The Impact of Comorbid Anxiety on Treatment Outcome of a Family-Based Psychoeducational Psychotherapy Program for Children With Mood Disorders

Dissertation

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Abstract

Comorbid conditions are the rule for children with mood disorders, and they pose complications when evaluating treatment studies. Comorbid anxiety disorders, in particular, have been found to predict an earlier age of onset and more hospitalizations in youth with bipolar disorder (Dickstein et al., 2005) and higher depression index scores in youth with depression (Rohde, Clarke, Lewinsohn, Seeley, & Kaufman, 2001). These studies suggest mood disorders with comorbid anxiety may represent a more severe form of illness than mood disorders alone. Few controlled trials have examined the comorbidity of anxiety disorders in children with mood disorders (Kendall, Kortlander, Chansky, & Brady, 1992), particularly pediatric bipolar disorder (Dickstein et al., 2005). Even fewer studies have examined the differential impact of treatment on children with mood and anxiety disorders. Family-based psychoeducational psychotherapy is one psychosocial intervention investigated for children with mood disorders. One goal of psychoeducational psychotherapy is to help parents become better advocates for their children, selecting more appropriate treatments to help manage mood disorders and comorbidities.

Multifamily Psychoeducational Psychotherapy (MF-PEP) groups are an eight-session, manual-driven treatment for children with mood disorders designed
as an adjunct to current medications and psychotherapy. 165 children with mood disorders, age 8-11, participated. Approximately 70% of participants were diagnosed with bipolar spectrum disorders (BPD), 30% with depressive spectrum disorders. Most had both comorbid behavioral (97%) and anxiety (69%) disorders. Assessments were conducted four times: at baseline, 6, 12, and 18 months. Approximately half \( n=78 \) were randomized into immediate treatment and half \( n=87 \) into a one-year wait-list condition. All were encouraged to continue treatment-as-usual.

The first objective was to examine the prevalence of comorbid anxiety disorders among MF-PEP participants. There were a mean number of 1.4 anxiety disorders per child. There were no differences in the number or prevalence of anxiety disorders between patients with BPD versus patients with depressive disorders. The two most common comorbid anxiety disorders were specific phobia and GAD.

Analyses were conducted at both the diagnostic and symptom level. At baseline, participants with comorbid anxiety disorders (+ANX) had higher levels of depressive symptom severity, but showed no difference in manic symptom severity, global functioning, and suicidality on either parent or child report compared to participants without comorbid anxiety disorders (-ANX). Higher levels of anxiety symptomatology were associated with greater functional
impairment and greater depressive symptom severity at baseline, but no difference in manic symptom severity.

MF-PEP did not lead to a significant reduction in anxiety symptoms post-treatment. +ANX showed similar improvement to –ANX as a result of MF-PEP on both parent and child-reported depressive and manic symptom severity ratings and overall functioning. Anxiety symptomatology did not have an effect on improvement in manic or depressive symptom severity as a result of MF-PEP. Children with higher anxiety symptomatology showed greater improvement in global functioning scores as a result of MF-PEP, perhaps due to their lower global functioning scores at baseline. Clinical implications and directions for future research are discussed.
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Chapter 1: Introduction

Mood disorders in childhood are associated with significant morbidity, mortality, distress and impairment. Post and Kowatch (2006) suggested that controversies surrounding the diagnosis of childhood-onset bipolar disorder, in particular, can be harmful for the treatment of these children. “An egregiously large number of the children with manic and depressive symptoms associated with moderate-to-severe-dysfunction were neither diagnosed nor treated for 10 to 15 years,” most likely resulting in “extremely adverse circumstances” (Post & Kowatch, 2006, p. 116). Regarding major depressive disorder (MDD), Ginsburg, Albano, Findling, Kratochvil, and Walkup (2005) stated positively that although it remains a “common, recurrent, and impairing disorder” in children and adolescents, “during the past 30 years, the field has progressed from debating about the very existence of pediatric depression to the development and implementation of effective psychotherapies and pharmacotherapies to treat the disorder in youth” (p. 252).

Further complicating research and treatment of childhood mood disorders are comorbid conditions, which are the rule, not the exception, for children with mood disorders. Comorbidity refers to the presence of two or more distinct, co-occurring disorders in one patient (Klein & Riso, 1993), first introduced to the medical literature by Feinstein in 1970. Individuals with more than one diagnosis
were found to be more likely than single diagnosis individuals to use mental health services and report more suicide attempts, periods of disability, greater life dissatisfaction, less job satisfaction, and less social stability (Newman, Moffitt, Caspi, & Silva, 1998). They also were less likely to attend college and had more physical health problems (Newman et al., 1998). Belzer and Schneier (2004) describe comorbidity as “largely the product of a nosological system that classifies mental disorders categorically, presupposing discrete diagnostic entities or disease states” (p. 297). Dimensional approaches may be more accurate in describing disorders that frequently co-occur. Nonetheless, “regardless of how co-occurring symptom complexes are described, clinicians and researchers must continue to grapple with the challenges involved in assessing and treating patients with complex combinations of symptoms” (Belzer and Schneier, 2004, p. 297).

In 1999, Angold, Costello, and Erkanli observed that research on comorbidity in children and adolescents had shown dramatic increases. A recent PubMed search of the phrase, “psychiatric comorbidity in children and adolescents” revealed 1058 articles published between 2003 to 2008, compared to just 656 articles published between 1998 to 2003, so research on the topic appears to continue to increase. Comorbid anxiety disorders, the focus of this dissertation, are found to be particularly common in children with mood disorders. Research studies have found wide ranges, suggesting comorbid anxiety disorders occur in rates of 20% to 75% in children with depression (Avenevoli, Stolar, Li, Dierker, & Merikangas, 2001) and 10% (Moreno et al., 2007) to 70% (Wilens et al., 2003) in
children with bipolar disorder. Further, comorbid anxiety disorders can worsen the course and prognosis of bipolar disorder (Dickstein et al., 2005) and depression (Rohde, Clarke, Lewinsohn, Seeley, & Kaufman, 2001), and frequently complicate treatment (Young, Mufson, & Davies, 2006). These studies suggest mood disorders with comorbid anxiety may represent a more severe form of illness than mood disorders alone.

Despite recent increases in research attention to comorbidity in children and adolescents, more research is needed on the comorbidity of anxiety disorders in children with mood disorders (Kendall, Kortlander, Chansky, & Brady, 1992), particularly pediatric bipolar disorder (Dickstein et al., 2005). Even fewer have examined the effect of intervention on this group. Family-based psychoeducational psychotherapy is one psychosocial intervention investigated for children with mood disorders. One goal of psychoeducational psychotherapy is to help parents become better advocates for their children, selecting more appropriate treatments to help manage their mood disorders and comorbid illnesses. Further, several components of psychoeducational psychotherapy, including problem-solving, verbal and nonverbal communication, identifying feelings, and affect regulation skills are applicable to managing anxiety as well as mood symptoms.

Seligman and Ollendick (1998) state, “Surprisingly, little effort has been put forth to explicate the meaning behind the high comorbidity of anxiety and affective disorders in youth” (p. 3). We know anxiety disorders occur in high rates and lead to significant impairment and poor prognosis in children with mood
disorders. Despite this knowledge, strikingly few studies have examined the effect of anxiety disorders on treatment outcome in children with mood disorders.

To address this gap in knowledge, steps need to be taken to clarify the existence of comorbid anxiety disorders and to identify effective treatment approaches for these children. In this dissertation, I first describe what is known about the comorbidity of anxiety disorders with depression and bipolar disorder (BPD). Next, I review the research regarding the effectiveness of treatment, medication and psychotherapy, for children with comorbid mood and anxiety disorders. Then, I describe an important psychosocial treatment modality, psychoeducational psychotherapy. Finally, a specific psychoeducational psychotherapy program, Multi-Family Psychoeducational Psychotherapy (MF-PEP), and its implications for children with comorbid mood and anxiety disorders are discussed. I expected children with comorbid anxiety disorders will present with poorer functioning and greater symptomatology at baseline and will therefore show slower improvement over time compared to the children without comorbid anxiety. However, as many of the goals of MF-PEP pertain to anxiety symptoms as well and aim to help families become better consumers of care, I expected MF-PEP will be effective in reducing the number of anxiety symptoms for all children participating.

Major Depressive Disorder

Although somewhat neglected in earlier research, the number of studies on childhood depressive disorders has increased significantly in recent decades.
Population studies have reported prevalence rates of depression in children ranging from 0.4% to 2.5% (Anderson & McGee, 1994; Fleming & Offord, 1990). Stark, Napolitano, Swearer, Schmidt, Jaramillo, and Hoyle (1996) asserted that an early-onset depressive disorder is “a risk factor for later episodes, impacts the youngster’s dyads, and has potentially life-threatening consequences” (p. 59). Children’s episodes of depression may have shorter durations, but they tend to recur (Kovacs, Feinberg, Crouse-Novak, Paulauskas, & Finkelstein, 1984) and can lead to a poor adult outcome, predicting a variety of disorders in adulthood, including depression, bipolar disorder, anxiety disorders, substance abuse, conduct disorder, and antisocial personality disorder (Weissman et al., 1999).

**Anxiety Comorbidity**

*Phenomenology.* According to Axelson and Birmaher (2001), existing research on comorbid anxiety and depressive disorders is “somewhat limited” (p. 67). Great variability exists on estimates of anxiety comorbidity for children with depression. Yorbik, Birmaher, Axelson, Williamson, and Ryan (2004) compared comorbid conditions in children with MDD to adolescents also with MDD. In the child sample, 34.8% suffered from any anxiety disorder (18.9%, generalized anxiety disorder [GAD]; 18.4%, separation anxiety disorder [SAD]; and 4.5%, social phobia). Avenevoli and colleagues (2001) describe anxiety disorders as the most common co-occurring psychiatric disorders in children with depression, with estimates ranging from 20% to 75%. In children with anxiety, rates of depression are generally lower, ranging from 5% to 55%. Lewinsohn and colleagues (1997)
found major depression to be significantly associated with most types of anxiety disorder, including panic disorder, SAD, overanxious disorder, and social and simple phobias. They did not find a relationship between depression and obsessive-compulsive disorder (OCD), however.

Specific anxiety disorders. Patients with dythymic disorder (DD) and GAD (DD + GAD) were compared to patients with DD and no GAD (DD - GAD). The DD + GAD group had more internalizing disorders (other comorbid anxiety disorders), while the DD - GAD group had more externalizing disorders (ADHD, oppositional defiant disorder, and conduct disorder). The authors hypothesized that, “a comorbid anxiety disorder can reduce the behavioral discharge and increase, on the contrary, agitation and internal tension,” which, “may provoke a self-destructive impulsive rather than an aggressive acting out” (p. 256). There were no differences between the groups in number of depressive symptoms and functional impairment (Masi, Mucci, Favilla, & Milliepiedi, 2001).

A few studies have examined comorbidity from the opposite perspective, looking at comorbid depression within anxiety disorders. Adolescent inpatients with OCD were found to have higher levels of depression compared to control subjects (87 community controls matched for age, sex, and socio-economic status), but no differences compared to other inpatients. The authors suggest these high scores on the Beck Depression Inventory (BDI) may be a response to having a severe mental disorder and requiring hospitalization. It should be noted only 40 of the 348 inpatients had OCD, so the sample size was low (Apter et al., 2003). Masi,
Favilla, Mucci, and Millepiedi (2000), examined the effect of depressive comorbidity and GAD in children. In a sample of 108 children with GAD, 55 (51%) had comorbid depression. Although the groups did not differ significantly by age, gender, and socioeconomic status, the patients with comorbid depression had significantly more anxiety symptoms than those without.

**Age of onset.** Research suggests onset of anxiety often occurs before onset of depression. For instance, in a longitudinal follow-up study, two-thirds of children with comorbid anxiety and depression had onset of their anxiety disorder before onset of depression (Kovacs, Gatsonis, Paualauskas, & Richards, 1989). Further, comorbid depressed and anxious children had an earlier age of onset of their depressive disorder compared to the depressed children without comorbid anxiety. Lewinsohn and colleagues (1997) found simple phobia, SAD, overanxious disorder, and social phobia more often precede diagnoses of MDD, but OCD and panic disorder appeared more likely to occur after the onset of depression. Avenevoli and colleagues (2001) found the onset of depressive disorders typically followed the onset of behavioral and anxiety disorders, except for panic disorder.

Based on retrospective reports in a subset of the participants in the Oregon Adolescent Depression Project, SAD in childhood was found to be a strong risk factor for panic disorder and depression in adulthood (Lewinsohn, Holm-Denoma, Small, Seeley, & Joiner, 2008). Cole, Peeke, Martin, Truglio, and Seroczynski (1998) discovered, in a community sample, high rates of self- and parent-reported anxiety predicted self- and parent-reported depression over time. However, the
opposite was not found; in fact, parents who reported their child as more depressed at one assessment point appeared to report their child as less anxious at a later assessment. This six-wave, three year, longitudinal study, controlling for prior depression, strongly supports the idea that anxiety frequently precedes depression in children.

**Conclusions.** Depression and anxiety disorders frequently co-occur, and this comorbidity can suggest further morbidity and impairment. Research lends support to the idea that anxiety frequently precedes depression. As only a few studies exist on specific types of anxiety disorders that frequently co-occur with depression (e.g., GAD), more research examining the co-occurrence of depression with specific anxiety disorders is needed.

*Bipolar Disorder*

Research on bipolar disorder in children is less common. For instance, although adolescents report lifetime prevalence rates of bipolar disorder of approximately 1% (Lewinsohn, Klein, & Seeley, 1995), similar epidemiological data are not available for children. It should be noted that Lewinsohn and colleagues’ figures came from interviews of students attending school, and may underestimate true rates, as children suffering from a severe mental illness are more likely to be absent from school or to have dropped out (Berg et al., 1993; Newacheck et al., 1998). In a national survey of individuals with bipolar disorder, 33% of respondents reported that they were under age 15 when symptoms of bipolar disorder first appeared, 27% were between 15 and 19, and only 39% were
age 20 or older (Hirshfeld, Lewis, & Vornik, 2003). In a second retrospective study of adults with BPD, Chengappa and colleagues (2003) found 37% of people from a 1900-1939 birth cohort reported onset of BPD before age 19, compared to 53% from a 1940 to 1959 birth cohort. Leverich and colleagues (2007) found 36% of 480 adults diagnosed with BPD reported an adolescent onset and 14%, a prepubertal onset. Further, a childhood-onset was associated with long delays in treatment-seeking. Bipolar disorder appears to be present in some patients even at very young ages; Tumuluru, Weller, Fristad, and Weller (2003) found 17% of hospitalized preschoolers on an inpatient unit known to specialize in mood disorders to have a bipolar illness.

Bipolar disorder is clearly a serious disorder causing multiple impairments to those who suffer from it. Wozniak and colleagues (2004) found children with bipolar depression to have: higher rates of comorbidity; more severe depression (including more severe symptoms of suicidality, anhedonia, and hopelessness); lower Global Assessment of Functioning (GAF) scores; and higher rates of hospitalization when compared with children with unipolar depression. In her review article, Weckerly (2002) argued, “pediatric mania represents a distinct, genetically mediated, severe subtype of BP that differs in presentation, correlates, and treatment from the adult form of the disorder” (p. 43). It is considered more severe than adult-onset bipolar disorder, often causing substantial psychosocial impairment and multiple psychiatric hospitalizations (Weckerly, 2002; Wozniak et al., 1995).
Anxiety Comorbidity

Phenomenology. Data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) are particularly valuable in understanding the effects of anxiety disorder comorbidity on adults with bipolar disorder. The STEP-BD is a multi-center, National Institute of Mental Health (NIMH)-funded project examining the longitudinal course of BPD in adults, including a large, prospective study and several randomized controlled trials. Simon, Otto, Wisniewski, and colleagues (2004) examined baseline data on anxiety comorbidity status on the first 500 patients enrolled in the study. The prevalence of any lifetime anxiety disorder was 51.2% and 30.5% for any current anxiety disorder, and patients showed significantly higher prevalence rates for each anxiety disorder compared to the general population. Current anxiety diagnosis rates were as follows: panic disorder, 8%; agoraphobia without panic disorder, 4.4%; social anxiety disorder, 12.7%; OCD, 5.7%; PTSD, 5.1%; GAD, 2.3%. Lifetime prevalence rates were: panic disorder, 17.3%; agoraphobia without panic disorder, 8.5%; social anxiety disorder, 22%; OCD, 9.9%; PTSD, 17.2%; GAD, 18.4%. Patients with BP-I showed greater overall anxiety comorbidity than patients with BP-II, although this difference only achieved significance for current PTSD and lifetime agoraphobia without panic (Simon et al., 2004).

Further, patients with comorbid lifetime anxiety disorders showed: a lower age of onset; less education completed; dramatically fewer days euthymic; less likely to be considered “recovering” or “recovered” at baseline; poorer functioning;
and a poorer quality of life. The presence of multiple anxiety disorders was associated with further impairment in quality of life and global functioning. As the patients with anxiety disorders had higher prevalence rates of lifetime alcohol and substance use disorders, the investigators re-examined the above associations while controlling for lifetime substance use. The above associations still occurred even after controlling for lifetime substance use disorders and current bipolar clinical state (e.g. depressed, manic, euthymic). The authors concluded that anxiety disorder comorbidity appears to be associated with greater severity of bipolar illness and poorer functioning. More research is necessary on treatment response in patients with comorbid anxiety and bipolar disorders, although “the field has been slow to develop specific anxiety-targeted interventions for patients with bipolar disorder and anxiety comorbidity” (Simon et al., 2004, p. 2227).

The authors further examined current anxiety comorbidity in the first 1,000 participants in the STEP-BD program (Otto et al., 2006). Rates were similar to those found in the first 500 participants (any anxiety disorder, 31.9%; social anxiety disorder, 13.3%; GAD, 13.3%; panic disorder with and without agoraphobia, 8.5%; OCD, 6.8%; PTSD, 4.8%; agoraphobia without panic disorder, 4.1%). Having at least one current comorbid anxiety disorder was associated with significantly fewer days well than the sample without anxiety disorders. Multiple anxiety disorders appeared to have an additive influence on fewer days well. Current anxiety disorder status was associated with a risk of relapse, lower likelihood of recovery from depression, lower quality of life, and poorer role
function. The authors suggest, “This potential for a reciprocal negative influence of anxiety comorbidity and bipolar disorder could serve to maintain the anxiety disorder and worsen the course of bipolar disorder” (Otto et al., 2006, p. 24).

The occurrence of anxiety disorders in youth with BPD has been called “a neglected comorbidity” (Masi, Toni, et al., 2001, p. 797). In a sample of 43 youth outpatients with DSM-IV-TR diagnosed BPD, only 23.5% percent did not present with an anxiety disorder. Lifetime comorbidities, evaluated with the Diagnostic Interview for Children and Adolescents-Revised (DICA-R), were as follows: 44.2% OCD; 39.5% social phobia; 25.6% panic disorder or agoraphobia; 16.3% SAD; and 18.6% GAD (Masi, Toni, et al., 2001). Moreno and colleagues (2007) found, looking at patient visits (age 0 to 19 years) from the National Ambulatory Medical Care Survey with a BPD diagnosis, only 10.0% presented with an anxiety disorder, much lower than other estimates among outpatient youth with BPD. However, comorbid disorders were determined via chart documentation. If only the primary diagnosis was recorded, many comorbid disorders may have been missed, resulting in an underestimate of true diagnoses.

Harpold and colleagues (2005) found youth with BPD (n = 297) were significantly more likely than youth with a disruptive behavior disorder (n = 1100) to report all anxiety disorders examined using the Kiddie Schedule for Affective Disorders and Schizophrenia- Epidemiologic Version (K-SADS-E), which included PTSD, OCD, SAD, simple phobia, social phobia, overanxious disorder, agoraphobia, and panic disorder. Youth with BPD also presented with significantly
more anxiety disorder syndromes and were more likely to report multiple anxiety syndromes than the youth with disruptive behavior disorders.

Dickstein and colleagues (2005), as part of a larger study, compared rates of anxiety disorders using the Kiddie-Schedule for Affective Disorders- Present and Lifetime Version (K-SADS-PL) in a narrow-phenotype sample (31 children who met stringent DSM-IV-TR criteria for BPD) to a broad-phenotype sample (32 children who met their research criteria for severe mood dysregulation--SMD). Among the narrow phenotype group, researchers found rates of: 43%, GAD; 9%, OCD; 6%, panic disorder; 13%, PTSD; 42%, SAD, 13%, social phobia; and 45%, specific phobia. The broad phenotype group showed much lower rates: 34%, GAD; no OCD or panic disorder; 3%, PTSD; 25%, SAD; 3%, social phobia; and 9%, specific phobia. Interestingly, in the narrow phenotype group, children with comorbid anxiety disorders had a significantly earlier age of onset of BPD and more psychiatric hospitalizations compared to those without anxiety. However, in the broad phenotype group, children with comorbid anxiety were not significantly more impaired than those without comorbid anxiety. The researchers suggest that narrow phenotype BPD plus anxiety may represent a more severe phenotype of BPD (Dickstein et al., 2005). Masi, Perugi, et al. (2007) found youth with Bipolar-II (BP-II) had higher rates of comorbid anxiety disorders than youth with Bipolar Disorder-I (BP-I) or Bipolar Disorder-Not Otherwise Specified (BP-NOS), particularly panic disorder and GAD. Comorbid anxiety disorders may be more common in narrow phenotype BPD and also in BP-II.
In a study of 49 preschool children (age four to six) with BPD, few
significant differences in rates of DSM-III-R anxiety disorders were found in
comparison to 29 school-age comparison children (age seven to nine) who also had
BPD (Wilens et al., 2003). Specifically, preschool-age children showed rates of
70% of any anxiety disorder, including: SAD, 57%; panic disorder, 5%;
agoraphobia, 36%; social phobia, 14%; simple phobia, 16%; overanxious disorder,
34%; and OCD, 9%. The school-age children showed rates of 76% of any anxiety
disorder, including: SAD, 48%; panic disorder, 17%; agoraphobia, 38%; social
phobia, 21%; simple phobia, 17%; overanxious disorder, 45%; and OCD, 10%.
The two groups only differed significantly on rates of overanxious disorder. Thus,
BPD and comorbid anxiety disorders are prevalent even in preschool-age children
(Wilens et al., 2003).

