and Standard Deviations for Children with Bipolar Disorder on Mania Rating Scales

	M	SD
CMRS	22.5	4.1
PGBI-SF-10	21.95	8.20
P-MDQ	8.17	3.42
P-YMRS	15.40	8.64

Table 3-5. Correlations between Symptom Severity Ratings as Indexed by the Conners' Parent Rating Scale (CPRS) and Mania Rating Scales

	ADHD Index	DSM-IV Inattentive	DSM-IV Hyperactive-Impulsive
CMRS	.26	.18	.36*
PGBI-SF-10	.12	.05	.19
P-MDQ	.28*	.23	.33*
P-YMRS	.07	.03	.09
CBQ	.24	.14	.37*

* $p < .05$ level

Table 3-6. Participants Meeting Published Cutoff Scores on Mania Rating Scales

		Yes (Percent)	No (Percent)
CMRS cut score 20	Controls	0 (0%)	18 (100%)
	ADHD only	7 (33.3%)	14 (66.7%)
	ADHD + ODD	15 (83.3%)	3 (16.7%)
	ADHD + Depression	2 (13.3%)	13 (86.7%)
PGBI-SF-10 cut score 5	Controls	0 (0%)	18 (100%)
	ADHD only	11 (52.4%)	10 (47.6%)
	ADHD + ODD	16 (88.9%)	2 (11.1%)
	ADHD + Depression	10 (66.7%)	5 (33.3%)
PGBI-SF-10 cut score 10	Controls	0 (0%)	18 (100%)
	ADHD only	5 (23.8%)	16 (76.2%)
	ADHD + ODD	16 (88.9%)	2 (11.1%)
	ADHD + Depression	6 (40%)	9 (60%)
P-MDQ cut score 5	Controls	2 (11.1%)	16 (88.9%)
	ADHD only	16 (76.2%)	5 (23.8%)
	ADHD + ODD	16 (88.9%)	2 (11.1%)
	ADHD + Depression	9 (40%)	6 (60%)
P-YMRS cut score 17	Controls	0 (0%)	18 (100%)
	ADHD only	2 (9.5%)	19 (90.5%)
	ADHD + ODD	12 (66.7%)	6 (33.3%)
	ADHD + Depression	6 (40%)	9 (60%)
CBQ cut score 4	Controls	0 (0%)	18 (100%)
	ADHD only	14 (66.7%)	7 (33.3%)
	ADHD + ODD	17 (94.4%)	1 (5.6%)
	ADHD + Depression	12 (80%)	3 (20%)

CHAPTER 4 DISCUSSION

During recent years increasing attention has been given to bipolar disorder in children and adolescents. As existing diagnostic criteria have focused on symptoms displayed by adults, it is perhaps not surprising that controversy has ensued regarding the prevalence of the disorder in children, particularly in regards to the disorder being described as being both over and under diagnosed. Current evidence that the diagnosis of childhood bipolar disorder has increased significantly in the past decade (Youngstrom et al., 2006; Moreno et al., 2007) has raised important questions regarding the degree to which this increase may relate to diagnostic criteria overlap between the dominant manic symptoms of bipolar disorder and other disorders such as ADHD and commonly occurring comorbid conditions.

Here, the symptom overlap between mania and ADHD include symptoms such as distractibility, talkativeness, and psychomotor agitation. Additionally, there are high comorbidity rates between bipolar disorder and ADHD: research suggests that 75-87% of children with bipolar disorder also meet diagnostic criteria for ADHD (Tillman et al., 2003). Other disorders, including depression and oppositional defiant disorder, are also important to consider in making a diagnosis of bipolar disorder. Some depressive symptoms can mimic symptoms of mania, including irritability, insomnia, psychomotor agitation, and problems concentrating. Although ODD does not share specific diagnostic criteria with bipolar disorder, the explosive, aggressive outbursts seen in some children with bipolar disorder may reflect diagnostic criteria for ODD. Also, 46-79% of children with mania meet diagnostic criteria for ODD (Tillman et al., 2003).

With the increasing diagnostic rates of bipolar disorder in children and adolescents, more and more emphasis is being placed on the development and clinical utility of rating scales to examine symptoms of mania in children and adolescents. Rating scales can be quick, informative

screeners, but should not be strictly used as diagnostic instruments. Parent-report, child-report, and teacher-report measures have been examined with bipolar disorder populations, with parent-report measures typically outperforming child-report and teacher-report measures. Parent-report measures appear to be able to accurately discriminate bipolar disorder cases from controls. Some measures have also been shown to discriminate between children with bipolar disorder and children with ADHD. However, none of the mania rating scales have been administered to ADHD groups with comorbid conditions, including ODD and depression, and no investigation has studied all five of these current parent-report mania rating scales together.

Given the significantly higher rates of bipolar disorder in children and adolescents, the increased use of rating scales to screen for pediatric bipolar disorder, along with the possible overlap between mania, ADHD, and commonly occurring comorbidities, the present study sought to examine five parent-report mania rating scales with different ADHD populations. The five mania rating scales used in this study were the Child Mania Rating Scale (CMRS), Parent General Behavior Inventory Short Form 10 (PGBI-SF-10), Parent Mood Disorder Questionnaire (P-MDQ), Parent Young Mania Rating Scale (P-YMRS), and the Child Bipolar Questionnaire (CBQ) core index subscale. The study groups on which the rating scales were compared included children with ADHD only, children with both ADHD and ODD, children with both ADHD and depression, and controls. This study attempted to examine the clinical utility of these parent-report mania rating scales in clinical populations where ADHD with comorbidities are common.

The first aim of this study was to compare the four study groups on their scores on each of the five mania rating scales in order to examine whether children with ADHD and ODD or ADHD and Depression scored higher on these rating scales than either the ADHD only group or controls. Results indicate that the ADHD with ODD group scored higher than all other groups on

all scales except for the P-MDQ. Here, there was no difference between this group and the ADHD-only or ADHD with depression group. There was no significant difference between scores of the ADHD-only and the ADHD with depression groups on any of the scales. However, the control group was significantly lower than all three ADHD groups on all scales.

The second aim of the study was to compare the four study groups' mean scores with previously published means for children with bipolar disorder on the five mania rating scales. Here the scores of the control group were found to be significantly lower than bipolar group means on two of the four scales (PGBI-SF-10, CMRS) for which published bipolar disorder means were available. Group differences on one other scale (P-MDQ) for the control group approached significance. For the ADHD-only group, no scales were significantly lower than bipolar disorder means. Likewise, the mean scores for the ADHD with ODD and ADHD with depression groups were not found to be significantly different from bipolar disorder means. Only for the PGBI-SF-10 did the ADHD only and ADHD with depression groups approach statistical significance for differences between these groups and children with bipolar disorder.

The third aim of the study was to document the relationship between various ADHD symptom severity scores of the Conners Parent Rating Scale and scores on the five mania rating scales. It was hypothesized that scores on the DSM IV Hyperactive-Impulsive scale would be significantly and positively correlated with mania rating indices. Indeed, significant positive correlations were found between scores on the DSM-IV Hyperactive-Impulsive subscale and scores on the P-MDQ, CMRS, and CBQ scales. Only the P-MDQ was positively correlated with the ADHD Index, and no scales were correlated with the DSM-IV Inattentive subscale. Given that the ADHD Index and DSM-IV Inattentive subscale mainly reflect symptoms of inattention, it makes sense that the mania rating scales were more positively correlated with a subscale

reflecting symptoms of hyperactivity and impulsivity, as these features seem to overlap more with mania symptoms.