Tillman and colleagues (2003) compared comorbidities in two groups of
youth, age seven to 16, as part of an ongoing trial. The pediatric BPD group (PEA-
BP) subjects were required to meet DSM-IV criteria for BP-I and ADHD subjects
were required to meet DSM-IV criteria for ADHD. Comorbid syndromal and
subsyndromal SAD was significantly higher in the PEA-BP group compared to the
ADHD group. The PEA-BP group showed prevalence rates of 8.6% and 17.2% for
syndromal and subsyndromal SAD; 7.5% and 17.2% for syndromal and
subsyndromal OCD; 5.4% and 7.5% for syndromal and subsyndromal GAD; 4.3%
and 32.3% for syndromal and subsyndromal specific phobia; 3.2% and 4.3% for
syndromal and subsyndromal panic attacks; 3.2% and 11.8% for syndromal and
subsyndromal social phobia; 0% for both syndromal and subsyndromal panic disorder without agoraphobia; and 0% and 1.1% for syndromal and subsyndromal agoraphobia without panic. The ADHD group showed prevalence rates of 2.5% and 1.2% for syndromal and subsyndromal SAD; 2.5% and 3.7% for syndromal and subsyndromal OCD; 2.5% and 2.5% for syndromal and subsyndromal GAD; 6.2% and 29.6% for syndromal and subsyndromal specific phobia; 2.5% and 0% for syndromal and subsyndromal panic attacks; 0% and 6.2% for syndromal and subsyndromal social phobia; 1.2% and 0% for syndromal and subsyndromal panic disorder without agoraphobia; and 0% for both syndromal and subsyndromal agoraphobia without panic. Further, a significantly greater percentage of PEA-BP subjects compared to ADHD subjects had greater than or equal to one comorbidity, not just anxiety, (97.9% versus 45.7%), greater than or equal to two comorbidities (81.7% versus 18.5%), greater than or equal to three comorbidities (41.9% versus 22.6%), and greater than or equal to four comorbidities (20.4% versus 1.2%).

**Specific anxiety disorders.** Some researchers have hypothesized links between panic disorder and BPD. Chen and Dilsaver (1995) found lifetime prevalence rates of panic disorder to be 20.8% for adult patients with BPD, compared to only 10% in patients with depression and 0.8% in comparison subjects. Patients with panic disorder have a high risk for suicidality (Fawcett, 1992). Adult patients with early-onset panic attacks were found to be more likely to have an earlier age of onset of depression and mania and increased risk and lethality of suicide attempts compared to patients with later-onset panic attacks.
(Goodwin & Hamilton, 2002a; Goodwin & Hamilton, 2002b). Approximately half of an outpatient sample of patients with BP-I reported “panic spectrum features,” which were associated with more depressive episodes, higher levels of depressive symptoms, and greater suicidal ideation (Frank et al., 2002).

Research on youth with BPD and comorbid panic disorder is rare; however, rates of BPD in youth with panic disorder are reported to range from 19% to 52% (Biederman et al., 1997; Birmaher et al., 2002). Birmaher and colleagues (2002) found youth with panic disorder were more likely to have comorbid BPD than youth with other anxiety disorders and youth with disorders other than anxiety. Bipolar symptom severity did not differ between youth with and without comorbid panic disorder. Likewise, panic symptom severity did not differ between youth with and without comorbid BPD. However, youth with both panic disorder and BPD had significantly more psychotic symptoms and suicidal ideation than youth with either panic disorder and no BPD or vice versa (Birmaher et al., 2002). Biederman and colleagues (1997) reported 52% of children and adolescents who reported panic disorder also met criteria for BPD. Masi and colleagues (2007) examined youth diagnosed with BPD with a mean age of 13.8. Their sample came from a larger cohort of youth screened and admitted to a unit for children with mood and anxiety disorders over a five year period. They found panic disorder to occur in one out of four of the youth with BPD, and primarily occurred in females with BP-II. Interestingly, patients with panic disorder + BPD were found to be less severely impaired at baseline. The authors suggest this may have occurred due to
the more frequent occurrence of panic disorder among BP-II patients, who suffer from hypomania as opposed to mania. The authors suggest that BPD with comorbid panic disorder may represent a different subtype of BPD (Masi et al., 2007). The link between BPD and panic disorder warrants further research in children.

Masi and colleagues (2004) examined the association between OCD and BPD in a clinical sample of youth with BPD, OCD, or both BPD and OCD. In the sample of 102 children and adolescents (65 inpatients and 37 outpatients), 36.3% were diagnosed as BPD, 34.3% were diagnosed as OCD, and 29.4% were diagnosed as BPD-OCD. Of the patients with OCD or BPD, 45% showed a lifetime prevalence of the other disorder. Age of onset of BPD was not affected by comorbid OCD, although BP-II was more common in the BPD-OCD group compared to the just BPD group. Interestingly, patients with OCD and no BPD had more compulsions, particularly ordering compulsions, but patients with OCD and BPD had more existential, philosophical, odd, or superstitious obsessions (Masi et al., 2004). A naturalistic, retrospective study of children and adolescents with OCD compared clinical features of patients with and without comorbid BPD (Masi et al., 2007). Compared to the patients without BPD, patients with comorbid BPD (36%) had an earlier onset of OCD, greater symptoms severity and functional impairment, more frequent hoarding obsessions and compulsions, higher comorbidity with ODD and ADHD, and a lower comorbidity with GAD (Masi et al., 2007).
Researchers involved in the STEP-BD program examined associations between PTSD and BPD (Pollack et al., 2006). They hypothesized that patients with BPD were at a higher risk for developing PTSD after media exposure to the September 11th terrorist attacks. The authors examined the 137 BPD patients whose baseline assessments occurred before September 11th, 2001 at two of their sites (Boston and Pittsburgh) using self-reports. Twenty percent of these patients developed “probable” PTSD as a response to the attacks lasting, on average, for up to one year after the attacks. This is a notably higher rate than the general population, and also of those local to the terrorist strike, as documented in another study, which demonstrated that 0.6% of New Yorkers developed PTSD in response to the attacks (Galea et al., 2003). Older patients were more likely to develop PTSD, as were those in a hypomanic, manic, or mixed state. Importantly, patients with a lifetime history of any anxiety disorder (including past PTSD) were not more likely to develop PTSD as a response. The development of PTSD was associated with television viewing of September 11th-related material in the 10 days after the attacks, although the degree to which participants changed their viewing habits to reduce anxiety (sought out versus avoided media coverage of the attacks) and participants’ level of identification with the victims were not associated with the development of PTSD. The authors suggest a potential mediator could be the higher levels of hyperarousal or greater elevations in anxiety sensitivity (Simon et al., 2003) in manic states (Pollack et al., 2006).
Cognitive processes. Brotman and colleagues (2007) found children with BPD and a comorbid anxiety disorder (BPD+ANX) demonstrated a bias toward threatening faces, while children with BPD and no comorbid anxiety disorder (BPD-ANX) and controls demonstrated no bias toward or away from threatening faces. Differences in attention allocation suggest BPD+ANX and BPD-ANX may require different treatment approaches.

Conclusions. Anxiety disorders are a significant problem for youth with BPD. In fact, Masi and colleagues (2007) suggest, “Multiple anxiety disorders may represent one possible pathway to early-onset bipolarity” (p. 48). However, prevalence estimates of comorbid anxiety disorders vary greatly. Some research seems to suggest no link to any anxiety disorder in particular for children with BPD (e.g. Goldstein & Levitt, 2007), although other research suggests a higher occurrence of panic disorder among children with BPD. Panic disorder in patients with BPD may predict worse prognosis and more morbidity and impairment. Patients with BPD may be more likely to develop PTSD than the general population in response to a traumatic event. Further research is needed to better understand this phenomenon, particularly in children. Overall, much more work is needed to clarify the presence and theories surrounding the occurrence of anxiety disorders in youth with BPD. Table 1.1 presents the prevalence estimates of comorbid anxiety disorders among children with mood disorders found in the literature.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Sample characteristics</th>
<th>Prevalence Rates</th>
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| Dickstein et al. (2005) | Compared two groups of pediatric BPD-narrow-phenotype (n = 31) and broad phenotype (n = 32)  
Age 7 to 17  
Enrolled in an ongoing longitudinal neurocognitive and neuroimaging study                                                                                     | Lifetime Dx:  
Narrow phenotype: Any anx = 77.4%; GAD = 42%; OCD = 9%; PD = 6%; PTSD = 13%; SAD = 42%; SocPh = 13%; SpecPh = 45%  
Broad phenotype: Any anx = 46.9%; GAD = 34%; OCD = 0%; PD = 0%; PTSD = 3%; SAD = 25%; SocPh = 3%; SpecPh = 9% |
| TADS Team (2005)        | 439 adolescents, aged 12 to 17, who met DSM-IV criteria for MDD  
Part of the TADS study and randomly assigned to one of four acute tx conditions                                                                                  | Current anx dx: any anx = 27.4% current, 10.32% past; GAD = 15.26% current, 3.2% past; SocPh = 10.71% current, 3.42% past; Special phobia = 5.24% current, 2.29% past; PTSD = 3.65% current, 2.51% past; OCD = 2.05% current, 0.46% past; PD = 2.05% current, 0% past; SAD = 2.05% current, 2.28 past; ASD = 0.23% current, 0.68% past |
| Brent et al. (1998)     | 107 adolescents; age 13 to 19, dx with DSM-III-R MDD  
Randomly assigned to one of three manual-based, brief, psychosocial treatments: CBT, SBFT; or NST                                                                 | Any anx dx  
CBT group = 37.8%; SBFT = 28.6%; NST = 28.6%                                                                                                                                                              |
| Goldstein et al. (2005) | 405 children and adolescents, age 7 to 17, fulfilled DSM-IV criteria for BP-I, BP-II, and BP-NOS, part of a multi-site longitudinal study of pediatric BP (Course and Outcome of Bipolar Youth) | 45% who had made a lifetime suicide attempt had a lifetime dx of an anxiety disorder compared with 38% of non-attempters                                                                                       |

Table 1.1 Literature review of prevalence estimates of comorbid anxiety disorders among children with bipolar and depressive disorders. (Continued)
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<th>Authors</th>
<th>Sample characteristics</th>
<th>Prevalence Rates</th>
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<tr>
<td>Harpold et al. (2005)</td>
<td>297 youth, aged 6 to 18 years, met full criteria for a DSM-III/IV diagnosis of BP-I or BP-II</td>
<td>Lifetime anxiety dx: Any anx= 76%; PTSD = 12%; OCD = 15%; SAD = 44%; Simple Phobia = 22%; SocPh = 26%; Overanxious disorder = 43%; Agoraphobia = 28%; PD = 15%</td>
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<tr>
<td>Masi, Perugi, Millepiedi, Mucci, Pari, Pfanner, Berloffa, &amp; Toni (2007)</td>
<td>Naturalistic study based on a database of 217 patients diagnosed with BPD and were admitted and screened for treatment in a unit for inpatient and outpatient mood and anxiety disorders</td>
<td>Lifetime anx. dx BP-I patients: Any anx = 69.2%; SAD = 17.9%; PD = 15.4%; SocPh = 25.6%; Simple Phobia = 6.4%; GAD = 28.2%; OCD = 35.9% BP-II patients: Any anx = 83.5%; SAD = 28.9%; PD = 37.1%; SocPh = 24.7%; Simple Phobia = 9.3%; GAD = 42.3%; OCD = 48.5% BP-NOS patients: Any anx = 61.9%; SAD = 26.2%; PD = 4.8%; SocPh = 14.3%; Simple Phobia = 2.4%; GAD = 16.7%; OCD = 61.9%</td>
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<tr>
<td>Masi, Perugi, Toni, Millepiedi, Mucci, Bertini, &amp; Akiskal (2004)</td>
<td>102 inpatient and outpatient youth aged 7 to 18 with BP, OCD, or BP-OCD</td>
<td>Lifetime anx dx BPD-OCD: SocPh = 26.7%; PD-agoraphobia = 33.3%; SAD = 16.7%; GAD = 16.7% BPD: SocPh = 32.4%; PD-agoraphobia = 13.5%; SAD = 16.2%; GAD = 13.5%</td>
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<tr>
<td>Masi, Toni, Perugi, Mucci, Millepiedi, &amp; Akiskal (2001)</td>
<td>43 outpatients, age 7 to 20; diagnosed with BP-I or BP-II</td>
<td>Lifetime anx dx&lt;br&gt; All: OCD = 44.2%; SocPh = 39.5%; PD = 25.6%; SAD = 16.3%; GAD = 18.6%&lt;br&gt; Childhood BP-onset: OCD = 40%; SocPh = 40%; PD = 20%; SAD = 15%; GAD = 20%&lt;br&gt; Adolescent BP-onset: OCD = 47.8%; SocPh = 39.1%; PD = 30.4%; SAD = 17.4%; GAD = 17.4%&lt;br&gt; W/Externalizing: OCD = 33.3%; SocPh = 33.3%; PD = 16.7%; SAD = 16.7%; GAD = 16.7%&lt;br&gt; W/out Externalizing: OCD = 48.4%; SocPh = 41.9%; PD = 29%; SAD = 16.1%; GAD = 19.3%</td>
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<tr>
<td>Rohde, Clarke, Lewinsohn, Seeley, &amp; Kaufman (2001)</td>
<td>151 adolescents age 14 to 18, met criteria for MDD, DD, or double depression, originally recruited and treated in two treatment trials</td>
<td>Lifetime comorbid dx&lt;br&gt; Any anx = 21.2%; SpecPh = 7.9%; SocPh = 6.6%; overanxious disorder = 6%</td>
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<tr>
<td>Moreno et al. (2007)</td>
<td>Chart review of youth, age 0 to 19, with BPD</td>
<td>10% had a comorbid anxiety disorder diagnosis</td>
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<td>Study</td>
<td>Participants</td>
<td>Lifetime dx</td>
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<td>Wilens et al. (2003)</td>
<td>44 preschool children age 4 to 6 and 29 school age children age 7 to 9 referred for clinical care to a pediatric psychopharmacology clinic</td>
<td>Preschoolers: Any anx = 70%; SAD = 57%; PD = 5%; Agoraphobia = 36%; SocPh = 14%; Simple Phobia = 16%; Overanxious = 34%; OCD = 9% School age: Any anx = 76%; SAD = 48%; PD = 17%; Agoraphobia = 38%; SocPh = 21%; Simple Phobia = 17%; Overanxious = 45%; OCD = 10%</td>
</tr>
<tr>
<td>Tillman et al. (2003)</td>
<td>93 youth age 7 to 16 years meeting criteria for a current DSM-IV manic episode</td>
<td>Anx dx: SAD = 8.6% syndromal, 17.2 subsyndromal; OCD = 7.5% syndromal, 17.2% subsyndromal; GAD = 5.4% syndromal, 7.5% subsyndromal; SpecPh = 4.3% syndromal, 32.3% subsyndromal; Panic attacks = 3.2% syndromal, 4.3% subsyndromal; SocPh = 3.2% syndromal, 11.8% subsyndromal; PD w/out agoraphobia = 0% syndromal, 0% subsyndromal; agoraphobia w/out panic = 0% syndromal, 1.1% subsyndromal</td>
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<tr>
<td>Young, Mufson, &amp; Davies (2006)</td>
<td>63 adolescents age 12 to 18 with a DSM-IV diagnosis of MDD, DD, adjustment disorder with depressed mood, or depression-NOS</td>
<td>Anx dx: any anx = 68%; SocPh = 32%; panic = 38%; GAD = 41%</td>
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Table 1.1: Continued

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<th>Authors</th>
<th>Sample characteristics</th>
<th>Prevalence Rates</th>
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<tr>
<td>Yorbik, Birmaher, Axelson, Williamson, &amp; Ryan (2004)</td>
<td>916 youth age 5.6 to 17.9 years with DSM MDD</td>
<td>Current Anx Dx</td>
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<tr>
<td></td>
<td></td>
<td>Children: Any anx = 34.8%; GAD/overanxious = 18.9%; SAD = 18.4%; OCD = 1.5%; SocPh = 4.5%</td>
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<tr>
<td></td>
<td></td>
<td>Adolescents: Any anx = 27.7%; GAD/overanxious = 15.7%; SAD = 3.1%; OCD = 2.2%; SocPh = 4.9%</td>
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Note. BPD = bipolar disorder; Dx = diagnosis; anx = anxiety disorder; GAD = generalized anxiety disorder; OCD = obsessive compulsive disorder; PD = panic disorder; PTSD = post-traumatic stress disorder; SAD = separation anxiety disorder; SocPh = social phobia; SpecPh = specific phobia; MDD = major depressive disorder; TADS = Treatment for Adolescents with Depression Study; tx = treatment; ASD = acute stress disorder; NOS = not otherwise specified; CBT = cognitive behavioral therapy; SFT = systematic-behavioral family therapy; NST = nondirective supportive therapy; BP-I = bipolar I disorder; BP-II = bipolar II disorder; BP-NOS = bipolar disorder not otherwise specified; DSM-IV = diagnostic and statistical manual of mental disorders, 4th edition; DSM-III = diagnostic and statistical manual of mental disorders, 3rd edition; DSM-III-R = diagnostic and statistical manual of mental disorders, 3rd edition, revised.
Angold and colleagues (1999) assert that the study of comorbidity is an important task because understanding why comorbidity occurs between particular disorders may help us better understand the development of psychopathology. There is no question that anxiety and mood disorders have high rates of co-occurrence. Issler, Sant-Anna, Kapczinski, and Lafer (2004) state, “The complexity of clinical presentations and the association patterns between these disorders does not allow [identification of] an exclusive model to explain the phenomenon of comorbidity between mood and anxiety” (p. 34).

Nonetheless, a few researchers have begun to investigate different models and theories to explain the occurrence of these comorbidities. Several include Seligman and Ollendick’s (1998) four explanations for the comorbidity of anxiety and depression, Clark and Watson’s (1991) Tripartite Model, Freeman, Freeman, and McElroy’s (2002) three explanations for the comorbidity of BPD and anxiety, and Gray’s (1987) Behavioral Activation and Behavioral Inhibition Systems. A thorough and complete explanation of each of these theories and supporting research is beyond the scope of this dissertation. However, I will briefly discuss each of the four models below.

**Comorbidity of Anxiety and Depression**

Little is known about the conditions under which anxiety and depressive symptoms occur and why they occur so frequently (Seligman & Ollendick, 1998). Several researchers have begun to question this relation and challenge the current diagnostic system. Seligman and Ollendick (1998) propose and examine four
explanations: (1) comorbidity between anxiety and depression in youth is due to the overlap in definitions; (2) comorbidity between anxiety and depression in youth is due to the fact that anxiety and depression represent two indicators of a single construct; (3) comorbidity between anxiety and depression in youth is due to the overlap in risk factors; (4) anxiety causes or puts youth at risk for depression. They conclude that, while some of these theories are promising, more research is warranted before we can settle on a reasonable explanation (Seligman & Ollendick, 1998).

Axelson and Birmaher (2001) pose the question, “Given the symptom overlap and high intercorrelation of assessment measures, the following question arises: are depression and anxiety in children actually manifestations of a single construct or are they separate but related domains?” (p. 68). Anxiety and depression are difficult to discriminate in community samples, but as symptomatology reaches clinical levels, they are easier to discriminate. A factor analysis of youth below diagnostic threshold for disorders suggested a single dimension of anxiety and depressive symptoms (Gurley, Cohen, Pine, & Brook, 1996).

The Tripartite Model of Anxiety and Depression (Clark & Watson, 1991) theorizes that anxiety and depression share a general factor, negative affectivity (NA), while two specific factors, physiological hyperarousal (PH) and (low) positive affect (PA), are common to anxiety and depression, respectively. Research on this model in adults has yielded mixed results, some data support the model (Clark & Watson, 1991), while other data suggest the model does not uniformly
apply to all anxiety disorders (Brown, Chorpita, & Barlow, 1998; Mineka, Watson, & Clark, 1998).

Researchers are gradually beginning to examine the Tripartite Model in children. Some studies have demonstrated support for the model in both pediatric inpatients (Joiner, Catanzaro, & Laurent, 1996) and from teacher, parent, peer, and self reports in sixth graders (Cole, Truglio, & Peeke, 1997). Olino, Klein, Lewinsohn, Rohde, and Seeley (2008) compared a one factor model and a three factor model in a study of adolescents followed to age 30. They found the three factor model fit best and concluded that depression and anxiety appear to be explained by a combination of stable shared and unique factors, consistent with the Tripartite Model. Lonigan, Phillips, and Hooe (2003) conducted a longitudinal study of school children in fourth through 11th grades looking at the relation between NA and PA and changes in children’s symptoms of anxiety and depression. Overall, they found support for the two factors. Specifically, NA and PA provided a good fit to the children’s self-reported affect and also showed stability over time. Further, NA and PA were related as hypothesized by the tripartite model (Lonigan et al., 2003).

Some studies show partial, but not complete, support for the model. In a school sample of 1,578 children, NA was positively related to anxiety and depression and PA was negatively correlated with depression. However, PH was only positively related to panic (Chorpita, 2002). An examination of parent and child-reported anxiety and automatic arousal measures showed PH to occur in both
anxiety and depression (Greaves-Lord et al., 2007). A study of the Tripartite Model in elementary and high school boys and girls found the tripartite model to be a good fit (Jacques & Mash, 2004). Specifically, PA was correlated with depression, PH was correlated with anxiety, and NA correlated with both depression and anxiety. Contrary to expectations, PA was also correlated with anxiety, and PH was correlated with depression. The best fit was for high school girls (Jacques & Mash, 2004). The Tripartite Model was supported in a sample of African American, urban youth, grades six through nine, but the dimensions showed a lack of discriminant validity (Lambert, McCrery, Joiner, Schmidt, & Ialongo, 2004).

Finally, a few studies show a lack of support for the model. Ollendick, Seligman, Goza, Byrd, and Singh (2003) compared one-factor (negative affectivity), two-factor (anxiety and depression), and three-factor models (Tripartite Model) in 510 fourth, seventh, and tenth graders. They found a two-factor model fit the entire sample and for each grade level. Opposite to Jacques and Mash (2004)’s findings, a better fit was found for boys and for younger children as opposed to adolescents. Lee and Rebok (2002) found in a school sample, PA and NA scales were significantly negatively correlated cross-sectionally and longitudinally, suggesting a new model is needed to describe mood disorders in children. Cole and colleagues (1997) found evidence for a unified model of anxiety and depression for third graders. However, Turner and Barrett (2003) followed up with these analyses, testing the Tripartite Model in three age cohorts to see if developmental differences call for a revision of the Tripartite Model in younger
ages. Contrary to Cole and colleagues’ findings, they found a correlated Tripartite Model provided a good fit across the age groups.

Thus, studies on the Tripartite Model have produced varying results, providing support, partial support, and lack of the support for the model. These variations could be the result of methodological differences between the studies. Regardless, they suggest further research, and perhaps a modified model, is necessary to truly understand the relationship of anxiety and depression in youth.

*Comorbidity of Anxiety and BPD*

Currently, no models are widely accepted to explain the frequent co-occurrence of bipolar and anxiety symptoms (Tamam, 2007). Freeman, Freeman, and McElroy (2002) discuss three conceptual models that may explain the frequent comorbidity of BPD and anxiety disorders and symptoms. Specifically, they suggest: (1) anxiety and BPD are separate disorders and their pathophysiological basis and comorbidity is the result of a high prevalence of both disorders in the general population; (2) anxiety and BPD are separate, but pathophysiologically related; or (3) BPD and anxiety disorders are different reflections of a common pathophysiological anomaly. In this model, general anxiety, social anxiety, panic attacks, and compulsions are considered pathological affective conditions similar to mania and depression evidenced in BPD. Freeman and colleagues (2002) emphasize that none of these three models are necessarily or universally correct, but each may apply to a different subgroup of patients diagnosed with both anxiety and BPD.
**Behavioral Inhibition System (BIS)/Behavioral Activation System (BAS)**

One theory hypothesized to explain the frequent comorbidity of mood disorders and anxiety disorders is Gray’s (1987, 1991) BIS and BAS. According to Gray, two main brain systems regulate approach and withdrawal behavior in response to the environment: the BIS and the BAS. Activity in the BIS causes feelings of anxiety and leads to withdrawal behavior, while activity in the BAS produces impulsive behavior, with little attention to the possibility of negative consequences. Expanding on this theory, several types of psychopathology are thought to be explained by the BIS/BAS. For instance, high levels of BIS activity are thought to be linked to anxiety symptoms (Gray, 1982), and low levels of BIS activity are thought to be associated with ADHD (Quay, 1997) and psychopathy (Fowles, 1980). High levels of BAS activity are hypothesized to be related to conduct disorder and antisocial personality disorder (Quay, 1993), and low levels are hypothesized to be related to depressive symptoms (Depue et al., 1987). BAS hypersensitivity, or extreme over and underactivity, is theorized to be associated with BPD (Depue, Krauss, & Spoont, 1987).

However, little research exists on the relationship between the BIS/BAS and mood and anxiety disorder comorbidity (Johnson, Turner, & Iwata, 2003). Research is particularly scarce in children. Muris, Meesters, de Kanter, and Timmerman (2005) examined the BIS/BAS scales in school children, age eight to 12. They found the BIS/BAS scales were theoretically meaningful in the sample. BIS was connected to higher levels of internalizing symptoms, while BAS was
related to externalizing symptoms. BIS was related to children-reported Strength and Difficulties Questionnaire (SDQ-C) emotional problems and Revised Child Anxiety and Depression Scale (RCADS) anxiety problems, but only small correlations between SDQ-C hyperactivity/conduct problems and Child Rating of Aggression (CRA) emerged. BIS was significantly correlated with parent-reported SDQ emotional problems and RCADS anxiety and depression, while BAS was only related to SDQ-P hyperactivity/conduct problems (Muris et al., 2005).

Although Gray’s original theory asserts that the BAS and BIS systems function independently of each other, Corr (2002) theorizes they may act interdependently and jointly influence behavior. In Kambouropoulos and Staiger’s (2004) study, participants completed two questionnaires and two behavioral measures of BIS/BAS activity. The authors found that, for one of the behavioral tasks, the Q-TASK, a combination of high levels of both appetitive and aversive motivations facilitated behavioral inhibition. A similar but non-significant pattern was found for the other behavioral task, the CARROT, a measure of reward responsiveness. The authors suggest that the approach-avoidance conflict in participants on the Q-TASK may have elicited anxiety and led to anxiety and inhibition.

Coplan, Wilson, Frohlick, and Zelenskis (2006) found child reports of BIS sensitivity were significantly associated with increased depressive symptoms, greater negative affect and social anxiety, and less positive reports of subjective well-being. BAS was significantly negatively associated with internalizing
problems but had no associations with subjective well-being. Children high in BIS and low in BAS reported more depressive symptoms, negative affect, social anxiety, and less positive affect and subjective well-being (Coplan et al., 2006). Children high in BIS and low in BAS may represent children with comorbid anxiety and depression.

Alloy and colleagues (2008) examined the BAS hypersensitivity model in individuals with BPD by examining whether self-reported sensitivity of the BAS and BIS predicts time to new onsets of hypomanic and depressive episodes. The BAS hypersensitivity model suggests a BAS that is overly reactive to external cues may predict vulnerability to BPD. An overly reactive BAS can lead to increased BAS response to reward and goal cues, and even anger evocation. This activation is theorized to lead to euphoric and/or irritable mood, increased self-confidence, increased goal-oriented behavior, and decreased need for sleep (Depue & Iacono, 1989). Alloy and colleagues (2008) followed 136 patients diagnosed with BP-II and 158 normal controls for 33 months with BIS/BAS scales and symptom measures. In the patient group, higher BAS sensitivity at Time 1 prospectively predicted a shorter time to onset of hypomanic and manic episodes (Alloy et al., 2008). Wright, Lam, and Brown (2008) hypothesized that adults with BPD would take a longer time than healthy controls to return to baseline levels of BAS activity after exposure to high levels of reward or frustration. No differences were found between groups among levels of frustration or reward experienced or time to return to baseline. However, the data were also examined taking into account number of
previous episodes. In these analyses, time to recover (measured by the time taken for Behavioral Engagement Scale [BES] score to return to baseline levels) after reward increased with higher numbers of previous manic episodes, while time to recover (again, time taken for BES scores to return to baseline levels) after frustration increased with higher number of episodes of both mania and depression. Urošević, Abramson, Harmon-Jones, & Alloy (2008) assert that, “Longitudinal research is needed to examine whether measures of weak regulation of BAS interact with the occurrence of BAS activation-and BAS deactivation-relevant events to predict hypomanic/manic and depressive episodes, respectively, in individuals with bipolar spectrum disorders” (p. 1202).

Johnson et al. (2003), in what they called the first study of the significance of BIS and BAS levels for comorbidity, examined the effect of BIS and BAS levels, as measured by the Behavioral Inhibition/Behavioral Activation System Scales, on lifetime prevalence of depression, anxiety, alcohol abuse or dependence, drug abuse or dependence, and ADHD or conduct disorders. Lifetime psychiatric disorders were measured with the Composite International Diagnostic Interview (CIDI). The authors found support for BIS and BAS levels in adults relating to drug abuse, anxiety disorders, and noncomorbid alcohol-related diagnoses. However, they found little support for the role of the BIS and BAS in explaining comorbidity. Further research is necessary examining the BIS and BAS, particularly regarding comorbidity and in children.
Anxiety Sensitivity Versus Neuroticism

Simon and colleagues (2003) examined the theory of anxiety-related traits to determine patterns of anxiety disorders in BPD versus depressive disorders in adults. Specifically, they theorized that anxiety sensitivity, or the tendency to fear arousal and sensations of anxiety due to the belief that these sensations have catastrophic consequences (Reiss, 1991), is associated with BPD. They suggested neuroticism, the predisposition to experience psychological distress and negative affect (Clark et al., 1994), may be more associated with depressive disorders. In a preliminary examination of this theory, the authors sought to determine if each of these anxiety profiles were more common in patients with depressive disorders versus those with BPD, as evidenced by the particular anxiety disorders found in BPD and MDD patients. The authors found that panic disorder and GAD was more common in the bipolar patients versus the depressed patients, even after controlling for age, gender, and other anxiety comorbidity. Panic disorder is found to be associated with anxiety sensitivity (Schmidt et al., 1997), so this may indicate that anxiety sensitivity is elevated in patients with BPD. Further research is needed.

Biological Theories

Depression and Anxiety

Genetics. Given the frequent comorbidity of anxiety and depression, research has investigated whether they share any common genetic factors (Axelson & Birmaher, 2001). Thapar and McGuffin (1997) examined analyses of symptoms of depression and anxiety in a twin sample. They determined that genetic effects on
anxiety symptoms are explained by common genetic factors with depressive symptoms, while depression has a small, unique genetic component. A separate study determined that children of parents with panic disorder with agoraphobia (both with and without comorbid MDD) had significantly higher rates of MDD and anxiety disorders compared to children of parents without psychiatric conditions ((Biederman, Rosenbaum, Bolduc, Faraone, & Hirshfeld, 1991). Likewise, children of depressed parents had nearly three times the risk of having an anxiety disorder compared to children of parents without psychiatric illness (Weissman, Warner, Wickramaratne, & Prusoff, 1997). Interestingly, this effect was only present for childhood-onset anxiety disorders (Wickramaratne & Weissman, 1998). In a twin study examining the genetic relationship between MDD, panic disorder, agoraphobia and social phobia, common genetic factors were found to explain a moderate proportion of the variance among these four disorders (Mosing et al., 2009). In sum, these genetic studies point to a shared genetic component of anxiety and depression which may help explain their frequent comorbidity.

**Biological.** Since anxiety and depression both respond to Selective Serotonin Reuptake Inhibitors (SSRIs), several researchers have hypothesized that anxiety and depression may arise from the similar effects of brain function (Nutt & Stein, 2006). While a thorough examination of theories surrounding the neurobiology of anxiety and depression is beyond the scope of this paper, a few interesting hypotheses warrant comment.
Several theories have hypothesized the relationship between anxiety and depression to be due to prolonged exposure to stress. Gray (1982) theorized that anxiety is the product of the stimulation of the septohippocampal system by the locus coeruleus, while depression is secondary to the exhaustion of noradrenergic input to the hypothalamus. This noradrenergic exhaustion is due to repeated stimulation of neuronal cell bodies found in anxiety. In other words, unremitting stress (due to anxiety) can cause the septohippocampal system to “crash,” resulting in a state of depression (Gray, 1982). A similar theory suggests that prolonged stress, or anxiety, activates g-aminobutyric acid (GABA) transmission. Prolonged stress causes the GABAergic-mediated inhibition of noradrenergic neurons to eventually fail, leading to depression (Paul, 1988). Future research on the biological factors associated with depression and anxiety is needed (Cameron, Abelson, & Young, 2004).

*Bipolar Disorder and Anxiety*

Less research has been conducted on genetic and biological factors related to the comorbidity of BPD and anxiety. In their review, Freeman, Freeman and McElroy (2002) theorize that “a complicated interplay among various neurotransmitter systems and neuromodulator contributes to their overlap” (p. 6). They describe several possible systems which may be involved in this interplay. First, an underlying noradrenergic hyperactivity appears to be involved in both BPD (i.e. Post et al., 1989) and certain anxiety disorders, particularly panic disorder and PTSD (Hoehn-Sarin & McLeod, 1993; Kosten, Mason, Giller, Ostroff, 1996).
Harkuess, 1987; Yehuda, Southwick, Giller, Ma, & Mason, 1992). Preliminary research also suggests excessive dopaminergic activity in both mania (Joyce, Fergusson, Woollard, Abbott, Horwood, & Upton, 1995; Potter, Rudorfer, & Goodwin, 1987), as well as panic disorder and PTSD (Azorin et al., 1990). Medications that act on the GABA system have been effective in treating both BPD (Bowden et al., 1994; McElroy & Keck, 2000) and GAD, social anxiety, and panic disorder, which suggests the GABA system may be involved in explaining comorbidity (Freeman et al., 2002). Finally, Freeman and colleagues (2002) theorize that dysregulation of serotonin function may also be involved in the frequently overlap of anxiety and BPD.

**Suicidality**

Suicide is the third leading cause of death in children age 10-14 in the United States, and the leading cause of death in this age group in China, Sweden, Ireland, Australia, and New Zealand (Goldsmith, Pellmar, Kleinman, & Bunney, 2002). In a sample of 1,285 youth age 9 through 17, 97 (7.5%) had thoughts of suicide within 6 months of the assessment and 42 (3.3%) had ever attempted suicide. Of those who had a history of attempted suicide, 32 (76.2%) met DSM-III criteria for a psychiatric disorder. Of the suicide attempters, 45.2% meet criteria for a mood disorder (Gould et al., 1998).

King, Hovey, Brand, Wilson, and Ghaziuddin (1997) found that, among 66 hospitalized, suicidal adolescents, 28.8% had made serious suicide attempts, 18.2% made mild suicide attempts, 33.3% were hospitalized with serious suicidal intent,
and 19.7% were hospitalized for significant suicidal ideation. In their review of the literature, King and Merchant (2008) assert that researchers and clinicians should take into account “the importance of social variables – social integration, perceptions of family and peer support, childhood abuse/neglect, and peer victimization – to our understanding of suicidal ideation and behavior among adolescents” (p. 192).

**Depression**

Suicidality remains a major problem in depression. Lui and colleagues (2006) examined suicidality in 553 children and adolescents who were currently in an MDD episode. The researchers examined current and lifetime suicidality with the Interview Schedule for Children and Adolescents-Diagnostic Version (ISCA-D and found that, in their lifetime, 68% the sample reported recurrent thoughts of death, 48% reported suicidal ideation, 30%, a suicide plan, and 12% reported having attempted suicide (Liu et al., 2006).

Mixed results exist on anxiety comorbidity and suicidality. Gould and colleagues’ (1998) study, referenced above, found that nearly half of those in their sample who had attempted suicide had more than one superordinate diagnosis. Superordinate diagnoses included any mood, any anxiety, any substance abuse, or any disruptive behaviors. Lui and colleagues (2006) found in a sample of youth with current MDD, those who were suicidal were significantly more likely to have comorbid anxiety disorders than those who were not suicidal (38.2% versus 24.9%). Ryan, Puig-Antich, Ambrosini, and colleagues (1987) found, in children
with depression, those with comorbid SAD, phobia, and overanxious disorder did not have higher rates of suicidality than patients without these disorders. Lifetime comorbid disorders (including anxiety, DD, and disruptive disorders) were not significantly related to suicidality in children and adolescents with depression (Barbe et al., 2005). Yet, in another study, patients with DD and comorbid anxiety had higher rates of suicidal ideation than patients with DD and no comorbid anxiety (Masi, Mucci, et al., 2001). Liu and colleagues (2006) found suicidal adolescents were more likely to have comorbid anxiety disorders, and anxiety was found to be an independent predictor of at least one form of suicidal behavior. Surprisingly, in adolescent inpatients with OCD, suicide attempters had lower depression levels than suicide nonattempters (Apter et al., 2003).

**Bipolar Disorder**

Estimates of youth with BPD who attempt suicide range from 20% (Strober et al., 1995) to 47% (Bhangoo et al., 2003). Goldstein and colleagues (2005) found approximately one-third of their sample of 405 BPD patients, age seven to seventeen, had a lifetime suicide attempt. While anxiety comorbidity, in general, was not a significant predictor of a suicide attempt, panic disorder was significantly associated with a previous suicide attempt. In Apter and colleagues’ study (2003), discussed above, all the OCD inpatients who attempted suicide (n = 4) had a diagnosis of BPD. However, as the authors note, the very small sample size limits the scope of their findings. Papolos, Hennen, and Cockerham (2005) found several items on the Child Bipolar Questionnaire (CBQ), including “excessive
anxiety/worry,” were associated with parent-reported suicidal threats in children and adolescents.

In an initial study, adult patients in the STEP-BD study with lifetime anxiety comorbidity were found to have an elevated risk for suicide attempts (Simon et al., 2004). The authors conclude that further research is needed, but suggest patients with comorbid anxiety may be less capable of tolerating negative affect and may be less likely to utilize social supports or cognitive strategies (Simon et al., 2004). The authors followed up on these results with a more thorough evaluation of the relationship between anxiety disorder comorbidity, BPD, and suicidality. They found lifetime anxiety comorbidity doubled the odds of a lifetime suicide attempt, and current anxiety comorbidity was associated with more than double the odds of current suicidal ideation (Simon et al., 2007).

Patients with a current anxiety disorder also were more likely to believe that their problems would be solved if they committed suicide. However, the authors speculated that BPD severity may be associated with increased suicidality, as opposed to anxiety comorbidity itself. Since patients with current anxiety comorbidity were more likely to have a younger age of onset of BPD, once age at first mood episode was controlled for in comparisons of BPD patients with anxiety disorders to those without anxiety disorders, lifetime comorbidity no longer was related to lifetime suicide attempts. Additionally, current suicidal ideation was no longer associated with a current anxiety diagnosis once current bipolar state was controlled for. Nonetheless, the Suicide Behaviors Questionnaire (SBQ) score,
which assessed past and current suicidal ideation, beliefs and suicide and future plans, was significantly higher for patients with current anxiety comorbidity than those without, even after controlling for current bipolar state. The authors assert these mixed findings did not allow them to determine the direction of the relationship between suicidal ideation, anxiety disorders, and bipolar disorder, but they theorize that anxiety comorbidity may be a marker for a more severe phenotype of BPD, including early age of onset, greater severity of symptoms, and higher risk of suicidality (Simon et al., 2007).

**Anxiety**

Anxiety has also been speculated to contribute to suicidal behavior in adolescents. For instance, Allan and colleagues (1998) hypothesize that a subgroup of “anxious-suicidal” youth exist who present with significant impairment and are also at risk for self-harm. Allan and colleagues (1998) identified this subgroup among a group of suicidal children using the RCMAS, and found that they experienced a greater number of adverse life-events, had poorer social skills, and had more self-described hostile and anxious parents. In a study by Ghaziuddin, King, Naylor, and Ghaziuddin (2000), RCMAS scores were found to account for 24% of the variance in the Suicidal Ideation Questionnaire-Junior high school version (SIQ-JR), and CDRS-R scores accounted for 55% of the variance. Finally, the authors found that both the self-reported RCMAS and clinician-rated Anxiety Rating Scale for Children (ARC) scores were correlated with CDRS-R and SIQ-JR. Clinician-rated suicidality scores, the Spectrum of Suicidal Behavior (SSB), were
not correlated with any of the anxiety or depressive symptom scores. The authors concluded that, “depression and anxiety not only go hand in hand but the evaluation of suicidal behavior is likely to be more complete when both depression and anxiety are included in the assessment” (Ghaziuddin et al., p. 117).

_Treatment Response_

Despite knowledge that comorbidity can significantly change treatment outcome, few studies have examined the effect of comorbidity on treatment interventions. Emslie, Mayes, Laptook, and Batt (2003) assert that determining which children respond to which treatments, or treatment moderators, would greatly improve outcomes and have lifelong impact for patients with mood disorders. Below, I discuss the effect of comorbid anxiety on the treatment of children with mood disorders; first, medications, then therapy.

_Medication Treatment_

_Depression_. Few studies currently exist of medication response in children with comorbid mood and anxiety disorders. For adults with comorbid anxiety and depression, Dunlop and Davis (2008) argue for the use of combination treatment of benzodiazepines and SSRI s to allow for more rapid relief of anxiety symptoms, reduction of early SSRI-induced anxiety or agitation, improved adherence, and improved control of situational anxiety. Even in adults, Sekula, DeSantis, and Gianetti (2003) assert, “until further research is available regarding any differential treatment of comorbid depression and anxiety, definitive guidelines cannot be documented” (p. 30). The authors suggest beginning treatment with an SSRI, then,
if there is no response, the prescriber should consider augmentation with a second
drug, or a trial with a different SSRI or a different class of antidepressants.
Psychoeducation is necessary when prescribing medications for individuals with
comorbid anxiety and depression, including education about conceptual models of
the disorder, the role of medications, and side effects. A strong alliance with the
clinician is helpful (Sekula et al., 2003).

Pini and colleagues (2003) examined the effect of comorbid anxiety
disorders in adults with depression on treatment with paroxetine and moclobemide.
They split their sample into three groups: patients with comorbid panic disorder (n
= 32), patients with comorbid GAD (n = 80), and patients with comorbid “other
anxiety disorders” (n = 11). Both medication groups (the patients given paroxetine
versus those given moclobemide) experienced significant reductions of symptoms
of depression and anxiety. However, when compared across anxiety diagnosis,
paroxetine was superior to moclobemide in reducing symptoms of depression and
anxiety in the panic disorder group (Pini et al., 2003).

In treatment guidelines for childhood depression, the authors elected not to
develop a specific treatment algorithm, but “rather this was left to the individual
clinician’s discretion” (Hughes et al., 1999, p. 1449). The authors state that since
the pharmacotherapy literature on childhood anxiety disorders “has been
disappointing,” comorbid anxiety disorders may be more appropriately addressed
with psychotherapies. More recently, as SSRIs are a first-line medication treatment
for children with anxiety disorders (Baldwin et al., 2005) and depression (Birmaher
& Brent, 2002), they represent a promising first choice medication in addressing both sets of symptoms (Hughes et al., 2007). Finally, psychotherapy, particularly cognitive behavior therapy (CBT), is recommended for youth (Hughes et al., 2007).

A few studies examined the effects of depressive comorbidity on response in children with anxiety disorders. A 12-week, open label study found paroxetine effective in reducing children’s symptoms of OCD (as measured by the Maudsley Obsessive Compulsive Inventory; MOCI), and improving Clinical Global Impressions- Severity of Illness (CGI-SI), and Children’s Depression Inventory (CDI) scores. Although 11/42 patients had MDD, there was no significant difference in mean changes in MOCI and CGI-SI scores at week twelve between children with and without MDD. Further, anxiety symptoms and depressive symptoms decreased with the treatment of paroxetine, despite the presence of comorbid anxiety and depressive diagnoses (Diler & Avci, 2000). In another study of children with OCD, patients treated with sertraline showed significantly greater improvement than placebo-treated patients on the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS), the NIMH Global Obsessive Compulsive Scale (GOCS), and the NIMH Clinical Global Impressions of Improvement (CGI-I) rating scales. In the sertraline group, 21% presented with comorbidity, including ADHD, 7%; Tic disorder, 5%; another anxiety disorder, 2%; and depression, 2%. In the placebo group, 18% presented with comorbidity, including ADHD, 3%; Tic disorder, 3%; anxiety, 5%; and depression, 2%. Effects were found after only three weeks and continued to end of the 12 week follow-up.
Comorbidity did not have an effect on treatment response. It is noteworthy that only two percent of the sample had a comorbid depressive disorder, however (March et al., 1998).

*Bipolar disorder.* According to current treatment guidelines, psychopharmacology is the primary treatment for children with BPD (McClellan et al., 2007). However, several complications can arise when faced with concomitant symptoms of anxiety and BPD. Although SSRIs are considered a first line medication treatment for children with anxiety (Baldwin et al., 2005), when they are prescribed for patients with anxiety comorbid with BPD, some researchers suggest there is a danger of an antidepressant-induced manic switch (Apter et al., 2003; Keck, Strawn, & McElroy, 2006; Keller, 2006). Go, Malley, Birmaher, and Rosenberg (1998) document evidence of fluoxetine-induced mania in 30% of treated patients with OCD and comorbid mood disorders. Therefore, often other options must often be considered. In adults, atypical antipsychotics have shown to have a beneficial effect on anxiety disorders (McIntyre & Katzman, 2003). Keck and colleagues (2006) conducted a literature search and found mostly case reports and open label studies on anxiety disorder response to mood stabilizers and atypical antipsychotics, but no specific studies targeting patients with anxiety and co-occurring mood disorders. They conclude the initial goal for patients with BPD and co-occurring anxiety should still be mood stabilization. Ideally, the prescriber should find a medication which also targets the anxiety disorder; but given the
limited data, “this goal presents a common clinical challenge” (Keck et al., 2006, p. 8).