Lastly, this study sought to examine the percentages of cases in each group that met established cutoff criteria for probable bipolar disorder diagnoses. Surprisingly, a large proportion of participants in the ADHD + ODD group met established cutoff criteria for the mania rating scales, ranging from 66.7% to 94.4% for the scales. There were less participants who met cutoff score criteria for the ADHD only (23.8% to 76.2%) and the ADHD with depression groups (13.3% to 80%). The CBQ had the most participants meeting cutoff criteria for the three ADHD groups, as 43 out of 54 participants (79.6%) met cutoff criteria. The P-MDQ had the second highest number of participants in the three ADHD groups meeting cutoff criteria (n = 41, 75.9%). The P-YMRS had the least number of participants in the ADHD groups meeting cutoff criteria, 20 out of 54 participants (37%). Only one of the scales, the P-MDQ, had any participants in the control group (n = 2) meeting cutoff criteria.

Current published literature on the five mania rating scales has suggested that these measures discriminate well between children with bipolar disorder and controls. The current study supports the literature in this respect, as controls do appear to score significantly lower on the mania rating scales compared to published means for children with bipolar disorder.

Additionally, controls scored lower than the three ADHD groups in the present study.

Previous research for the CBQ and PGBI-SF-10 demonstrated that these scales differentiated between children with ADHD and children with bipolar disorder (Papolos et al., 2006; Youngstrom et al., 2008a). Although this analysis could not be performed for the CBQ because published bipolar disorder means were not available for the measure, results for the PGBI-SF-10 in the current study do suggest that the difference between children with ADHD

and children with bipolar disorder on this scale approaches significance. Published research on the CMRS, P-MDQ, and P-YMRS had not yet examined the clinical presentation of children with ADHD on these scales. Additionally, the clinical presentation of children with ADHD with ODD and ADHD with depression had not been examined on any of the five mania rating scales.

The present study suggests that when children have comorbid diagnoses of ADHD and ODD, their scores on the PGBI-SF-10 and the other mania rating scales are not significantly different than scores for children with bipolar disorder. The present study was the first study to examine the mania rating scales with children with ADHD and depression, thus providing research to suggest that the addition of depression to ADHD symptomatology does not increase scores on these scales.

While the current study provides important information about these parent-report mania rating scales, it is important to address certain limitations of the current study. Although the study has yielded significant findings with good power, replication of the study with a larger sample size is important. For example, a larger sample size with multiple participants within each of the ADHD subtypes (Combined, Hyperactive-Impulsive, Predominately Inattentive) would allow analysis of the mania rating scales as a function of subtype. Also, the current study's ADHD with depression group included children with major depressive disorder, dysthymia, and depression not otherwise specified. There were not enough participants in this group to allow analysis of specific depression diagnoses. Replicating this study with a larger sample size in the ADHD with depression group, with enough participants with the three depression diagnoses, will be important in order to examine the mania rating scales with the different depression diagnoses in conjunction with ADHD.

A larger sample size would also allow analyses by age groups, in order to examine whether there are significant differences on scores on the mania rating scales by age. A replication study would also be useful in order to determine whether the study results are similar in other clinical settings. An additional limitation of this study was that the principal investigator administered the WASH-U-KSADS and made diagnostic decisions for the study. Although good inter-rater reliability was established with an independent clinician, in a larger replication study other researchers should conduct the diagnostic interviews in order to reduce the chance of any bias by the principal investigators.

To summarize the findings of the current study, it appears that children with both ADHD and ODD tend to score much higher on mania rating scales than children with ADHD only or ADHD with depression. There was almost no difference between published means for bipolar disorder and means for the three ADHD groups in the current study. This suggests that these scales may not discriminate very well between children with bipolar disorder and children with ADHD, particularly ADHD with ODD. Additionally, a significant proportion of participants, especially children with both ADHD and ODD, met established cutoff criteria for probable bipolar disorder diagnoses.