In the 2005 treatment guidelines for children with BPD, Kowatch and colleagues also advise prescribers to first stabilize the child’s BPD symptoms, and then address anxiety concerns. “It is important to emphasize that there are very few controlled studies for the treatment of comorbid disorders in youth with BPD and that almost all the literature is anecdotal” (Kowatch et al., 2005, p. 226). Treatment plans must be modified to include comorbid anxiety disorders, and all comorbid disorders must be monitored over time. Once the mood has been stabilized, if the patient’s comorbid anxiety symptoms continue to cause significant impairment, that disorder must be addressed. Cognitive-behavioral therapy (CBT) is recommended as the first adjunctive treatment, followed by SSRIs if the former is not available or not effective in ameliorating anxiety symptoms.

Henry and colleagues (2003) examined the impact of anxiety disorders on BPD adults’ response to mood stabilizers (lithium and anticonvulsants). The researchers found although the patients with lifetime comorbid anxiety disorders (24%) did not show greater illness severity (i.e., number of hospitalizations, psychotic symptoms, alcohol and drug use, suicide attempts), they responded significantly less well to anticonvulsant medications than patients without comorbid anxiety disorders. Both groups responded equally well to lithium. The researchers concluded, “Ours is the first study that has dealt with the impact of
anxiety comorbidity as a whole on the outcome of bipolar disorder” (Henry et al., 2003, p. 334).

Tohen and colleagues (2007) examined the effect of comorbid anxiety on adults with bipolar depression. This was part of an 8-week, double-blind, randomized placebo-controlled study of the effectiveness of the combination of fluoxetine and olanzapine. The patients with comorbid anxiety (43%) were more likely to have a history of suicide attempts and a higher use of concomitant benzodiazepine use. They also had significantly higher scores on the Montgomery-Asberg Depression Rating Scale (MADRS) and on the Young Mania Rating Scale (YMRS) at baseline and were less likely to achieve response and remission regardless of treatment group. The researchers found in the comorbid anxiety population, as with the full sample, combination treatment with olanzapine-fluoxetine was significantly more effective in reducing symptoms of anxiety and depression (Tohen et al., 2007).

Looking at baseline data from STEP-BD, Simon and colleagues (2004) found in patients with BPD, the presence of comorbidity was only minimally associated with pharmacotherapy, and medications to specifically target the comorbidity were particularly uncommon. This suggests patients with BPD may infrequently treat their comorbid conditions with pharmacotherapy. The authors found similar results looking specifically at anxiety disorders. Most patients with a current comorbid anxiety disorder were not taking anxiety-specific pharmacotherapy. The authors concluded that perhaps this lack of treatment of
comorbid conditions may have occurred for a number of reasons, including lack of focus on comorbidity by the clinician, concerns of the risk of treating patients with medications such as antidepressants or benzodiazepines, a preference for psychosocial treatments by the clinician, or treatment noncompliance by the patient (Simon et al., 2004).

In a naturalistic sample of routine clinical practice in Italy, 20 of 40 children with BPD were classified as “responders” according to their Clinical Global Impression—Improvement (CGI-I) scores. All patients were treated with mood stabilizers; some received antidepressant treatment. Comorbid anxiety disorders, including panic disorder, OCD, and social phobia (found in 72.5% of the full sample) were not found to be significant predictors of nonresponse (Masi et al., 2004). In a retrospective, naturalistic study of children and adolescents with OCD, Masi and colleagues (2007) reported that those with comorbid BPD were found to have an overall poorer response to treatment compared to those without comorbid BPD. However, final analyses showed comorbidity with ODD and conduct disorder to be significant predictors of negative treatment outcome. Therefore, the authors hypothesized that the more frequent occurrence of disruptive behavior disorders in the subset of patients with comorbid BPD led to poorer treatment response, rather than the BPD itself. Further, patients with comorbid BPD received more mood stabilizers compared to patients without BPD. Thirty percent of the comorbid BPD individuals did not receive SSRIs due to fear of a pharmacological-induced mania (Masi et al., 2007).
Conclusions. Several conclusions can be drawn from existing psychopharmacology studies of patients with depression and BPD and comorbid anxiety. First, patients with comorbid anxiety disorders frequently present with greater morbidity and impairment at baseline. Some studies suggest they are more likely to be taking a higher number of medications, while other studies, such as STEP-BD, suggest they do not treat comorbid anxiety disorders with medications. Second, patients may be less likely to achieve remission, and therefore, may be more difficult to treat. Third, some medications may be effective in reducing symptoms of patients with comorbid anxiety and mood disorders, including paroxetine for depression, and lithium and olanzapine-fluoxetine combination treatment for BPD. SSRIs are a promising medication treatment for patients with comorbid anxiety and depression, but they may exacerbate manic symptoms in patients with BPD and comorbid anxiety. Fourth, much more research on the effects of psychopharmacology in individuals with comorbid anxiety and mood disorders, especially in children, is warranted. Fifth, psychotherapy in addition to medications is recommended.

Therapy

Several studies examined the effect of comorbid anxiety on treatment outcome in patients with mood disorders. No studies examined programs specifically designed for patients with mood disorders and comorbid anxiety, but all looked at anxiety comorbidity as a potential moderator of treatment. As discussed above, patients with mood disorders and comorbid anxiety are found to
be more ill and have higher levels of impairment, suicidality, and a worse treatment course (e.g. Frank et al., 2002; Lee & Dunner, 2008).

*Depression.* Psychotherapy provides an important component in the treatment of children with mood disorders. In a cost-effectiveness analysis of adults with mood disorders, Antonuccio, Thomas, and Danton (1997) found CBT alone to be the most cost-effective choice. Over the course of two years, fluoxetine showed 33% higher costs, and combination treatment showed 23% higher costs than CBT alone. The authors concluded, “When long-term outcome for depression is considered, it appears that CBT may be more clinically effective and more cost-effective than antidepressant medication alone” (Antonuccio et al., 1997, p. 204). Although conducted with adults, this study suggests the importance of including therapy in the treatment of mood disorders. No health economic studies have been conducted with children with mood disorders.

The Treatment for Adolescents with Depression Study (TADS), a National Institute of Mental Health-funded, multicenter, randomized, masked trial that compared the effectiveness of fluoxetine alone, CBT alone, CBT plus fluoxetine, and placebo, provides support for combination treatment (TADS Team, 2004). CBT plus fluoxetine led to the highest rates of response, followed by fluoxetine alone, then CBT alone, and finally placebo, with response rates of 71.0%, 60.6%, 43.2%, and 34.8%, respectively (TADS team, 2004). The authors also found that patients who were less severely impaired responded better to acute treatment (week 12). Specifically, patients with mild or moderate depression on the CGI-S had
better results with CBT plus fluoxetine than fluoxetine alone or CBT alone. CBT alone and placebo showed no difference based on severity of baseline symptoms. Patients with severe levels of depression responded equally well to CBT plus fluoxetine and fluoxetine alone. For these patients, CBT and placebo did not differ (Curry et al., 2006). Also, patients with comorbid anxiety disorders benefited less from acute intervention (Curry et al., 2006). Long-term outcomes of patients with comorbid anxiety disorders are not yet published, but by week 24, all three active treatments (CBT plus fluoxetine, fluoxetine alone, and CBT alone) showed similar remission outcomes (Kennard et al., 2009).

Brent and colleagues (1998) examined three psychosocial treatments for adolescent depression: CBT, systematic-behavioral family therapy (SFT), and nondirective supportive therapy (NST). Overall, they found CBT resulted in a more rapid and complete relief of depression symptoms compared with those treated with SFT or NST. They later examined the predictors of treatment outcome, including comorbid anxiety disorders. They found comorbid anxiety predicted depression at the end of acute treatment. They also found comorbidly anxious patients responded better to CBT than the other two treatments. The researchers theorized that patients with comorbid anxiety disorders may exhibit shared cognitive distortions, which CBT targets. Further, patients with comorbid anxiety disorders and depression would benefit from treatments targeted to both conditions (Brent et al., 1998). Treatment did not have any acute effects on anxiety symptoms. At 24-month follow-up, however, CBT and NST tended to be
associated with a more consistent reduction in anxiety symptoms compared to SFT (Kolko, Brent, Baugher, Bridge, & Birmaher, 2000).

Rohde and colleagues (2001) examined the effect of comorbidity on a CBT group treatment for adolescent depression, the Adolescent Coping with Depression Course (CWD-A), hypothesizing that comorbidities “negatively effect treatment in various ways” (p. 795). The researchers found depressed adolescents with comorbidity, anxiety disorders in particular, entered the study more depressed and more functionally impaired than adolescents with depression and no comorbidity. However, the researchers found comorbid anxiety disorders had no impact on course of recovery or recurrence of their depressive disorder. In fact, the researchers observed, “Comorbid anxiety disorder was associated with better outcome, as measured by reductions in depression scores (BDI) during treatment,” a finding probably due to comorbidly anxious patients’ higher scores of depression pre-treatment (Rohde et al., 2001, p. 801-802). Thus, the authors conclude that comorbid anxiety disorders did not have an impact on treatment outcome, and, if anything, patients with comorbid anxiety had greater improvements in depression symptoms. Importantly, however, post-treatment and at the end of follow-up, Global Assessment of Functioning scores (GAF) in patients with comorbid disorders were lower than in patients without comorbidity. This suggests the remaining functional impairment in comorbid patients may require supplemental treatments targeted towards the comorbid disorder. For this specific analysis, the
researchers did not analyze specific comorbid diagnoses separately, but rather looked at youth with and without any comorbidity (Rohde et al., 2001).

A final study by Young and colleagues (2006) examined the impact of comorbid anxiety in an effectiveness study of Interpersonal Psychotherapy for Depressed Adolescents (IPT-A). The authors hypothesized that, first, comorbidly anxious adolescents would have higher depression scores and worse functioning at baseline than adolescents without anxiety. Replicating Rohde and colleagues’ (2001) finding, patients with comorbid anxiety disorders had more severe depression at study entrance; however, they did not have greater functional impairment. The authors suggested that adolescents without comorbid anxiety had other comorbid conditions that affected their functioning. Second, they hypothesized comorbidly anxiety adolescents will have higher depression scores and worse functioning post-treatment. They found that patients with and without comorbid anxiety had similar levels of functioning post-treatment, but patients with comorbid anxiety had higher depression scores post-treatment than patients without comorbid anxiety. The authors asserted, “This suggests that the depression in these comorbid adolescents is not only more severe but also more difficult to treat than uncomplicated depression” (Young et al., 2006, p. 909).

Third, Young and colleagues (2006) hypothesized that IPT-A would be more effective than control (usual care) in treating depression in comorbidly anxious adolescents. As hypothesized, patients with comorbid anxiety disorders and depression treated with IPT-A had significantly lower depression scores post-
treatment compared to usual care, a finding not detected in the group without comorbid anxiety. Specifically, the presence of comorbid anxiety disorders appeared to magnify differences between IPT-A and usual care. Finally, the authors hypothesized that anxiety would improve during the course of treatment. The authors also found as a whole, anxiety did not decrease significantly post-treatment, although patients who no longer met criteria for an anxiety disorder post-treatment reported better overall functioning and depressive symptoms. Young and colleagues postulate depression and anxiety may improve together. The authors suggest, “For patients with mild to moderate anxiety, it may not be necessary to tailor the depression intervention to address the anxiety” (Young et al., 2006, p. 911).

Thus, findings from the TADS study suggest psychotherapy plus medication appears to be the treatment of choice for adolescents with depressive disorders as indicated by Curry and colleagues (2006). Future research is required to determine the most efficacious treatments for depression in children and adolescents. Mixed results exist from treatment studies of youth with depression and comorbid anxiety disorders. Patients with comorbidity tend to enter treatment more severely depressed. Depressive and anxious symptoms may improve together. CBT and IPT-A may be effective treatments for patients with depression and comorbid anxiety, although this may be a result of more severe symptoms at baseline. Debate exists as to whether supplemental treatments to target anxiety symptoms are necessary in addition to the treatment for depression.
Bipolar disorder. Treatment guidelines describe psychotherapeutic interventions as an essential component of treatment for children with BPD, stating “a comprehensive, multimodal treatment approach that combines psychopharmacology with adjunctive psychosocial therapies is almost always indicated for early-onset BPD” (McClellan et al., 2007, p. 120). Psychosocial treatment should include psychoeducational therapy, relapse prevention, individual psychotherapy, social and family functioning, academic and occupational functioning, and community consultation (McClellan et al., 2007). Comorbid anxiety disorders, in particular, may require psychotherapy, as a balance must be drawn between pharmacological treatments such as SSRIs, which may trigger manic or mixed episodes. Acknowledging this, Kowatch and colleagues (2005) conclude, “Currently, there are very few other pharmacological alternatives for the management of anxiety symptoms in patients with BPD” (p. 228).

Feske and colleagues (2000) examined the effect of comorbid anxiety symptoms on adults diagnosed with Bipolar I Disorder (BP-I). Patients were randomly assigned to acute-phase treatment with either interpersonal social rhythm therapy (ISRT) or intensive clinical management (ICM). Pharmacology guidelines were constant across treatment conditions. Preliminary analyses of treatment effects revealed no significant differences between patients treated with ISRT and ICM on outcome variables, including remission status and time to remission. Therefore, for the current analyses of comorbid anxiety symptoms, the authors did not control for treatment group, but rather grouped ISRT and ICM participants together.
Interestingly, the researchers found, the 45.2% of patients who experienced anxiety symptoms required a larger total number of medications, particularly patients with panic attacks. Patients with a history of anxiety and panic attacks also reported more side effects. Further, a history of panic attacks was associated with nonremission, and anxiety symptoms were associated with a longer time to remission. The authors suggest patients with comorbid anxiety symptoms should receive psychotherapies that have components that specifically target the anxiety symptoms in addition to medication (Feske et al., 2000).

*Treatment components.* No studies have specifically examined a treatment catered to children with mood disorders and comorbid anxiety disorders (Manassis & Monga, 2001). However, several researchers have theorized about necessary components of such a treatment for patients with concomitant anxiety and depression. Hudson, Krain, and Kendall (2001) discuss this issue from the perspective of clinicians at the Child and Adolescent Anxiety Clinic, working with children with anxiety disorders and comorbid disorders. They assert their experience suggests more complicated comorbid cases are more time-consuming, and force the therapist to be creative and work flexibly with the treatment manual; in their case, Kendall’s (1992) Coping Cat Therapist manual. Kendall et al. (1992) state, “A range of cognitive and behavioral interventions have been developed to address anxiety and depression separately, but there are currently no outcome data on the treatment of children comorbid for anxiety and depression” (p. 875).
It is more common to find patients suffering from anxiety disorders without depression, but somewhat uncommon to find patients with depression and no anxiety; therefore, therapists working with children with depression will more often have to adapt their treatment protocols. Further, children comorbid with anxiety and depression have very different presentations, so clinicians should be prepared to design and implement treatments adjusted for each child’s individual symptom profile (Kendall et al., 1992). Kendall and colleagues describe several important treatment components, including affective education, behavioral procedures, cognitive interventions, and peer and parental involvement. With affective education, or helping the child differentiate between feelings, the child may require help learning a wider range of feelings, including positive and negative emotions. Further, the therapist should consider that while thoughts related to depression tend to be global, thoughts of anxiety are more situation-specific. Therefore, thoughts and feelings of anxiety may not be as readily accessible depending on the type of anxiety disorders.

Behavioral procedures typically involve relaxation training, enactive programming, and reinforcement. For comorbid children, relaxation training should both involve control of physiological arousal and the pleasurable aspects of relaxation. Enactive programming differs for anxious and depressed children. Anxious children are taught to overcome fears of threat and an inability to cope, while depressed children gradually develop competency through “mastery experiences that require the child to experience only a modest amount of the
negative emotional state” (Kendall et al., 1992, p. 876). Depressed children also practice scheduling and engaging in pleasurable activities. Therefore, behavioral procedures are different for depression and anxiety children, and Kendall and colleagues (1992) offer several suggestions. For instance, clinicians can separate the anxiety and depression components, perhaps treating the more impairing one initially. Children can participate in both exposure to anxiety-provoking situations, and hypothesis-testing experiments regarding their beliefs about themselves (Hudson et al., 2001). Cognitive interventions should be directed to help comorbidly anxious and depressed children more realistically self-evaluate. For instance, cognitive restructuring can focus on both threat-related self-talk and on loss and/or hopeless and self-blaming cognitions (Hudson et al., 2001). The last component discussed by Kendall and colleagues, peer and parental involvement, has significant overlap in treating anxious and depressed children. Social skills training, including encouraging the child to engage with peers (Manassis & Monga, 2001) and parental involvement can help both anxious and depressed children, and particularly comorbidly anxious and depressed children (Kendall et al., 1992).

Manassis and Monga (2001) suggest several important concepts for therapists working with children with anxiety and other comorbid disorders. They propose structured diagnostic interviews and involving children and parents in identifying and prioritizing symptoms. Increasing structure in the home can be helpful, as children with anxiety disorders and comorbid conditions are often susceptible to unpredictability. Children with anxiety disorders often have highly
anxious parents, so careful communication with families is necessary, including identifying clear objectives and monitoring treatment progress throughout. Communication with schools is important, as academic impairment is common.

*Psychoeducational psychotherapy.* In addition to the important components of treatment discussed above, current treatment guidelines for depression and BPD in children advocate for psychoeducation in addition to medication and psychotherapy. McClellan and colleagues (2007) state psychoeducational therapy should provide information to the patient and family about symptoms and course of the disorder, treatment, impact of BPD on family functioning, and the heritability of BPD. In their treatment algorithm, Hughes and colleagues (1999) assert psychoeducation is “a critical element of medication treatment” (p. 1443). Ginsburg and colleagues (2005) claim that regardless of what type of treatment is implemented, psychoeducation remains a crucial part of treatment. They define psychoeducation as the teaching of critical information about the disorder, its symptoms, course, and treatment information, including “current standard of care …, essential components of treatment, time demand, duration, adherence, potential benefits and risks, management of treatment compliance or side effects, and management of no or partial response” (p. 257).

Klaus and Fristad (2005) assert that psychoeducational psychotherapy should contain three important components: education, support, and skill-building, and should help decrease environmental stress, such as expressed emotion (Fristad, Gavazzi, & Mackinaw-Koons, 2003; Klaus & Fristad, 2005). Psychoeducational
psychotherapy, adjunctive to current treatment, teaches families about the
symptoms of BPD as well as its biopsychosocial management, which includes
improving family problem solving and communication skills to better manage
symptoms. Goldberg-Arnold, Fristad, and Gavazzi (1999) found their
psychoeducational psychotherapy treatment program for children with mood
disorders (MF-PEP) led to improved knowledge, specific skills, and support in
parents, and that some improvements (e.g., increased knowledge, perception of
social support) were found immediately following treatment for most families.

Fristad, Verducci, Walters, and Young (2009) found that youth who
received treatment with MF-PEP had a significantly greater decrease in mood
severity index (MSI) scores at follow-up compared to waitlist control. This
symptom improvement appeared to be maintained through the 18-month follow-up
period. The waitlist group experienced similar improvement after they received
treatment. In further analyses, Mendenhall, Fristad, and Early (2009) found that
participation in MF-PEP improved service utilization by participating families (as
indicated by increases in clinician-rated quality of services), which was mediated
by increased parental knowledge and beliefs about treatment. Further,
improvements in service utilization mediated the relationship between participation
in MF-PEP and improvements in MSI scores. Thus, psychoeducation appears to be
a valuable tool for the treatment of children with mood disorders.
Treatment for Anxiety Disorders

A full discussion of the literature on the treatment for anxiety disorders is far beyond the scope of the dissertation. However, in this section, I very briefly discuss some components necessary for the treatment of anxiety in childhood. Current treatment guidelines for anxiety disorders call for a multimodal approach, including consideration of parent and child education about the anxiety disorder, consultation with school and physicians, possibly pharmacotherapy, and psychotherapy. Treatment guidelines also suggest that treatment of childhood anxiety disorders, at least those of mild severity, should begin with psychotherapy (Connolly et al., 2007). Exposure-based CBT is by far the most-widely researched and utilized treatment for childhood anxiety disorders (Compton et al., 2004), particularly the Coping Cat Program, designed for children with SAD, GAD, and social phobia (Kendall, 1990). Albano and Kendall (2002) describe five components of CBT for childhood anxiety disorders: psychoeducation, somatic management skills training, cognitive restructuring, exposure methods, and relapse prevention plans. Exposure, in particular, is useful for the treatment of childhood anxiety disorders because anxious children tend to avoid rather than approach fearful stimuli. Avoidance prevents the child from learning that: (1) negative events are not as likely as s/he may have thought; (2) a feared consequence is less likely and less negative than anticipated; and (3) s/he can cope with the feared stressor (Kendall, Aschenbrand, & Hudson, 2003).
Silverman and Pina (2008) conducted a literature review on the efficacy of treatments targeted to specific phobia and found four, all of which involved the use of graded behavioral exposures. These included emotive imagery for darkness phobia (Cornwall, Spence, & Schotte, 1996), in vivo exposures for spider phobia (Muris, Merckelbach, Holdrinet, & Sijsenaar, 1998), exposures with contingency management or self-control (Silverman et al., 1999), and one-session in vivo exposure for various fears (Ost, Svensson, Hellstrom, & Lindwall, 2001). In their review, Silverman, Pina, and Viswesvaran (2008) describe Group CBT and social effectiveness training for children with social phobia was “probably efficacious.” Panic disorder may be best treated with Panic Control Treatment (Barlow, 1988; Barlow, Gorman, Shear, & Woods, 2000), which Ollendick (1995) and Hoffman and Mattis (2000) have adapted for adolescents. Key components include correcting misinformation about panic, breathing retraining, cognitive restructuring, and interoceptive and in vivo exposure. Findings have shown these techniques to be successful in reducing panic symptoms (Ollendick and Pincus, 2008).

For OCD, CBT with exposure and response prevention is the most empirically supported treatment modality in youth (Storch et al., 2008). In their review, Barrett, Farrell, Pina, Peris, and Piacentini describe exposure-based CBT as a “probably efficacious” treatment. The goal of exposure-based CBT is to teach the individual that, with repeated exposure to the feared object or behavior, the obsession-triggered anxiety will dissipate. As the individual reaches habituation,
s/he learns that the “feared consequences of not ritualizing will not materialize” (Barrett et al., 2008, p. 133). For youth with PTSD, exposure-based CBT appears to represent the “best practice” based on the current literature (La Greca, 2008). Silverman, Ortiz, and colleagues (2008) described Trauma-Focused CBT as a “well-established” treatment for traumatized youth. Trauma-Focused CBT should contain the following components: working with children individually; training in cognitive and behavioral procedures; and conducting some form of exposure with the children, perhaps through imaginal exposure or constructing narratives. Thus, several treatments for anxiety disorders have shown efficacy in the research literature. Many, if not all, require some form of exposure to best target specific anxiety symptoms. These findings should be considered in light of the current study.

Two studies examined the effect of comorbid depression on treatment for childhood anxiety disorders. Barrett, Dadds, and Rapee (1996) compared CBT to CBT with a family anxiety management program to a waitlist control for treatment for childhood anxiety. Although both treatment conditions were significantly more efficacious than the waitlist, the CBT plus family treatment was significantly better than CBT alone on a number of the study’s measures. Treatment effects on depressive symptomatology were measured via the CDI; no difference was noted between the waitlist and treatment conditions post-treatment and at follow-up. The authors noted CDI scores were below the clinical level, so it was not surprising that no statistically significant changes in scores occurred. Only six percent of the
children had comorbid depression, which explains the low occurrence of depressive symptoms in their sample (Barrett et al., 1996).

Mendlowitz and colleagues (1999) examined the effect of parental involvement in a CBT group treatment for childhood anxiety disorders. They had three groups – parent-only, child-only, and parent and child. They found all three treatment groups had a decrease in depressive and anxiety symptoms, while waitlist groups showed no decrease. Unlike Barrett and colleague’s study, Mendlowitz and colleagues found a decrease in CDI scores as a result of treatment. This occurred despite few concurrent depression diagnoses and generally low CDI scores in all groups. The authors speculated treatment may result in higher senses of self-efficacy due to better coping among the children, resulting in lower CDI scores. The authors also observed the high occurrence of worry symptoms on the CDI, which may have confounded anxiety and depression in the study (Mendlowitz et al., 1999).

**Current Study**

Psychoeducational psychotherapy is strongly recommended for the treatment of children with MDD or BPD and comorbid anxiety disorders. As discussed above, these comorbid children and their families are often faced with an earlier age of onset of problems, possibly a more severe illness course, higher risk for suicidality, and the challenge of managing treatment for at least two distinct and impairing disorders, anxiety and depression/BPD. Although MF-PEP’s focus is on the treatment of children with mood disorders, comorbidity is addressed in
treatment. As discussed above, anxiety disorders frequently require specific
treatments targeted to address anxiety symptomatology, such as exposure.
However, many components of MF-PEP are useful to managing anxiety symptoms,
as well. Treatment programs for anxiety that implement family participation were
found to led to a more rapid reduction of anxiety symptoms in anxious children
than CBT alone (Wood, Piacentini, Southam-Gerow, Chu, and Sigman, 2006). A
goal of MF-PEP is to help patients select more appropriate treatments to target their
mood disorder, and comorbidities as well. I believe MF-PEP will be useful in
reducing the number of anxiety symptoms post-treatment by providing patients
with CBT strategies that are crucial in the treatment of both anxiety and mood
disorders, as well as helping patients select appropriate adjunctive treatments. MF-
PEP provides families with techniques that address anxiety symptoms as well as
mood symptoms. Parents are provided with basic information about comorbid
disorders and symptoms in the first session of MF-PEP. Families learn to better
manage and track their child’s medications and to manage systems of care,
including school and treatments teams. This may be particularly helpful to children
with comorbid anxiety, who may present with greater impairment and
symptomatology. MF-PEP’s discussion of symptoms management, coping skills,
and family communication may also be helpful in reducing both mood and anxiety
symptoms. Children practice identifying feelings, learn about medications, and
create a Tool Kit to help regulate their moods. They also practice social skills
training and learn CBT techniques, all of which are helpful in the treatment of anxiety symptoms as well as mood symptoms.

Thus, MF-PEP provides families with strategies to address mood symptoms that are hypothesized to be also helpful in reducing anxiety symptoms. Nonetheless, MF-PEP is a treatment geared towards mood disorders and lacks some treatment components identified as particularly crucial to addressing anxiety symptoms and disorders. MF-PEP does not provide somatic management skills training or exposure methods, which are considered important for the treatment of anxiety disorders (Albano and Kendall, 2002). MF-PEP’s cognitive behavioral techniques are not specific to anxiety symptoms, and families may have difficulty applying these strategies to different disorders. Thus, although I believe MF-PEP will help families in reducing their overall number of anxiety symptoms, I believe children with comorbid anxiety disorders may continue to have greater impairment and symptomatology after MF-PEP compared to children without comorbid anxiety.

Furthermore, although the consensus of the current research suggests comorbid anxiety disorders complicate treatment and worsen prognosis of mood disorders, leading to greater impairment, no researchers have currently suggested or tested a model as to why (Keller, 2006; McIntyre, Soczynska, Bottas, Bordbar, Konarski, & Kennedy, 2006). El-Mallakh and Hollifield (2008) acknowledge that the co-occurrence of anxiety disorders and bipolar disorder is associated with a poorer prognosis of bipolar illness and poorer functioning, but it is unclear if this is
“an expression of the pathology of two disorders, or an additive interaction of the existing disorders” (p. 145). Keller (2006) suggests, “Anxiety in patients with bipolar disorder tends to have an adverse affect by intensifying symptoms of bipolar disorder and other comorbid disorders, which consequently has a negative impact on the patients and on the course of the bipolar illness” (p. 6).

Since anxiety symptoms and mood symptoms are highly correlated in the literature, and anxiety symptoms tend to predict a worse course of illness and greater severity of depressive and manic symptoms, I believe that children with comorbid anxiety disorders will have poorer outcomes after MF-PEP compared to children without comorbid anxiety disorders. The mechanism through which I believe this will occur is poorer overall functioning. Mood disorders are particularly debilitating illnesses, and anxiety represents an additional, debilitating illness that can lead to much impairment for the patients in the home, at school, and with peers (Barrett, 1999; Wood, 2006). These impairments in functioning may cause greater stress for the family and may make engagement in treatment particularly difficult. MF-PEP is a positive first step in helping families select appropriate treatment and helping them learn to deal with their mood symptoms; however, patients with comorbid anxiety disorders particularly require additional treatment beyond MF-PEP to improve their overall functioning and achieve symptom remission.

The current study examined, first, demographic characteristics of the children with mood disorders and comorbid anxiety in the MF-PEP sample.
Research suggests these children may be more severely impaired, may require a larger amount of medications, and may suffer from greater illness severity and suicidality. Further, although several theories of the occurrence of mood and anxiety symptoms (e.g. Clarke and Watson’s Tripartite Model for anxiety and depression; frequent co-occurrence of BPD with panic disorder) have been proposed, we continue to know very little about the co-occurrence of these symptoms. Analyses at the symptom level could help clarify some questions about these co-occurrences. Also, as many symptoms of anxiety frequently co-occur with mood symptoms and many components of MF-PEP can be applied to anxiety symptoms, the current study examined the impact of MF-PEP on anxiety at the symptom level in the full sample. Finally, studies suggest individuals with mood and anxiety disorders may be more difficult to treat, although research is very mixed. I addressed many of these unanswered questions in this study.

I tested the following hypotheses on my sample.

**Description of the Sample**

1. Prevalence of the various anxiety disorders, including separation anxiety disorder, specific phobia, social phobia, generalized anxiety disorder, stress disorders (post-traumatic stress disorder and acute stress disorder), and obsessive-compulsive disorder will be explored in the full sample. The occurrence of these anxiety disorders will be compared between children with BPD and children with depressive disorders. In addition, rates of multiple anxiety disorders for children with depressive
spectrum and BPD spectrum disorders will document how many children with mood disorders have one or more than one anxiety disorder and the pattern of overlap among those anxiety disorders.

Comparisons of Children with Anxiety Disorders to Those without Anxiety Disorders

2. Compared to children without comorbid anxiety disorders, children with comorbid anxiety disorders will have at baseline:
   
   a. poorer functioning
   b. higher depression symptoms severity scores
   c. higher mania symptoms severity scores
   d. a larger number of medications prescribed
   e. greater amount of suicidality

Correlations with Anxiety Symptoms

3. At baseline, number of anxiety symptoms in the full sample will be significantly and:

   a. positively correlated with depression symptom severity scores
   b. positively correlated with mania symptom severity scores
   c. negatively correlated with measures of global functioning.

Effects of MF-PEP on Anxiety Symptoms

4. As many MF-PEP components may alleviate anxiety as well as mood symptoms, MF-PEP will be effective in reducing the number of anxiety symptoms, as demonstrated by a decrease in the number of anxiety symptoms.
symptoms at one year follow-up in the immediate (IMM) group compared to the waitlist control (WLC) group.

*Effect of Anxiety Diagnoses on MF-PEP Outcomes*

5. Children with comorbid anxiety disorders will experience slower rates of improvement in manic symptom severity scores compared to children without comorbid anxiety disorders.

6. Children with comorbid anxiety disorders will experience slower rates of improvement in depressive symptom severity scores compared to children without comorbid anxiety disorders.

7. Children with comorbid anxiety disorders will experience slower rates of improvement in global functioning compared to children without comorbid anxiety disorders.

*Effect of Anxiety Symptoms on MF-PEP Outcomes*

8. Greater anxiety symptomatology will predict slower rates of improvement in manic symptoms for children in MF-PEP.

9. Greater anxiety symptomatology will predict slower rates of improvement in depressive symptoms for children in MF-PEP.

10. Greater anxiety symptomatology will predict slower rates of improvement in global functioning for children in MF-PEP.
Chapter 2: Method

Participants

One hundred sixty-five children with mood disorders participated in the MF-PEP study. Each child had one or two parents, legal guardians and/or caregivers (hereafter referred to as parents) who participated as well. If two parents per family participated, one parent was selected to be the primary informant, and the other served as the secondary informant. Families were recruited in 11 sets of 15 families with a set being recruited every three months. Within each family set, seven families were randomized into immediate treatment (IMM) and eight families were randomized into a one-year wait-list control group condition (WLC). One family was erroneously assigned to IMM who should have been in WLC, resulting in 78 families participating in the IMM group, and 87 in the WLC group. All families received treatment-as-usual (TAU) throughout the study (i.e., they were encouraged to continue receiving any existing mental health or school-based services throughout their participation in MF-PEP, and make any changes to their treatment they felt were warranted). Figure 2.1 illustrates the size of the sample at the different time points during which assessments were conducted and treatment was received for the two groups.
Table 2.1 Sample size by group at each time point.

<table>
<thead>
<tr>
<th>Total Sample</th>
<th>Group</th>
<th>Time 1 Month 0</th>
<th>Time 2 Month 6</th>
<th>Time 3 Month 12</th>
<th>Time 4 Month 18</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Imm+ TAU</td>
<td>Baseline: Pre-treatment</td>
<td>Follow-up</td>
<td>Follow-up</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n = 78</td>
<td>n = 70</td>
<td>n = 61</td>
<td>n = 56</td>
</tr>
<tr>
<td></td>
<td>WLC+ TAU</td>
<td>Baseline</td>
<td>Follow-up</td>
<td>Pre-treatment</td>
<td>Follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n = 87</td>
<td>n = 74</td>
<td>n = 61</td>
<td>n = 53</td>
</tr>
</tbody>
</table>

*Note:* Imm + TAU = Immediate Treatment Group + Treatment As Usual; WLC = Wait-List Control + Treatment As Usual.

Participants were between the ages of 8 and 11 at study entry ($M = 9.9$, $SD = 1.3$). The mean age of participating parents was 40.8 ($SD = 7.8$) at baseline. Most (90.9%) of the children were White, 6.7% of the children were African American, 1.8% were mixed race, and 0.6% were Hispanic. A majority (73%) were male. The children’s IQ, assessed by the Kaufman Brief Intelligence Test (K-BIT), ranged from 71 to 148 ($M = 106.9$, $SD = 14.9$). The median family income of the sample was between $40,000 and $59,000 per year and ranged from less than $20,000 to over $100,000. All participants in the study were diagnosed with an
Axis I mood disorder; most (70%, n = 115) had a bipolar spectrum disorder. The remainder (30%, n = 50) were diagnosed with a depressive disorder, MDD or DD. Half met criteria for BP-I (n = 62; 37.5%) or BP-II (n = 22; 13.3%). The rest of the sample met criteria for BP-NOS (n = 29, 17.5%), Substance-Induced Mood Disorder (n = 1 within BP spectrum; n = 1 within depressive spectrum), Mood Disorder-NOS (n = 1), MDD (n = 38, 23%), DD (n = 5) and both MDD and DD (n = 6). Of the participants who met criteria for a depressive diagnosis (n = 50), 74% showed some symptoms of mania. All participants were diagnosed with a comorbid behavior disorder and/or a comorbid anxiety disorder (100 %, n = 165). Most (97%) were diagnosed with a comorbid behavioral disorder (e.g., ADHD, ODD) and 69% of the participants were diagnosed with a comorbid anxiety disorder (e.g. GAD, OCD).

Measures

The *Children’s Interview for Psychiatric Syndromes- Child and Parent Forms* (ChIPS, P-ChIPS; Weller, Weller, Rooney, & Fristad, 1999a; Weller, Weller, Rooney, & Fristad, 1999b) was administered to each parent and child to determine study diagnosis and comorbid disorders upon entry and at one-year follow-up. The ChIPS screens for 20 Axis I disorders and psychosocial stressors, and is based on the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV). Its reliability and validity as a diagnostic instrument in clinical research has been demonstrated in child and adolescent samples, age six to 18 years (Weller, Weller, Fristad, Rooney, & Schecter, 2000).
Besides providing information about the number and types of diagnoses, the ChIPS also provided information about number and types of symptoms, particularly of anxiety disorders for the purpose of this project. Cerel and Fristad (2001) discussed the technique of creating BAMO scores (Behavior, Anxiety, Mood, Other) from a structured interview. This technique was applied to the P-ChIPS and the ChIPS. Briefly, for each disorder, the number of symptoms was divided by the total number of possible symptoms of that disorder on the P-ChIPS and the ChIPS. This technique created standardized numbers, between zero and one, which allowed comparison between disorders. These scores were then summed across to create an index score for anxiety symptoms, an index score for depressive symptoms, and an index score of manic symptoms. The index score for anxiety symptoms included the symptoms from the following disorder categories on the P-ChIPS and the ChIPS: specific phobia, social phobia, SAD, GAD, OCD, and PTSD. This technique allowed for analyses of both categorical and dimensional data (Cerel & Fristad, 2001).

A Mood Disorder Timeline was generated for each child after every interview. The timeline incorporated information such as lifetime history of mood symptoms and episodes, psychosocial events, comorbid conditions, treatment history and response, and any other important information collected during a clinical assessment (Danner, Young, & Fristad, 2009).

The Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) was administered to each child upon study entry to estimate IQ. The K-BIT is
designed to assess intelligence in persons ages four through 90, and consists of three subtests, two which provide verbal intelligence through vocabulary and naming, and one which assesses nonverbal intelligence through various visuospatial exercises (Kaufman & Kaufman, 1990). The K-BIT has been shown to be a reliable and valid screening measure of verbal, nonverbal, and general intellectual ability (Naugle, Chelune, & Tucker, 1993).

The Children’s Depression Rating Scale - Revised (CDRS-R; Poznanski, Grossman, Buchsbaum, Banegas, Freeman, & Gibbons, 1984) and the Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler, & Meyer, 1978) were administered to each parent and child upon study entry and at each follow-up. The CDRS-R is conducted in interview format, and assesses the severity of 17 symptoms of depression. It has demonstrated good psychometric properties, showing adequate reliability and validity (Poznanski et al., 1984). The YMRS is an 11-item interview that assesses severity of manic symptoms. It has demonstrated good psychometric properties (Double, 1990; Fristad, Weller, & Weller, 1992; Fristad, Weller, & Weller, 1995; Youngstrom, Danielson, Findling, Gracious, & Calabrese, 2002). A mood severity index score (MSI) was then calculated from each child’s CDRS-R and YMRS score, with the formula: (CDRS-R score – 17 x 11/17) + MRS score. This formula takes in consideration the greater number of items on the CDRS-R and the scaling differences between the instruments (i.e., fact on the CDRS-R, a score of 1 indicates no symptoms, whereas on the YMRS, a score of 0 indicates no symptoms). MSI scores were operationally defined in terms
of mood severity, where scores of less than 10 represent minimal symptoms, 11 to 20 represent mild symptoms, 21 to 35 represent moderate symptoms, and greater than 35 indicates severe symptoms.

Suicidality ratings, another variable used in this study, were calculated by summing each participant’s scores on two questions on the CDRS-R that relate to suicidality and morbid ideation. The morbid ideation question ranged from 1 (“none”) to 7 (“preoccupied with death themes or morbid thoughts that are elaborate, extensive, bizarre and occur on a daily basis”). The suicidal ideation question also ranged from 1 (“understands the word suicide but does not apply to term to self”) and 7 (“has made suicide attempt within the last month or is actively suicidal”). Thus, the lowest possible suicidality rating was a 2 and the highest was a 14.

The Medication Usage Grid (Goldberg-Arnold, 1999) is a semi-structured parent interview that gathers information regarding the numbers and types of medications in the sample, as well as their perceived effectiveness and related side effects. This information was generated at the initial interview for each participant then reviewed at each time period to assess any changes (Goldberg-Arnold, 1999).

The Children’s Global Assessment Scale (C-GAS) is a clinician rating of global functioning based on assessment of a child’s school, home, and peers. The C-GAS ranges from one (indicating severely impaired functioning) to 100 (indicating very superior functioning) (Shaffer et al., 1983). Two clinical psychologists (blinded to group status) separately reviewed reports and then held a
consensus meeting to arrive at one C-GAS score. The C-GAS was completed upon study entry and at each follow-up. The inter-rater reliability between the two raters was substantial (kappa = 0.68). See Appendix A for the C-GAS rating scale.

Procedures

All assessments and MF-PEP group sessions occurred at the Ohio State University Child Mood Disorders Program. Trained interviewers, including child clinical psychology graduate students and postdoctoral trainees, administered assessments. Interviewer training included rating mock, videotaped, and live interviews. After establishing reliability (kappas ≥ .70), interviewers were videotaped performing live interviews. Interviewers could conduct interviews independently after establishing reliability of videotaped interviewers (kappas ≥ .70). To maintain reliability, 10% of all interviews were videotaped. Study reliability for the ChIPS was .82, and reliability for the P-ChIPS was .78. Study reliability for the CDRS-R was .68, and reliability for the YMRS was .71.

Children were recruited from health care providers, media coverage, and fliers, and word-of-mouth. After each participant completed phone pre-screening to determine if the child likely met diagnostic criteria for a mood disorder and if the child lived with one or more parent, the family was scheduled for a baseline assessment. Participants were paid to attend assessments, but not for treatment.

After the baseline assessment, the assessment team, including the principal investigator, project coordinator, and parent and child interviewers, met within 48 hours after the interview to determine study eligibility and diagnostic category (i.e.,
bipolar spectrum disorder or depressive spectrum disorder). The primary investigator determined study eligibility and diagnostic category based on the information described above, except in those cases where there were obvious reasons to disregard information from one informant (e.g., a child refused to answer questions seriously or a parent clearly provided exaggerated responses).

Balanced randomization was used after each set of 15 families completed their baseline assessment. Randomization was balanced to ensure that IMM and WLC had approximately equal distribution of mood diagnostic category, comorbid conditions (i.e., behavior disorders-present/absent; anxiety disorders-present/absent), and demographics. The project coordinator summarized these variables and the primary investigator (who was masked to other information) completed randomization.

Subsequently, the interviewers prepared a report summarizing their findings which was reviewed by two clinical researchers, both licensed psychologists, experienced in childhood mood disorders, at which time a precise diagnosis (e.g., bipolar disorder Type I, major depressive disorder + dysthymic disorder) was given.

Treatment

MF-PEP consisted of eight 90-minute sessions that began and ended with parents and children together. The majority of each session was held separately for parents and children. The child group was led by a group leader (a post-doctoral trainee or advanced level graduate student) and co-leader (an advanced level
graduate student). Each session covered a specific topic (see Appendix B for details). Although no one session was devoted strictly to anxiety comorbidity, comorbidity was discussed throughout group.

Each session began with a check-in meeting of parents and children, at which time they discussed projects assigned and issues from the previous week. Parent and child groups then separated to complete their particular goals, topics, and activities. After their “lesson of the day,” children received 15 to 20 minutes of social skills training via noncompetitive group recreational activities. At the end of each session, children rejoined their parents to discuss what they learned and their upcoming family projects (Fristad et al., 2003).

Parent Sessions

The topic of the first parent session was “Learn about symptoms and disorders.” Parents introduced themselves and symptoms of bipolar disorder and depression were discussed. Goals for treatment were presented to the parents, including: 1) Learn about depression and BPD in children; 2) Learn about the bi-psycho-social treatment of childhood mood disorders; 3) Learn how to work with the school system and mental health system; 4) Learn new communication and problems solving strategies to manage mood symptoms and improve family life. Parents were taught the motto of MF-PEP, “It’s not your fault, but it’s your challenge.”

Also in the first parent session, types of comorbid disorders were discussed, including behavior disorders, anxiety disorders, eating disorders, learning
disorders, and pervasive developmental disorders. The group leader explained some co-occurring disorders can be successfully treated in part by treatments for mood disorders, including many anxiety disorders. However, most comorbid conditions require some other specialized intervention, such as medication and psychotherapy, school intervention, and learning to cope with symptoms.

The second parent session discussed medications. Parents were taught medication management strategies, specific classes of medications, and how to manage side effects. The third parent session addressed the school and treatment team. Parents were taught to consider themselves the most important member of their children’s treatment team, along with their child. Techniques such as providing organized records, understanding diagnostic procedures, and following up with treatment were discussed. Parents discussed the members of the treatment team, types and goals of psychotherapies, and ways to work with the school system.

The purpose of the fourth family session was to talk about the negative family cycle and how to change it. Mood disorders can result in problems among family members, in part due to misconceptions about the disorder. The “can’ts” and the “won’ts,” learning what a child cannot do (i.e., when severely impaired by mood symptoms) versus what he will not do (i.e., when the child volitionally chooses to disobey), were discussed. Parents were taught positive strategies to help their child function at home, including empathy, a structured environment, communication, praise, and phrasing commands. The focus of the fifth session was
developing problem-solving and coping skills. Parents were taught coping skills -
what to avoid, and how to manage symptoms of depression and mania.

The sixth session taught and discussed verbal and nonverbal communication
skills. Parents were taught the communication cycle and differences between
hurtful versus helpful communication. Session seven addressed symptom
management. Parents discussed strategies to manage their child’s depression
and/or mania, and techniques for managing their own stress. In session eight, the
parents reviewed what they had learned, and a small graduation ceremony
occurred, during which the children received certificates for completing MF-PEP.