There did not appear to be a significant difference between children with ADHD only and ADHD with depression on their scores on the mania rating scales. While it was hypothesized that children with ADHD and depression would score higher than the ADHD only group, it appears that depressive symptoms do not mimic mania, although there may be some symptom overlap (e.g., irritable mood). There was not a single mania rating scale that appeared to outperform the others on these aims. Controls did not score high on any of the mania rating scales, suggesting

that these measures do discriminate well between children with bipolar disorder and controls without any psychological disorders.

Finally, when examining ADHD symptomatology, severity of hyperactive-impulsive symptoms seems to be positively correlated with scores on the mania rating scales. Although there were not enough participants with different subtypes of ADHD for analyses, further research in this area should be conducted. It will be important to understand what profile type of ADHD is more likely to mimic mania in order to help accurately differentiate this condition from bipolar disorder.

Results of the current study suggest that using these parent-report mania rating scales could lead to potentially making a wrongful diagnosis of bipolar disorder, especially in clinical settings where children with both ADHD and ODD are frequently seen. Children with ADHD and ODD appear to frequently meet established cutoff criteria for probable bipolar disorder diagnoses on these measures, score significantly higher on these measures than children with ADHD only or ADHD with depression, and their scores on the rating scales do not appear to be significantly different from published mean scores for children with bipolar disorder. Therefore, these scales should be cautiously used as screeners only to identify individuals for whom further assessment of bipolar disorder is warranted, such as through structured and semi-structured interviews. Using these scales as diagnostic instruments may lead to misdiagnosis and possibly erroneously medicating children with aggressive pharmacotherapy, which can have potentially dangerous consequences.

Additionally, clinicians should keep in mind that the profile of children with ADHD and ODD appears to mimic mania on these rating scales, and should use this information to make appropriate diagnoses. Indeed, epidemiological research suggests there are lower prevalence

rates of pediatric bipolar disorder in countries such as the United Kingdom, Ireland, Denmark, and Germany. When examining why there are significant differences in prevalence rates between these countries and the United States, research suggests that children presenting with aggression, inattention, and mood problems are often given severe disruptive behavior disorder diagnoses in these countries. However, children presenting with these same symptoms are often diagnosed with bipolar disorder in the United States (Soutullo et al., 2005; Holtmann et al., 2008).

Given the concerns that bipolar disorder in children and adolescents is being over-diagnosed, along with the results of the current study that demonstrate that children with both ADHD and ODD score very high on these mania rating scales, future research should continue in several areas. Research should focus on the development of more age-appropriate diagnostic guidelines for bipolar disorder in children and adolescents, with a consideration for how the presentation of ADHD with disruptive behavior disorders mimics mania. This could lead to a reduction in the over-diagnosis and misdiagnosis of bipolar disorder in children and adolescents. Given that the DSM-IV provides little information about the presentation of the disorder in children and young children, particularly in regards to symptom overlap between bipolar disorder and severe disruptive behavior disorders, development of these guidelines is crucial.

Additionally, further research on these mania rating scales should be continued. Administration of these rating scales to large samples of children and adolescents with bipolar disorder, and children with both ADHD and ODD, could allow symptom and item-level analyses to determine which symptoms and items on the mania rating scales best discriminate between the two groups. Such analyses could lead to construction of a new mania rating scale that adequately discriminates between pediatric bipolar disorder and severe disruptive behavior disorders. Such a

measure could provide more clinical utility than currently existing mania rating scales and could help reduce the over-diagnosis of the disorder that may be occurring.

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BIOGRAPHICAL SKETCH

Katherine Elizabeth Kiker was born in 1983 in Charlotte, North Carolina. She has since lived most of her life in Gainesville, Florida, with her mother and father. She graduated from the International Baccalaureate Program at Eastside High School in 2001, and proceeded to earn her Bachelor of Science in Psychology and Bachelor of Arts in Spanish in December 2004 from the University of Florida. In August 2005, Katherine entered the Doctoral Program in Clinical and Health Psychology at the University of Florida, and earned her Master of Science in psychology in May 2007.