Although discussed in the context of mood disorders, many of the
components of these parent sessions provide general skills which may be helpful
for anxiety disorders as well. The research previously discussed suggests treatment
of mood disorders with comorbid anxiety is particularly complex. Families of
children with comorbid mood and anxiety disorders may be particularly frustrated
and confused with the treatment options available to their child. Therefore, helping
families first better manage and track their child’s medications and, second, learn to
manage their systems of care (school and treatment teams), may be particularly
beneficial to this subgroup. Academic impairment is common (Kendall et al., 1992)
in children with anxiety disorders, so help navigating the school system is an
important resource for these families. Further, evidence suggests comorbid anxiety
disorders often worsen the course of mood disorders, leading to more severe
symptoms and suicidality. Discussion of symptom management techniques and
coping skills may be particularly important for these families. Finally, Kendall and colleagues (1992) identify the importance of parent involvement in the treatment of comorbid mood and anxiety disorders. Children with anxiety disorders are likely to also have anxious parents (Manassis & Monga, 2001), so negative family cycles are likely to occur in their homes.

**Child Sessions**

Throughout the child sessions, children practiced identifying feelings, as well as the strength and causes of these feelings. Children were taught affect regulation, problem-solving, and communication skills.

In session one, they learned about symptoms of mania and depression and then “other problems,” including ADHD, anxiety, and other comorbid disorders. Anxiety problems were described as “feeling scared and worried a lot of the time.” Children and parents both generated a “fix-it list” of problems within the home they would like to address.

During the child session two, the children first completed an exercise that demonstrated how their symptoms can mask positive traits and talents, and additionally, how treatment can help “put the symptoms behind the child and allow their true character and strengths to come into view” (Lofthouse & Fristad, 2004, p. 83). This exercise illustrates the important message for children that they are not to blame for their symptoms, nor are they the cause of their symptoms. Yet, they are responsible, with the help of their parents and treatment teams, for managing their symptoms. This is one of the pivotal messages of MF-PEP, “It’s not your fault, but
it’s your challenge.” This message could be applied to any type of symptoms, including anxiety.

Also in session two, the children discussed their medications, including antianxiety medications, and the “enemies” they target. Children learned common side effects and management techniques. In session three, the children generated a “Tool Kit” to help them regulate their moods. The Tool Kit included strategies in four realms: creative, physical, social, and rest and relaxation. In session four, children were taught the rubrics of cognitive-behavioral therapy, first learning the connection between thoughts, feelings, and actions then working through how to alter mood states by replacing negative, hurtful thoughts and actions with positive, helpful ones.

In session five, children reviewed and practiced problem-solving skills, applying them to situations in which their symptoms cause impairment at home, school or with peers. Sessions six and seven discussed communication techniques. In session six, children reviewed communication, types of communication, and the communication cycle. Nonverbal communication was the emphasis, as children were taught ways they express themselves without words (e.g. tone of voice, facial expression, body gestures, body posture, and personal space). The focus of session seven was on verbal communication, including ways it can be hurtful and helpful. In session eight, children reviewed what they have learned through a Jeopardy®-like game and had a graduation ceremony with their parents.
As with the parent group, several of the components of the child group could serve to reduce both mood and anxiety symptoms. Children with anxiety frequently have social skill deficits (Kendall et al., 1992); therefore, discussion of the communication cycle and appropriate communication techniques are helpful to this population. Children practice identifying feelings at the beginning of each session, which falls under the category of affective education, endorsed by Kendall and colleagues (1992). Cognitive-behavioral strategies help children manage their maladaptive thoughts and feelings, which Hudson and colleagues (2001) emphasize as an important component of treatment for children with comorbid mood and anxiety disorders. Further, children learn social skills by interacting with other group members in MF-PEP, also an important component in treatment for children with comorbid anxiety disorders (Manassis & Monga, 2001).

Therefore, the different techniques of MF-PEP, in both the child and parent sessions, might help to alleviate anxiety, as well as mood symptoms. As discussed by Kendall and colleagues (1992), no specific protocols have been developed to address both anxiety and depression; however, “informed suggestions for treatment rest on examining some of the distinctive and overlapping features of the disorders themselves as well as the treatments that have been used for each” (Kendall et al., 1992). MF-PEP’s main foci, including education regarding affective awareness, affect regulation skills, problem-solving, communication, cognitive-behavioral strategies and social skills, as well as helping families become better consumers of
care, can be applied broadly to help with both mood and comorbid anxiety disorders.

Data Analysis

Description of the Sample

Hypothesis One

First, descriptive statistics examined the representation of the different anxiety disorders in the population at baseline: separation anxiety disorder, specific phobia, social phobia, generalized anxiety disorder, stress disorders (acute stress disorder and post-traumatic stress disorder), and obsessive-compulsive disorder. Independent sample t-tests were run comparing the prevalence of these disorders in patients with BPD versus depressive disorders. In addition, rates of co-occurring anxiety disorders for children with depressive spectrum and BPD spectrum disorders were documented using descriptive statistics to determine how many children with mood disorders have one or more than one anxiety disorder and the pattern of overlap among those anxiety disorders.

Comparisons of Children with Anxiety Disorders To Those Without Anxiety Disorders

Hypothesis Two

A one-way, between subjects analysis of variance (ANOVA) compared participants with comorbid anxiety disorders to participants without anxiety disorders at Time 1. Anxiety comorbidity status was the independent variable, and global functioning (C-GAS), depression symptoms severity scores reported by the
primary caregiver (current CDRS-R ratings), mania symptoms severity scores reported by the primary caregiver (YMRS ratings), the number of current medications, and suicidality (CDRS-R) were the dependent variables. Children with comorbid anxiety disorders were expected to have lower C-GAS scores, higher CDRS-R scores, higher YMRS scores, a higher number of current medications, and a greater amount of suicidality.

_Correlations of Anxiety and Depressive Symptoms_

_Hypothesis Three_

Pearson correlations were run, correlating the number of anxiety symptoms (BAMO-anxiety) reported on the P-ChIPS and the ChIPS with depression symptoms severity scores (current CDRS-R ratings) in the entire sample at baseline. Parent BAMO-anxiety scores were correlated with parent CDRS-R ratings, and child BAMO-anxiety scores were correlated with child CDRS-R ratings. It was expected that the number of anxiety symptoms would be significantly and positively correlated with depressive symptom severity scores for both child and parent report.

Pearson correlations were calculated, correlating the number of anxiety symptoms (BAMO-anxiety) reported on the P-ChIPS and the ChIPS with mania symptoms severity scores (YMRS ratings) in the entire sample at baseline. Parent BAMO-anxiety scores were correlated with parent YMRS ratings, and child BAMO-anxiety scores were correlated with child YMRS ratings. It was expected
that number of anxiety symptoms would be significantly and positively correlated with mania symptom severity scores for both child and parent report.

Pearson correlations were run, correlating measures of global functioning (C-GAS) with the number of anxiety symptoms (BAMO-anxiety) reported on the P-ChIPS and the ChIPS in the entire sample at baseline. It was expected that number of anxiety symptoms would be significantly and negatively correlated with C-GAS scores for both the child and parent report.

*Effects of MF-PEP on Anxiety Symptoms*

**Hypothesis Four**

An analysis of covariance (ANCOVA) assessed the number of anxiety symptoms (BAMO-Anxiety scores) at Time 3 in the IMM group compared to the WLC group. BAMO-Anxiety scores at Time 1 will be used as a covariate. It was hypothesized that at Time 3, BAMO-Anxiety scores in the IMM group will be significantly lower than BAMO-Anxiety scores in the WLC, after covarying BAMO-Anxiety scores at Time 1.

*Effect of Anxiety Diagnoses on MF-PEP Outcomes*

**Hypothesis Five**

A three-way Linear Mixed Effects (LME) procedure assessed the effect of anxiety disorder diagnosis and participation in MF-PEP on YMRS scores over time. As anxiety disorders tend to complicate treatment, it was expected there would be a significant interaction between anxiety disorder diagnosis and participation in MF-PEP, such that children with anxiety disorders would show
slower improvement in YMRS scores over time compared to children without comorbid anxiety.

Hypothesis Six

A three-way LME procedure assessed the effect of anxiety disorder diagnosis and participation in MF-PEP on CDRS-R scores over time. As anxiety disorders tend to complicate treatment, it was expected there would be a significant interaction between anxiety disorder diagnosis and participation in MF-PEP, such that children with anxiety disorders would show slower improvement in CDRS-R scores over time compared to children without comorbid anxiety.

Hypothesis Seven

A three-way LME procedure assessed the affect of anxiety disorder diagnosis and participation in MF-PEP on C-GAS scores over time. As anxiety disorders tend to complicate treatment, it was expected there would be a significant interaction between anxiety disorder diagnosis and participation in MF-PEP, such that children with anxiety disorders would show slower improvement in C-GAS scores over time compared to children without comorbid anxiety.

Effect of Anxiety Symptoms on MF-PEP Outcomes

Hypothesis Eight

LME assessed the effect of participation in MF-PEP and anxiety symptoms on YMRS scores over time. Pre-treatment BAMO-anxiety scores were added to the model as a covariate. It was expected children with higher BAMO-anxiety scores would show slower improvement in YMRS scores over time.
Hypothesis Nine

LME assessed the effect of participation in MF-PEP and anxiety symptoms on CDRS-R scores over time. Pre-treatment BAMO-Anxiety scores were added to the model as a covariate. It is expected children with higher BAMO-Anxiety scores would show slower improvement in CDRS-R scores over time.

Hypothesis Ten

LME assessed the effect of participation in MF-PEP and anxiety symptoms on C-GAS scores over time. Pre-treatment BAMO-Anxiety scores were added to the model as a covariate. It was expected children with higher BAMO-Anxiety scores would show slower improvement in C-GAS scores over time.

Missing Data

Missing data were not common in this study and appeared to occur at random. The largest amount of missing data was found with child YMRS and CDRS ratings. If a child was unwilling or reluctant to answer questions, or if a child’s responses on these measures were considered unreliable, that child’s responses were considered missing. Child-reported data for the CDRS were missing for no participants at Time 1, four participants at Time 2, and seven participants at Time 3. Child-reported data for the YMRS were missing for two participants at Time 1, five participants at Time 2, and four participants at Time 3.

Further, anxiety comorbidity status did not appear to affect study drop-out. One hundred and thirteen children with comorbid anxiety disorders participated at Time 1, 94 at Time 2, and 79 at Time 3. Fifty-two children without comorbid
anxiety disorders participated at Time 1, 48 at Time 2, and 38 at Time 3.
Chapter 3: Results

Description of the Sample

Hypothesis One

First, randomization status did not have an effect on any of the following variables at baseline: K-BIT scores, number of medications, child and parent-reported suicidality, C-GAS scores, parent and child CDRS-R ratings, and parent and child YMRS ratings.

There were a mean number of 1.4 anxiety disorders per participant: 31.5% had no anxiety disorders; 29.7% had one anxiety disorder; 15.2% had two anxiety disorders; 18.8% had three anxiety disorders; 3.6% had four anxiety disorders; and 1.2% had five anxiety disorders. Independent t-tests revealed no difference in the number of anxiety disorders among the MDD ($m = 1.3$) versus BPD ($m = 1.4$) groups, $t(163) = 0.331, p < 0.741$. Power analyses were conducted using the G*Power3 program (Erdfelder, Faul, & Buchner, 1996). The effect size was considered low ($d = 0.18$) and observed power was also low ($\beta = 0.18$).

Descriptive statistics examined the representation of the different anxiety disorders in the population at baseline: separation anxiety disorder, specific phobia, social phobia, generalized anxiety disorder, stress disorders (acute stress disorder and
post-traumatic stress disorder), and obsessive-compulsive disorder. Figure 3.1 depicts the representation of anxiety disorders in the sample.

![Representation of Anxiety Disorders in the Sample](image)

*Note.* BPD = bipolar disorder; MDD = depressive disorder; SocPh = Social Phobia; SpecPh = Specific Phobia; SAD = separation anxiety disorder; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PTSD = post-traumatic stress disorder.

Figure 3.1. Representation of anxiety disorders in the sample.

In the full sample, 13.3% had social phobia, 42.4% had specific phobia, 33.3% had SAD, 41.8% had GAD, 3.0% had OCD, and 3.0% had PTSD. Pearson Chi-Squares were run comparing the frequencies of each anxiety disorder within the MDD versus BPD samples. No differences were found for any anxiety disorder, as shown in Table 3.1.
| Anxiety Disorder     | MDD  
(n = 50) | BPD  
(n = 115) | $\chi^2$ (1) | $p$ |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Phobia</td>
<td>14.0</td>
<td>13.0</td>
<td>0.028</td>
<td>0.868</td>
</tr>
<tr>
<td>Specific Phobia</td>
<td>48.0</td>
<td>40.0</td>
<td>0.913</td>
<td>0.339</td>
</tr>
<tr>
<td>SAD</td>
<td>26.0</td>
<td>36.5</td>
<td>1.736</td>
<td>0.188</td>
</tr>
<tr>
<td>GAD</td>
<td>38.0</td>
<td>43.5</td>
<td>0.430</td>
<td>0.512</td>
</tr>
<tr>
<td>OCD</td>
<td>4.0</td>
<td>2.6</td>
<td>0.230</td>
<td>0.632</td>
</tr>
<tr>
<td>PTSD</td>
<td>2.0</td>
<td>3.5</td>
<td>0.259</td>
<td>0.611</td>
</tr>
</tbody>
</table>

*Note.* BPD = bipolar disorder; MDD = depressive disorder; SAD = separation anxiety disorder; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PTSD = post-traumatic stress disorder.

Table 3.1. Prevalence (%) of anxiety disorders among MDD versus BPD participants.

An ANOVA was calculated comparing BAMO scores in patients with BPD versus depressive disorders. No differences were found among parent report (Table 3.2) or child report (Table 3.3) for any anxiety disorder.
<table>
<thead>
<tr>
<th>Variable</th>
<th>All $M (SD)$</th>
<th>MDD $M (SD)$</th>
<th>BPD $M (SD)$</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Phobia</td>
<td>0.20</td>
<td>0.20</td>
<td>0.19</td>
<td>0.172 (1) 0.679</td>
</tr>
<tr>
<td>Specific Phobia</td>
<td>0.19</td>
<td>0.22</td>
<td>0.20</td>
<td>0.188 (1) 0.665</td>
</tr>
<tr>
<td>SAD</td>
<td>0.19</td>
<td>0.195</td>
<td>0.18</td>
<td>0.068 (1) 0.795</td>
</tr>
<tr>
<td>GAD</td>
<td>0.42</td>
<td>0.42</td>
<td>0.42</td>
<td>0.001 (1) 0.960</td>
</tr>
<tr>
<td>OCD</td>
<td>0.12</td>
<td>0.16</td>
<td>0.11</td>
<td>1.796 (1) 0.182</td>
</tr>
<tr>
<td>PTSD</td>
<td>0.14</td>
<td>0.19</td>
<td>0.12</td>
<td>1.866 (1) 0.174</td>
</tr>
<tr>
<td>ASD</td>
<td>0.09</td>
<td>0.13</td>
<td>0.07</td>
<td>2.436 (1) 0.120</td>
</tr>
</tbody>
</table>

*Note. BPD = bipolar disorder; MDD = depressive disorder; SAD = separation anxiety disorder; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PTSD = post-traumatic stress disorder; ASD = acute stress disorder.*

Table 3.2. Analysis of variance of parent-reported BAMO-anxiety scores.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All $M (SD)$</th>
<th>MDD $M (SD)$</th>
<th>BPD $M (SD)$</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Phobia</td>
<td>0.16</td>
<td>0.20</td>
<td>0.15</td>
<td>1.062 0.304</td>
</tr>
<tr>
<td>Specific Phobia</td>
<td>0.16</td>
<td>0.19</td>
<td>0.15</td>
<td>1.623 0.204</td>
</tr>
<tr>
<td>SAD</td>
<td>0.23</td>
<td>0.20</td>
<td>0.25</td>
<td>0.800 0.372</td>
</tr>
<tr>
<td>GAD</td>
<td>0.26</td>
<td>0.32</td>
<td>0.23</td>
<td>1.755 0.187</td>
</tr>
<tr>
<td>OCD</td>
<td>0.04</td>
<td>0.05</td>
<td>0.03</td>
<td>0.663 0.417</td>
</tr>
<tr>
<td>PTSD</td>
<td>0.06</td>
<td>0.05</td>
<td>0.06</td>
<td>0.192 0.662</td>
</tr>
<tr>
<td>ASD</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.898 0.345</td>
</tr>
</tbody>
</table>

*Note. BPD = bipolar disorder; MDD = depressive disorder; SAD = separation anxiety disorder; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PTSD = post-traumatic stress disorder; ASD = acute stress disorder.*

Table 3.3. Analysis of variance of child-reported BAMO-anxiety scores.
In addition, rates of co-occurring anxiety disorders for children with depressive spectrum and BPD spectrum disorders were documented using descriptive statistics to determine how many children with mood disorders have one or more than one anxiety disorder and the pattern of overlap among those anxiety disorders. Table 3.4 depicts the prevalence of co-occurring anxiety diagnoses.

<table>
<thead>
<tr>
<th>Anxiety disorder</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. SpecPh (n = 70)</td>
<td>--</td>
<td>81.8</td>
<td>69.1</td>
<td>59.4</td>
<td>80</td>
<td>60</td>
</tr>
<tr>
<td>2. SocPh (n = 22)</td>
<td>25.7</td>
<td>--</td>
<td>21.8</td>
<td>17.4</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>3. SAD (n = 55)</td>
<td>54.3</td>
<td>54.5</td>
<td>--</td>
<td>44.9</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>4. GAD (n = 69)</td>
<td>58.6</td>
<td>54.5</td>
<td>56.4</td>
<td>--</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>5. OCD (n = 5)</td>
<td>5.7</td>
<td>4.5</td>
<td>3.6</td>
<td>5.8</td>
<td>--</td>
<td>20</td>
</tr>
<tr>
<td>6. PTSD/ASD (n = 5)</td>
<td>4.3</td>
<td>0</td>
<td>5.5</td>
<td>5.8</td>
<td>20</td>
<td>--</td>
</tr>
<tr>
<td>No additional anxiety diagnosis</td>
<td>20</td>
<td>4.5</td>
<td>20</td>
<td>30.4</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

*Note.* SpecPh = Specific Phobia; SocPh = Social Phobia; SAD = separation anxiety disorder; GAD = generalized anxiety disorder; OCD = obsessive-compulsive disorder; PTSD = post-traumatic stress disorder; ASD = acute stress disorder.

Table 3.4. Prevalence (%) of co-occurring anxiety diagnoses for participants.

Comparisons of Children with Anxiety Disorders to Those without Anxiety Disorders

**Hypothesis Two**

A one-way, between subjects analysis of variance (ANOVA) compared participants with comorbid anxiety disorders to participants without anxiety.
disorders at Time 1. Anxiety comorbidity status was the independent variable, and global functioning (C-GAS), depression symptoms severity scores reported by the primary caregiver and child (current CDRS-R ratings), mania symptoms severity scores reported by the primary caregiver and child (YMRS ratings), the number of current medications, and parent and child reported suicidality (CDRS-R morbid thoughts and suicidality ratings) were the dependent variables. Results are depicted in Table 3.5. Contrary to hypotheses, there was no difference in C-GAS, YMRS ratings, number of medications, and parent and child-reported suicidality scores between the –AnxDx and the +AnxDx groups. However, as hypothesized, the +AnxDx group had higher CDRS-R scores than the –AnxDx group based on both child and parents report. The –Anxiety group had a mean BAMO-anxiety score of 0.75 with a maximum score of 4.22, and 0.27 with a maximum score of 1.04, for the parent and child ratings respectively. The +Anxiety group had a mean BAMO-anxiety score of 1.64 with a maximum score of 6.11, and 1.19 with a maximum score of 4.08, for the parent and child ratings respectively.
### Table 3.5
Analysis of variance (ANOVA) of the effect of comorbid anxiety diagnoses on C-GAS, number of medications, parent-reported CDRS-R and YMRS, child-reported CDRS-R and YMRS, and parent and child-reported suicidality.

<table>
<thead>
<tr>
<th>Variable</th>
<th>-Anx M(SD)</th>
<th>+Anx M(SD)</th>
<th>ANOVA F (1, 162)</th>
<th>p</th>
<th>Observed Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-GAS</td>
<td>44.58 (10.00)</td>
<td>43.35 (7.59)</td>
<td>0.752</td>
<td>0.387</td>
<td>0.129</td>
</tr>
<tr>
<td># Meds</td>
<td>2.17 (1.63)</td>
<td>2.36 (1.43)</td>
<td>0.575</td>
<td>0.449</td>
<td>0.154</td>
</tr>
<tr>
<td>P-CDRS</td>
<td>34.56 (11.48)</td>
<td>42.61 (13.72)</td>
<td>13.54**</td>
<td>0.000</td>
<td>0.922</td>
</tr>
<tr>
<td>P-YMRS</td>
<td>20.48 (11.22)</td>
<td>20.64 (10.51)</td>
<td>0.008</td>
<td>0.931</td>
<td>0.005</td>
</tr>
<tr>
<td>C-CDRS</td>
<td>32.90 (11.22)</td>
<td>40.32 (15.45)</td>
<td>9.336**</td>
<td>0.003</td>
<td>0.845</td>
</tr>
<tr>
<td>C-YMRS</td>
<td>14.86 (10.51)</td>
<td>15.76 (9.58)</td>
<td>0.289</td>
<td>0.592</td>
<td>0.134</td>
</tr>
<tr>
<td>P-Suicidality</td>
<td>2.90 (1.75)</td>
<td>3.03 (1.79)</td>
<td>0.170</td>
<td>0.680</td>
<td>0.054</td>
</tr>
<tr>
<td>C-Suicidality</td>
<td>3.58 (1.97)</td>
<td>3.61 (2.31)</td>
<td>0.007</td>
<td>0.935</td>
<td>0.154</td>
</tr>
</tbody>
</table>

*Note. -Anx = no comorbid anxiety diagnosis; +Anx = comorbid anxiety diagnosis; C-GAS = children’s global assessment scale; P-CDRS = parent-reported children’s depression rating scale-revised ratings; P-YMRS = parent-reported young mania rating scale ratings; C-CDRS = child-reported children’s depression rating scale-revised ratings; C-YMRS = child-reported young mania rating scale ratings; P-Suicidality = parent-reported suicidality; C-Suicidality = child-reported suicidality. **p < 0.01*  

Correlations of Anxiety and Depressive Symptoms

**Hypothesis Three**

Pearson correlations were run, correlating the number of anxiety symptoms (BAMO-anxiety) reported on the P-ChIPS and the ChIPS with depression symptom severity scores (current CDRS-R ratings) in the entire sample at baseline. As hypothesized, parent BAMO-anxiety scores were significantly positively correlated with parent CDRS-R ratings, and child BAMO-anxiety scores were also
significantly positively correlated with child CDRS-R ratings. Thus, the number of anxiety symptoms were significantly and positively correlated with depressive symptom severity scores for both child and parent report. Parent BAMO-anxiety scores were positively correlated with child BAMO-anxiety scores. Although statistically significant, this correlation was low \((r = 0.169)\). However, parent CDRS-R ratings were not significantly correlated with child CDRS-R ratings.

Pearson correlations were run, correlating the number of anxiety symptoms (BAMO-anxiety) reported on the P-ChIPS and the ChIPS with mania symptoms severity scores (YMRS ratings) in the entire sample at baseline. Contrary to hypotheses, parent BAMO-anxiety scores were not correlated with parent YMRS ratings and child BAMO-anxiety scores were not significantly positively correlated with child YMRS ratings. Thus, number of anxiety symptoms was not significantly and positively correlated with mania symptoms severity scores for either child report or parent report. Parent YMRS ratings were positively correlated with child YMRS ratings.

Pearson correlations were run, correlating measures of global functioning (C-GAS) with the number of anxiety symptoms (BAMO-anxiety) reported on the P-ChIPS and the ChIPS in the entire sample at baseline. Parent BAMO-anxiety scores were significantly negatively correlated with C-GAS scores. However, child BAMO-anxiety scores were not. Thus, number of anxiety symptoms was significantly and negatively correlated with C-GAS scores for parent report, but not child report. Table 3.6 shows the results of all Pearson correlations.
Table 3.6. Pearson correlations of parent- and child-reported depression, anxiety, and global functioning ratings.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. P-CDRS</td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2. P-YMRS</td>
<td>0.297**</td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>3. C-CDRS</td>
<td>0.118</td>
<td>0.146</td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>4. C-YMRS</td>
<td>-0.030</td>
<td>0.316**</td>
<td>0.507**</td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>5. C-GAS</td>
<td>-0.325**</td>
<td>-0.437**</td>
<td>-0.092</td>
<td>-0.432**</td>
<td>1</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>6. P-BAMO</td>
<td>0.169*</td>
<td>0.035</td>
<td>0.066</td>
<td>0.036</td>
<td>-0.295**</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td>7. C-BAMO</td>
<td>0.124</td>
<td>0.011</td>
<td>0.342**</td>
<td>0.153</td>
<td>-0.095</td>
<td>0.202*</td>
<td>1</td>
</tr>
</tbody>
</table>

Note. P-CDRS = parent-reported children’s depression rating scale-revised ratings; P-YMRS = parent-reported young mania rating scale ratings; C-CDRS = child-reported children’s depression rating scale-revised ratings; C-YMRS = child-reported young mania rating scale ratings; P-BAMO = parent-reported BAMO-anxiety scores; C-BAMO = child-reported BAMO-anxiety scores.

** p < 0.01. * p < 0.05

Table 3.6. Pearson correlations of parent- and child-reported depression, anxiety, and global functioning ratings.

Effects of MF-PEP on Anxiety Symptoms

Hypothesis Four

An analysis of covariance (ANCOVA) assessed the number of anxiety symptoms (BAMO-Anxiety scores) at Time 3 in the IMM group compared to the WLC group. BAMO-Anxiety scores at Time 1 were used as a covariate. Parent-report and child-report results are presented in Table 3.7 and Table 3.8, respectively. Contrary to hypotheses, there was no difference between the IMM
group’s BAMO-Anxiety scores and the WLC group’s BAMO-Anxiety scores, after covarying BAMO-Anxiety scores at Time 1. Thus, MF-PEP does not appear to impact anxiety symptoms. Observed power was 0.08 and 0.127 for both parent and child analyses, respectively.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time 1 M (SD)</th>
<th>Time 2 M (SD)</th>
<th>ANCOVA F (1, 120)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Treatment</td>
<td>1.471 (1.413)</td>
<td>1.339 (1.528)</td>
<td>0.245</td>
<td>0.622</td>
</tr>
<tr>
<td>Waitlist Control</td>
<td>1.265 (1.296)</td>
<td>1.400 (1.342)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3.7. Analysis of covariance of parent-report BAMO-anxiety scores as a result of Multi-Family Psychoeducational Psychotherapy.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time 1 M (SD)</th>
<th>Time 2 M (SD)</th>
<th>ANCOVA F (1,118)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Treatment</td>
<td>0.905 (0.967)</td>
<td>0.642 (0.778)</td>
<td>0.660</td>
<td>0.418</td>
</tr>
<tr>
<td>Waitlist Control</td>
<td>0.908 (0.937)</td>
<td>0.559 (0.632)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3.8. Analysis of covariance of child-report BAMO-anxiety scores as a result of Multi-Family Psychoeducational Psychotherapy.

**MF-PEP Outcomes of Individuals with and without Anxiety Diagnoses**

**Hypothesis Five**

A three-way Linear Mixed Effects (LME) procedure assessed the effect of anxiety disorder diagnosis and participation in MF-PEP on YMRS scores over
time. Contrary to hypotheses, there was no significant interaction between anxiety disorder diagnosis and participation in MF-PEP. Thus, children with anxiety disorders showed similar improvement in YMRS scores over time compared to children without comorbid anxiety. These results occurred for both parent YMRS scores, $F(283.598) = 0.001, p = 0.980$ and child YMRS scores, $t(268.480) = 0.761, p = 0.384$. See Table 3.9 and 3.10 for mean YMRS parent-report and child-report scores over time for both groups. Figure 3.2 and 3.3 depict slopes of change over time for parent and child report respectively.

The four different groups for parent-reported YMRS showed the following slopes. The YMRS scores for IMM +ANX decreased at a rate of -4.32, compared to the YMRS scores for IMM -ANX that decreased at a rate of -2.95. The YMRS scores for WLC+ANX decreased at a rate of -1.77, compared to WLC-ANX which decreased at a rate of -0.034 over time. For child report, the YMRS scores for the IMM+ANX decreased at a rate of -1.71, compared to the YMRS scores for IMM-ANX that decreased at a rate of -2.93. The YMRS scores for WLC+ANX decreased at a rate of -2.84 and the YMRS scores for WLC-ANX decreased at a rate of -2.38. Sample size calculations for LME analyses were conducted using a procedure described by Diggle, Heagerty, Liang, and Zeger (2002). For the analysis of the parent-rated YMRS, a sample size of 8,809 per group was needed to achieve a sufficient power of 0.80. For the child-rated YMRS, a sample size of over 173 participants per group was needed to achieve a power of 0.80.
<table>
<thead>
<tr>
<th>Group</th>
<th>+ Anxiety</th>
<th>- Anxiety</th>
<th>+ Anxiety</th>
<th>- Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM</td>
<td>N = 52</td>
<td>N = 26</td>
<td>N = 47</td>
<td>N = 22</td>
</tr>
<tr>
<td></td>
<td>20.71 (10.04)</td>
<td>22.46 (11.13)</td>
<td>16.85 (10.40)</td>
<td>18.23 (9.88)</td>
</tr>
<tr>
<td></td>
<td>N = 39</td>
<td>N = 17</td>
<td>N = 40</td>
<td>N = 21</td>
</tr>
<tr>
<td>WLC</td>
<td>N = 61</td>
<td>N = 26</td>
<td>N = 47</td>
<td>N = 26</td>
</tr>
<tr>
<td></td>
<td>20.57 (10.98)</td>
<td>18.50 (11.17)</td>
<td>`16.57 (10.32)</td>
<td>`16.65 (10.86)</td>
</tr>
<tr>
<td></td>
<td>N = 40</td>
<td>N = 21</td>
<td>N = 79</td>
<td>N = 21</td>
</tr>
<tr>
<td>All</td>
<td>N = 113</td>
<td>N = 52</td>
<td>N = 94</td>
<td>N = 48</td>
</tr>
<tr>
<td></td>
<td>20.64 (10.51)</td>
<td>20.48 (11.22)</td>
<td>16.71 (10.30)</td>
<td>17.37 (10.34)</td>
</tr>
<tr>
<td></td>
<td>N = 79</td>
<td>N = 38</td>
<td>N = 79</td>
<td>N = 38</td>
</tr>
</tbody>
</table>

Note. IMM = immediate treatment group; WLC = waitlist control group.

Table 3.9. Linear Mixed Effects procedure on the effect of anxiety disorder diagnosis and participation in Multi-Family Psychoeducational Psychotherapy on parent-reported Young Mania Rating Scale scores over time.
Note. IMM = immediate treatment group; WLC = waitlist control group; -Anx = no comorbid anxiety diagnosis; +Anx = comorbid anxiety diagnosis.

Figure 3.2. Changes in parent-reported Young Mania Rating Scale scores over time for IMM versus WLC and anxiety comorbidity versus no anxiety comorbidity.
<table>
<thead>
<tr>
<th>Group</th>
<th>+ Anxiety</th>
<th>- Anxiety</th>
<th>+ Anxiety</th>
<th>- Anxiety</th>
<th>+ Anxiety</th>
<th>- Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM</td>
<td>N = 52</td>
<td>N = 26</td>
<td>N = 60</td>
<td>N = 25</td>
<td>N = 112</td>
<td>N = 51</td>
</tr>
<tr>
<td></td>
<td>14.52 (8.81)</td>
<td>15.08 (10.97)</td>
<td>16.83 (10.14)</td>
<td>14.64 (10.23)</td>
<td>15.76 (9.58)</td>
<td>14.86 (10.51)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>14.26 (8.62)</td>
<td>11.50 (8.11)</td>
<td>13.06 (8.90)</td>
<td>10.60 (9.96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N = 47</td>
<td></td>
<td>N = 20</td>
<td>N = 47</td>
<td>N = 45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10.76 (8.72)</td>
<td></td>
<td>9.56 (9.54)</td>
<td>10.55 (8.70)</td>
<td>10.31 (8.70)</td>
</tr>
<tr>
<td>WLC</td>
<td>N = 47</td>
<td>N = 20</td>
<td>N = 40</td>
<td>N = 25</td>
<td>N = 77</td>
<td>N = 39</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>13.06 (8.90)</td>
<td>10.60 (9.96)</td>
<td>13.66 (8.74)</td>
<td>11.00 (9.09)</td>
</tr>
<tr>
<td>All</td>
<td>N = 94</td>
<td>N = 45</td>
<td>N = 77</td>
<td>N = 39</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.65 (8.65)</td>
<td>10.31 (8.70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note.* IMM = immediate treatment group; WLC = waitlist control group.

Table 3.10. Linear Mixed Effects procedure on the effect of anxiety disorder diagnosis and participation in Multi-Family Psychoeducational Psychotherapy on child-reported Young Mania Rating Scale scores over time.
Note. IMM = immediate treatment group; WLC = waitlist control group; -Anx = no comorbid anxiety diagnosis; +Anx = comorbid anxiety diagnosis.

Figure 3.3. Changes in child-reported Young Mania Rating Scale scores over time for IMM versus WLC and anxiety comorbidity versus no anxiety comorbidity.

Hypothesis Six

A three-way Linear Mixed Effects (LME) assessed the effect of anxiety disorder diagnosis and participation in MF-PEP on CDRS-R scores over time. Contrary to hypotheses, there was no significant interaction between anxiety disorder diagnosis and participation in MF-PEP. Thus, children with anxiety disorders showed similar improvement in CDRS-R scores over time compared to children without comorbid anxiety. These results occurred for both parent CDRS-R
scores, $F(283.95) = 1.561$, $p = 0.213$ and child CDRS-R scores, $t(278.565) = 0.128$, $p = 0.721$. See Table 3.11 and 3.12 for mean CDRS-R parent-report and child-report scores over time for both groups. Figure 3.4 and 3.5 depict slopes of change over time for parent and child report respectively.

The four different groups for parent-reported CDRS-R showed the following slopes. The CDRS-R scores for IMM +ANX decreased at a rate of -2.55, compared to the CDRS-R scores for IMM -ANX that decreased at a rate of -4.52. The CDRS-R scores for WLC+ANX decreased at a rate of -1.81, compared to WLC-ANX which decreased at a rate of -0.01 over time. For child report, the CDRS-R scores for the IMM+ANX decreased at a rate of -3.47, compared to the CDRS-R scores for IMM-ANX that decreased at a rate of -1.27. The CDRS-R scores for WLC+ANX decreased at a rate of -3.34 and the CDRS-R scores for WLC-ANX decreased at a rate of -2.20. For LME analyses of the parent-rated CDRS-R scores, 398 participants per group were needed to achieve a power of 0.80. For LME analyses of the child-rated CDRS-R scores, 1514 participants per group were needed to achieve a power of 0.80.
<table>
<thead>
<tr>
<th>Group</th>
<th>+ Anxiety</th>
<th>M (SD)</th>
<th>Time 1</th>
<th>M (SD)</th>
<th>Time 2</th>
<th>M (SD)</th>
<th>Time 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM</td>
<td>N = 52</td>
<td>40.94 (13.72)</td>
<td>N = 47</td>
<td>37.43 (15.37)</td>
<td>N = 39</td>
<td>34.90 (18.75)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 26</td>
<td>38.19 (11.62)</td>
<td>N = 22</td>
<td>33.68 (13.10)</td>
<td>N = 17</td>
<td>28.47 (8.54)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 24</td>
<td>32.00 (11.78)</td>
<td>N = 25</td>
<td>38.52 (8.16)</td>
<td>N = 21</td>
<td>28.67 (10.17)</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>N = 113</td>
<td>42.61 (13.72)</td>
<td>N = 94</td>
<td>38.20 (16.77)</td>
<td>N = 79</td>
<td>38.06 (17.86)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N = 52</td>
<td>34.56 (11.48)</td>
<td>A = 48</td>
<td>33.29 (11.68)</td>
<td>A = 38</td>
<td>30.00 (8.36)</td>
<td></td>
</tr>
</tbody>
</table>

Note. IMM = immediate treatment group; WLC = waitlist control group.

Table 3.11. Linear Mixed Effects procedure on the effect of anxiety disorder diagnosis and participation in Multi-Family Psychoeducational Psychotherapy on parent-reported Children’s Depression Rating Scale-Revised scores over time.
Figure 3.4. Changes in parent-reported Children’s Depression Rating Scale-Revised scores over time for IMM versus WLC and anxiety comorbidity versus no anxiety comorbidity.

*Note.* IMM = immediate treatment group; WLC = waitlist control group; -Anx = no comorbid anxiety diagnosis; +Anx = comorbid anxiety diagnosis.
<table>
<thead>
<tr>
<th>Group</th>
<th>Time 1 $M$ (SD)</th>
<th>Time 2 $M$ (SD)</th>
<th>Time 3 $M$ (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Anxiety</td>
<td>N = 52 39.83 (16.51)</td>
<td>N = 47 36.40 (13.52)</td>
<td>N = 37 32.00 (10.61)</td>
</tr>
<tr>
<td>- Anxiety</td>
<td>N = 26 33.73 (10.83)</td>
<td>N = 20 34.55 (17.09)</td>
<td>N = 17 31.12 (12.74)</td>
</tr>
<tr>
<td>WLC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Anxiety</td>
<td>N = 61 44.03 (13.68)</td>
<td>N = 47 38.97 (18.19)</td>
<td>N = 40 41.14 (16.60)</td>
</tr>
<tr>
<td>- Anxiety</td>
<td>N = 26 30.92 (10.30)</td>
<td>N = 26 32.96 (10.59)</td>
<td>N = 21 31.24 (8.22)</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Anxiety</td>
<td>N = 113 40.32 (15.45)</td>
<td>N = 94 36.22 (13.78)</td>
<td>N = 77 32.99 (12.11)</td>
</tr>
<tr>
<td>- Anxiety</td>
<td>N = 50 32.90 (11.22)</td>
<td>A = 45 31.20 (13.10)</td>
<td>A = 38 29.76 (11.29)</td>
</tr>
</tbody>
</table>

*Note.* IMM = immediate treatment group; WLC = waitlist control group.

Table 3.12. Linear Mixed Effects procedure on the effect of anxiety disorder diagnosis and participation in Multi-Family Psychoeducational Psychotherapy on child-reported Children’s Depression Rating Scale-Revised scores over time.
Note. IMM = immediate treatment group; WLC = waitlist control group; -Anx = no comorbid anxiety diagnosis; +Anx = comorbid anxiety diagnosis.

Figure 3.5. Changes in child-reported Children’s Depression Rating Scale-Revised scores over time for IMM versus WLC and anxiety comorbidity versus no anxiety comorbidity.

**Hypothesis Seven**

A three-way LME procedure assessed the affect of anxiety disorder diagnosis and participation in MF-PEP on C-GAS scores over time. Contrary with hypotheses, children with anxiety disorders and children without anxiety disorders had similar improvement in C-GAS scores over time, $t (278.790) = 0.017$, $p =$
0.896. See Table 3.13 and mean C-GAS scores over time for both groups. Figure 3.6 depicts slopes of change over time for parent and child report respectively.

The four different groups for C-GAS showed the following slopes. The C-GAS scores for IMM +ANX increased at a rate of 2.52, compared to the C-GAS scores for IMM -ANX that increased at a rate of 2.34. The C-GAS scores for WLC+ANX increased at a rate of 1.21, compared to WLC-ANX which increased at a rate of 0.77 over time. For this LME analysis, 1211 participants per group were needed to achieve a power of 0.80.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time 1 M (SD)</th>
<th>Time 2 M (SD)</th>
<th>Time 3 M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMM + Anxiety</td>
<td>N = 52 43.00 (7.02)</td>
<td>N = 47 46.13 (8.07)</td>
<td>N = 38 48.26 (10.53)</td>
</tr>
<tr>
<td>IMM - Anxiety</td>
<td>N = 26 42.96 (9.83)</td>
<td>N = 22 47.36 (7.72)</td>
<td>N = 17 48.12 (12.12)</td>
</tr>
<tr>
<td>WLC + Anxiety</td>
<td>N = 61 43.66 (8.09)</td>
<td>N = 47 46.36 (9.89)</td>
<td>N = 38 46.50 (10.40)</td>
</tr>
<tr>
<td>WLC - Anxiety</td>
<td>N = 26 46.19 (10.08)</td>
<td>N = 26 46.96 (8.34)</td>
<td>N = 21 47.00 (7.69)</td>
</tr>
<tr>
<td>All + Anxiety</td>
<td>N = 113 43.35 (7.59)</td>
<td>N = 94 46.24 (8.98)</td>
<td>N = 76 47.38 (10.43)</td>
</tr>
<tr>
<td>All - Anxiety</td>
<td>N = 53 44.58 (10.00)</td>
<td>N = 48 47.15 (7.98)</td>
<td>N = 38 47.50 (9.79)</td>
</tr>
</tbody>
</table>

Note. IMM = immediate treatment group; WLC = waitlist control group.

Table 3.13. Linear Mixed Effects procedure on the effect of anxiety disorder diagnosis and participation in Multi-Family Psychoeducation Psychotherapy on Children’s Global Assessment Scale scores over time.
**Note.** IMM = immediate treatment group; WLC = waitlist control group. -Anx = no comorbid anxiety diagnosis; +Anx = comorbid anxiety diagnosis.

Figure 3.6. Changes in Children’s Global Assessment Scale scores over time for IMM versus WLC and anxiety comorbidity versus no anxiety comorbidity.

*Effect of Anxiety Symptoms on MF-PEP Outcomes*

*Hypothesis Eight*

LME assessed the effect of participation in MF-PEP and anxiety symptoms on YMRS scores over time. Pre-treatment BAMO-anxiety scores were added to the model as a covariate. Contrary to hypotheses, BAMO-anxiety scores did not have an effect on improvement in YMRS scores in IMM compared to WLC over time, $t$
(307.242) = 0.007, \ p = 0.936. \text{ For this analysis, 7034 participants were needed to achieve a power of 0.80.}

\text{Hypothesis Nine}

LME assessed the effect of participation in MF-PEP and anxiety symptoms on CDRS-R scores over time. Contrary to hypotheses, BAMO-anxiety scores did not have an effect on improvement in CDRS-R scores in IMM compared to WLC over time, \( t(301.136) = 0.114, \ p = 0.736. \) For this analysis, 3,781 participants were needed to achieve a power of 0.80.

\text{Hypothesis Ten}

LME assessed the effect of participation in MF-PEP and anxiety symptoms on C-GAS scores over time. Pre-treatment BAMO-Anxiety scores were added to the model as a covariate. As hypothesized, BAMO-anxiety scores had an effect on improvement in C-GAS scores over time, \( t(303.395) = 5.546, \ p = 0.019. \) However, this effect was opposite the expected direction. Specifically, higher anxiety symptomatology at baseline predicted greater improvements in C-GAS scores in IMM compared to WLC over time after participation in MF-PEP. For this analysis, 157 participants were needed to achieve a power of 0.80.

\text{Additional Analyses}

In an attempt to further understand the impact of overall symptom severity, rather than anxiety, per se, on baseline and outcome variables, several post-hoc analyses were conducted. The effect of behavior symptomatology and overall symptomatology (excluding anxiety) on baseline and outcome variables was
examined. The previously described BAMO method was used to calculate index scores for baseline behavioral symptoms (BAMO-B) and baseline symptoms of behavior, mood, and “other” disorders (BMO). Analyses were rerun, replacing parent-reported BAMO-A scores with parent-reported BAMO-B then BMO.

Pearson correlations were calculated to examine the associations between BAMO-B scores and depressive and manic symptom severity and global functioning. Higher BAMO-B scores were associated with significantly more dysfunction on all three baseline measures (higher CDRS-R scores and YMRS scores, lower C-GAS scores). When analyses were repeated replacing BAMO-B with BMO, higher BMO scores were significantly associated with significantly lower C-GAS scores. To avoid redundancy (as BMO contains mood symptom scores), BMO analyses were not conducted with mood symptom severity measures.

Next, a three-way LME procedure was utilized to determine the effect of BAMO-B and BMO scores at baseline on change in depressive and manic symptom severity and global functioning over time. Results mimicked findings with BAMO-A scores. Specifically, after participating in MF-PEP, children with higher baseline BAMO-B scores showed less improvement in CDRS-R scores over time. This effect, however, was only marginally significant. BAMO-B scores did not impact change in YMRS scores over time. Similar to the findings with anxiety, children with higher baseline BAMO-B scores showed significantly greater improvement in C-GAS scores over time following MF-PEP; the same was found with baseline BMO scores.
These additional analyses suggest that perhaps greater symptomatology (BAMO-A, BAMO-B, or BMO), not factors specific to comorbid anxiety, per se, may contribute to this study’s overall findings.

Finally, additional analyses were conducted to determine the impact of specific phobia diagnoses and symptoms on study outcomes. All ten hypotheses were re-tested using the same analytic procedures, only excluding all specific phobia symptoms and diagnoses. Results did not differ from the original findings. These post-hoc analyses indicate that the impact of comorbid anxiety symptoms and diagnoses on the sample were not affected by the large number of children who presented with symptoms and diagnoses of specific phobia.
Chapter 4: Discussion

Comorbidity is the rule, not the exception, for youth with mood disorders. Few researchers have considered comorbidity when evaluating treatment studies, despite the importance of this endeavor. No researchers to date have examined the mechanisms through which comorbidity impacts treatment outcome. Anxiety disorders are particularly debilitating disorders, causing substantial impairment to those who suffer from them. When comorbid with mood disorders, current research suggests they lead to further impairment, more severe symptomatology, greater suicidality, and poorer treatment outcome. In regards to BPD, Harpold and colleagues (2005) state, “Considering that bipolar disorder and anxiety disorders are highly morbid disorders in their own right, patients with comorbid BPD and anxiety disorders are at high risk for a particularly severe form of BPD” (p. 20).

Prevalence Rates

The first objective of this dissertation was to examine the prevalence of comorbid anxiety disorders in a population of children with mood disorders. There were a mean number of 1.4 anxiety disorders per child in the sample. Approximately one-third of the sample had no anxiety comorbidity, less than one-third had one anxiety disorder, one-sixth had two anxiety disorders, one-fifth had three anxiety disorders, and 5% had four or more anxiety disorders. There were no
differences in the number of anxiety disorders between patients with BPD versus patients with depressive disorders.

Nearly 70% of the MF-PEP sample had at least one comorbid anxiety disorder. The two most common comorbid anxiety disorders were specific phobia and GAD, both of which occurred in approximately 42% of the sample. The second most commonly occurring anxiety disorder was SAD, which occurred in one-third of the sample. Thirteen percent of the sample suffered from social phobia, 3% of the sample were diagnosed with OCD and 3% with PTSD. This distribution was similar in both children diagnosed with BPD and depressive disorders. These prevalence estimates are similar to those reported in the previous literature, presented in Table 1.1 (cf., Dickstein et al., 2005; Harpold et al., 2005; Masi et al., 2007; Wilens et al., 2003; and Yorbik et al., 2004).

Effect of Anxiety Comorbidity and Symptoms on Baseline Variables

The next hypothesis was that participants with comorbid anxiety disorders would experience higher depressive and manic symptomatology, poorer global functioning, and greater suicidality. Contrary to expectations, participants with comorbid anxiety disorders showed no difference in manic symptomatology, global functioning, and suicidality on either parent or child report. As expected, participants with comorbid anxiety disorders showed higher rates of depressive symptomatology based on both parent and child report.

These results appear to differ from the majority of the literature on the impact of comorbid anxiety disorders on the severity of bipolar illness, global
functioning, and suicidality. Many researchers have suggested that comorbid anxiety diagnoses may be associated with a more severe form of BPD (Simon et al., 2004) and depression (Rhode et al., 2001; Seligman & Ollendick, 1998). The current results demonstrate that anxiety comorbidity is associated with greater depressive symptomatology, but no difference in suicidality, global functioning, and manic symptomatology.

This may have occurred, in part, due to the decreased power evidenced by using categorical versus continuous data on anxiety comorbidity. Using diagnostic groups forces the data into two categories, one containing 70% of the sample (+Anxiety) and the other containing 30% of the sample (-Anxiety). As described by Streiner (2002), using categorical data when continuous data are available not only results in a loss of information, but it reduces the statistical power of the test and increases the probability of making a Type II error. Information was lost because it is incorrect to assume that the –Anxiety category did not have significant anxiety symptoms. In fact, the data suggest anxiety symptoms were present in this group, although these participants did not meet criteria for an anxiety diagnosis.

Results differed slightly when using continuous, rather than categorical evaluations of the impact of anxiety on functioning. Correlations suggest that a greater number of anxiety symptoms was associated with poorer global functioning and greater depressive symptom severity. A greater number of anxiety symptoms was not associated with greater manic symptom severity. A dimensional approach was useful in this situation, because it did not rule out children who experienced
significant anxiety symptomatology and impairment, but did not meet stringent DSM-IV categories. These continuous analyses also likely increased statistical power (Streiner, 2002).

Even with continuous analyses, there were no associations between anxiety symptoms and manic symptomatology. This is contrary to hypotheses, as several researchers have suggested that BPD with comorbid anxiety predicts a worse course of illness than BPD with no comorbid anxiety (Otto et al., 2006). Comorbid anxiety has been shown to suggest greater severity of BPD in an adult sample from STEP-BD (Simon et al., 2004) and a narrow phenotype child sample (Dickstein et al., 2005). Several possibilities for this finding exist. First, it is possible that the theory that manic symptom severity is associated with anxiety comorbidity is flawed. A few studies have demonstrated support for the current hypotheses, such as STEP-BD, but others have shown no differences in manic symptom severity between participants with and without comorbid anxiety (e.g. Birmaher et al., 2002; Masi et al., 2007). It is also important to consider that MF-PEP participants may not show the same effects of anxiety comorbidity as research conducted with adults (such as STEP-BD).

Second, although many MF-PEP participants had high levels of impairing manic symptomatology, only approximately half met stringent DSM-IV criteria for BP-I or BP-II. The rest of the sample met criteria for BP-NOS, Substance-Induced Mood Disorder, Mood Disorder-NOS, MDD, and/or DD. Of the participants who met criteria for a depressive diagnosis, close to three-fourths had some symptoms
of mania. Many of the participants in the previously described mania studies met DSM-IV criteria for BP-I or BP-II. Dickstein and colleagues (2005) found comorbid anxiety had an effect on age of onset of BPD and more psychiatric hospitalizations in a narrow-phenotype sample (31 children who met stringent DSM-IV-TR criteria for BPD). However, they did not find this in a broad phenotype (32 children who met their research criteria for severe mood dysregulation--SMD). Thus, it is possible that the MF-PEP participants are more representative of a “mixed” phenotype sample (broad and narrow), in which anxiety symptoms may not be associated with a more severe phenotype of BPD.

To test this, the analyses related to this hypothesis were re-run on the subsample of BP-I and BP-II participants. Even among BP-I and BP-II participants, findings for hypothesis two and hypothesis three did not change. Research on the severity of manic symptoms and broad versus narrow phenotype BPD warrants further exploration. These results indicate anxiety symptoms and diagnoses did not have a differential effect on narrow phenotype BPD participants.

Third, many of the anxiety disorders hypothesized to be associated with manic symptom severity were either not assessed or not prevalent in the MF-PEP sample. Research has explored connections between mania and panic disorder (e.g. Birmaher et al., 2002), which is not assessed in the ChIPS/P-ChIPS. PTSD and OCD, also hypothesized to be connected with BPD (e.g. Masi et al., 2004; Pollack et al., 2006) were only found in 3% of the sample. Perhaps the anxiety symptoms most common in MF-PEP participants, such as GAD and SAD, which are clearly
associated with depressive symptoms bear no particular relationship with manic symptoms.

However, previous research showed mixed results on the effect of panic disorder, OCD, and PTSD comorbidity on the manic symptoms. Birmaher and colleagues (2002) found youth with panic disorder had a three to four-fold increased risk for BPD compared to other patients in a clinic. Similarly, Masi and colleagues (2007) assert, “Recent evidence has also been advanced to support the hypothesis that differential risk for [panic disorder] comorbidity might represent a promising tool for distinguishing heterogeneous genetic subtypes of [bipolar disorder]” (p. 52). However, Masi and colleagues (2007) found BPD youth with comorbid panic disorder showed less severity at baseline and better treatment response compared to BPD without comorbid panic disorder. Birmaher and colleagues (2002) found panic disorder had no effect on manic and hypomanic symptoms among youth with BPD. Masi and colleagues (2004) also found that severity of symptomatology did not differ between patients with BPD and comorbid OCD and patients with BPD and no comorbid OCD.

Further, although Dickstein and colleagues (2005) found children with narrow phenotype BPD and anxiety had higher rates of psychiatric hospitalizations and earlier age of onset, GAD, SAD, and specific phobia were the most common anxiety comorbidities among participants. Research from the STEP-BD study in adults found anxiety symptoms predicted younger age of onset of bipolar illness, decreased likelihood of recovery, and less time euthymic, but again, social phobia
and GAD were the two most common comorbid anxiety diagnoses in the sample. Further research is needed to better understand the effect of specific anxiety diagnoses, such as panic disorder, OCD, and PTSD, on bipolar symptoms in youth.

Moreover, evidence suggests that the MF-PEP sample was considerably impaired and had significant mood symptoms. At baseline, the average MSI score was 31.9, which, according to operational guidelines, falls in the higher end of the moderate symptom range. Participants had high rates of comorbidity in addition to anxiety comorbidity; in fact, all participants presented with some form of comorbidity. Behavioral disorders were present in 97% of the sample, mirroring Tillman and colleagues’ (2003) findings that comorbid syndromal and subsyndromal ODD were significantly higher in a pediatric BPD group compared to an ADHD group (78.5% and 17.2% versus 61.7% and 24.7%). Participants were prescribed an average of 2.3 medications at baseline, and 70% of the sample took more than one medication. Many of the families in MF-PEP had tried a variety of services, but sought MF-PEP to help manage their child’s symptoms.

Thus, most MF-PEP participants presented with very impairing mood symptomatology. Families had likely tried many other treatments and medications, and some travelled far distances to attend MF-PEP sessions. As MF-PEP participants had at least moderate levels of mood symptoms and a comorbid behavior disorder in addition to a mood disorder, the presence or absence of anxiety symptoms may have had little association with manic symptoms.
Further, the findings of low associations between anxiety and mania may be due to this study’s operational definition of “manic symptom severity.” The YMRS was utilized, an interview that assesses current severity of manic symptoms. Anxiety may be associated with a worse course of BPD, but this may not be reflected on the YMRS. Previous data suggest anxiety predicted lower age of onset in children (Dickstein et al., 2005) and adults (Simon et al., 2004), more psychiatric hospitalizations in children (Dickstein et al., 2005), and dramatically fewer days euthymic, risk of relapse, and a poorer quality of life in adults (Simon et al., 2004). Perhaps, in MF-PEP participants, anxiety had negative associations with BPD illness, but these negative effects were not exposed with the YMRS. Moreover, the YMRS has limitations. Some items measured on the YMRS, including insight regarding symptoms, hypersexual behavior, and inappropriate dress and grooming, are indirect reflections of manic symptoms. At the same time, the YMRS excludes some symptoms in the diagnostic criteria for mania, including poor judgment and inflated self-esteem/grandiosity. Thus, the YMRS may not be the most accurate method to assess manic symptom severity in children.

Also contrary to hypotheses, there were no differences between number of medications and suicidality ratings among participants with comorbid anxiety disorders compared to participants without comorbid anxiety disorders. Psychiatrists may have been nervous about a manic-induced switch from a SSRI, or may simply not be focused on the patient’s anxiety in the light of the current mood problems. Treatment guidelines suggest psychosocial treatments should be used
wherever appropriate, as they can be used without risk of intensifying mood symptoms (Kowatch et al., 2005), so it is quite possible prescribers followed these guidelines. Further, the MF-PEP sample showed low rates of suicidality overall, most likely because suicidality is more common among older BPD youth (Goldstein et al., 2005). Although suicidality ratings had a potential range of 2 to 14, the mean scores for parent and child suicidality among MF-PEP participants were only 2.99 and 3.60, respectively. Thus, it is possible that, in a sample of older participants with more variance in levels of suicidality, such as reported by Liu and colleagues (2006) or the STEP-BD program, anxiety comorbidity would be associated with greater suicidality.

Thus, clinicians should consider anxiety at the symptom level as well as diagnostically. Anxiety symptoms appear to be associated with poorer functioning and greater severity of depressive symptoms. Further exploration between the associations with manic symptom severity and anxiety symptoms is warranted.

**Effect of MF-PEP on Anxiety Symptoms**

Current treatment guidelines for mood disorders suggest after clinicians stabilize the child’s mood, the second step is to address comorbid symptoms (Hughes et al., 1999, 2007; Kowatch et al., 2005; McClellan et al., 2007). The current study hypothesized that MF-PEP would lead to a reduction in the number of anxiety symptoms, as MF-PEP addresses the issue of anxiety comorbidity and provides coping skills that may be helpful for relieving anxiety symptoms as well as mood symptoms. Although, for the parent-report, the number of anxiety
symptoms decreased for IMM while the number of mood symptoms increased for WLC over time, this difference did not achieve statistical significance. There was also no difference in the number of child-reported anxiety symptoms pre- and post-treatment.

Not many studies have examined the effect of treatment for mood disorders on anxiety symptoms, but those that have found similar results (Kolko et al., 2000; Young et al., 2006). Mendlowitz and colleagues (1999) found that group-based CBT for children with anxiety led to both anxiety and depressive symptom reductions. It is possible that anxiety treatments may lead to reductions in symptoms of depression, while depression treatments may not necessarily reduce anxiety.

The current study hypothesized that several MF-PEP treatment components would help families better manage and treat anxiety symptoms in addition to mood symptoms and lead to anxiety symptom reduction. This does not appear to be the case. Although contrary to hypotheses, these findings are consistent with Kowatch and colleagues (2005) guidelines that, among children with bipolar disorder, comorbid symptoms should be carefully assessed before treatment. Once BPD symptoms are stabilized, the need for treatment of comorbid disorders should then be reviewed. Although MF-PEP has some components that may help decrease anxiety symptoms, children with comorbid anxiety still appear to require treatment in addition to MF-PEP to specifically target their anxiety.
Effect of Anxiety Diagnosis and Symptoms on MF-PEP Outcomes

Next, it was hypothesized that comorbid anxiety disorders would complicate treatment and therefore, children with comorbid anxiety diagnoses would show poorer improvements in global functioning, manic symptom severity, and depressive symptom severity. Contrary to hypotheses, children with comorbid anxiety diagnoses showed similar improvement as a result of MF-PEP on both parent and child-reported depressive and manic symptom severity ratings and overall functioning. The current study hypothesized that poorer overall functioning would be the mechanism through which participants with comorbid anxiety showed slower improvements in manic and depressive symptoms after MF-PEP. Since there were no differences in improvements in depressive, manic symptom severity, and global functioning after MF-PEP, it was not feasible to test this hypothesis. Thus, it appears that MF-PEP is similarly effective for both participants with and without comorbid anxiety in reducing depressive and manic symptom severity and global functioning.

These findings are inconsistent with previous research suggesting anxiety comorbidity predicts higher depression post-treatment (Brent et al., 1998; Curry et al., 2006; Young et al., 2006) and a longer time to remission among BPD adults (Feske et al., 2000). The current results are positive and suggest that psychoeducational psychotherapy is equally effective in treating mood symptoms and global functioning for comorbidly anxious children. MF-PEP appears to be successful in addressing this first step of treatment guidelines: stabilizing the
child’s mood (Hughes et al., 1999, 2007; Kowatch et al., 2005; McClellan et al., 2007). Clinicians treating children with mood disorders and comorbid anxiety can incorporate MF-PEP techniques in their practice to work to stabilize the mood, and then implement anxiety specific techniques, such as exposure-based CBT, to address anxiety symptoms.

When analyses were conducted at the symptoms level on parent report-measures, results differed slightly. Analyses at the diagnostic level pose many problems, particularly because they force researchers to group participants into categories, as opposed to using more dimensional approaches (Cerel & Fristad, 2001). Similar to the diagnostic analyses and contrary to hypotheses, the number of parent-reported anxiety symptoms did not have an effect on improvement in parent-reported manic symptom severity or parent-reported depressive symptom severity. These findings suggest, as discussed above, that MF-PEP does a good job at addressing mood symptoms despite levels of anxiety symptoms.

The number of parent-reported anxiety symptoms at baseline did have an effect on global functioning as a result of MF-PEP; however, this effect was not in the hypothesized direction. Specifically, higher parent-reported anxiety symptomatology at baseline predicted greater improvements in C-GAS scores as a result of MF-PEP.

These results suggest that children in the IMM group with higher anxiety symptomatology at baseline were able to make significantly greater improvements in C-GAS scores. These findings are surprising. No previous research looked at
the effect of anxiety symptomatology on treatment outcome in participants with mood disorders, so it is difficult to consider this finding within the context of the current literature. Nonetheless, it is an interesting finding, and it mirrors that of Young and colleagues (2006), who found that anxious and depressed adolescents treated with IPT-A had significantly lower post-treatment depression scores than adolescents without comorbid anxiety. Young and colleagues (2006) speculate that IPT-A may be more effective for this group than for their overall sample. The authors assert that it is unclear whether the anxiety symptoms or the more severe depression symptoms at baseline explained the greater response in this comorbid subgroup.

The NIMH Collaborative Multisite Multimodal Treatment Study of Children with ADHD (MTA Study) examined the effect of four different treatments, medication management, behavioral treatment, combination, and community comparison, on children with ADHD with a wide range of comorbid conditions. They found anxiety comorbidity moderated treatment. Specifically, children with comorbid anxiety responded equally well to MTA behavioral and medication treatments, while children with only behavioral disorders responded best to MTA medication treatments (with or without behavioral treatments). The authors asserted that comorbid anxiety had modest effects on baseline characteristics but had much stronger effects on response to treatment. The authors state, “as a general rule, [anxiety] status appeared to confer certain benefits on

Thus, MF-PEP participants with higher anxiety symptomatology were also more responsive in terms of improving their global functioning after treatment. This finding is unexpected, as anxiety symptoms did not show statistically significant decreases after involvement in MF-PEP. Several possible reasons may have caused participants with greater anxiety symptomatology to make further improvements in their overall functioning compared to participants without comorbid anxiety. First, participants with comorbid anxiety symptoms may be able to apply the behavioral strategies taught by MF-PEP to their anxiety disorder as well, and may experience greater improvements in functioning. As children with anxiety disorders often experience significant social skill deficits (Kendall et al., 1992), perhaps the emphasis MF-PEP placed on social skill building at each season was particularly helpful for this group in improving functioning. Further, one of the goals of MF-PEP is to help families become better consumers of care; perhaps this was especially beneficial for children with more impaired functioning at baseline.

Also, greater anxiety symptomatology was associated with more impairments in functioning at baseline. The average C-GAS for the entire sample was 43.74 at baseline, which indicates a moderate degree of interference in functioning in most areas of the child’s life. Patients with more anxiety symptoms were likely to have C-GAS scores below this mean, indicating major impairment in functioning. Lower C-GAS scores at baseline may indicate that participants with
more functional impairment at baseline had more room to improve. Once implementing MF-PEP strategies, these participants were able to narrow the gap between their level of functioning at baseline and their full potential. Participants with less functional impairment may have had fewer improvements to make and thus showed less improvement in global functioning.

Research is mixed in regards to the effect of initial severity on treatment outcome. In the adult depression literature, Elkin and colleagues (1995) assert, “Despite some ambiguity …, the general direction of findings might lead one to expect somewhat better outcome for more severely depressed (nonpsychotic) outpatients in pharmacotherapy and for less severity depressed in psychotherapy” (p. 841). However, Mufson and colleagues (2004) found that adolescents who were more severely depressed and exhibited greater functional impairment at baseline showed even larger treatment effects (improvements in HAMD and C-GAS scores) from IPT-A compared with treatment as usual. The researchers stated, “This finding suggests that milder depression in younger adolescents can be more easily treated with supportive psychotherapy, whereas more severe depression is more effectively treated with a structured treatment specifically targeted for adolescent depression” (p. 583).

Limitations

The current study had several limitations. First, a large number of analyses were conducted, increasing the chances of Type I error. This should be taken into account when considering analyses that achieved statistical significance. Also,
analyses were based on both parent and child report. Research suggests parents and children show poor agreement on ratings of children’s internalizing symptoms (Achenbach, McConaughy, & Howell, 1987) particularly anxiety (Engel, Rodrigue, & Geffken, 1994).

Further, the focus of the larger study was to examine the effect of psychoeducational psychotherapy on childhood mood disorders. Thus, most of the participants’ primary diagnoses were mood disorders. This study would have benefited from questionnaires specifically targeting anxiety disorders and symptoms, such as the RCMAS, the Anxiety Disorders Interview Schedule, or the Self-Report for Childhood Anxiety Related Disorders (SCARED) rating scales. Moreover, comorbid diagnoses may have been over-represented in participants compared to the general population, because individuals who suffer from multiple conditions are more likely to seek treatment (Berkson, 1946). However, MF-PEP participants are likely representative of a population that would seek adjunctive psychoeducational psychotherapy.

The current study sought to examine the effect of comorbid anxiety on depressive and manic symptom severity, global functioning, and treatment response. Theoretically, the current study would have benefited from the use of a comparison group to ensure that anxiety symptoms specifically led to further impairment and symptom severity, not just greater symptomatology in general. However, as 97% of the sample was diagnosed with a comorbid behavioral
disorder and 70% had an anxiety disorder, such a comparison group was not feasible.

Finally, most (90.9%) of the children who participated were white, which may limit the applicability of these findings to minority populations. Future trials should seek to “oversample” from minority populations, although limited research is available regarding particular recruitment methods to increase minority participation (Durant et al., 2007). Some strategies, including setting a priori minority recruitment goals (Durant et al., 2007) and specifically recruiting from places minorities may be more likely to go (Jones, Sleeves, & Williams, 2009), have been shown effective. Further, the majority (73%) of the participants were male. Although other studies have documented similarly higher rates of boys with mood disorders than girls (Dickstein et al., 2005; Harpold et al., 2005), it may be useful for future studies to specifically assess for gender differences in comorbidity in childhood mood disorders.

Clinical Implications and Directions for Future Research

This study has several important clinical implications. First, anxiety comorbidity appears very prevalent among children with bipolar and depressive disorders. Treatment guidelines suggest clinicians should carefully assess for comorbidity (Hughes et al., 2007; Kowatch et al., 2005). Comorbid anxiety may initially be overshadowed by the severity of the child’s mood symptoms, so they may not initially receive clinical attention, but the current findings indicate children with mood disorders are likely to suffer from one or more anxiety diagnoses.
Children who present with greater levels of anxiety symptomatology appear to also have greater depressive symptom severity and poorer global functioning. Thus, anxiety symptoms can have significant, negative effects on children with mood disorders, and clinicians should assess and monitor these symptoms over time.

Current treatment guidelines suggest clinicians should first work to stabilize the patient’s mood. Psychoeducational psychotherapy, MF-PEP, appears to work equally well among children with and without anxiety comorbidity at this first step. Higher numbers of anxiety symptoms did not appear to impact improvements in depressive symptom severity and manic symptom severity as a result of MF-PEP. The current findings suggest that psychoeducational psychotherapy may be particularly helpful for children with higher levels of anxiety symptomatology in making improvements in global functioning. This could be a result of participants having more room to improve as they implemented MF-PEP strategies. Thus, clinicians should utilize MF-PEP strategies for children both with and without anxiety symptomatology in order to treat mood symptoms. Families of children with a mood diagnosis and comorbid anxiety symptoms may especially benefit from education about both disorders and how to coordinate more complex medication regimens and systems of care.

However, psychoeducational psychotherapy targeted towards mood disorders does not appear to be effective in reducing anxiety symptoms. Following treatment guidelines, after mood symptoms have been stabilized, clinicians should treat children’s anxiety symptoms through strategies proven effective in previous
literature, such as exposure-based CBT. It is important for clinicians to educate families about managing both diagnoses, and clinicians who treat mood disorders must also be prepared and adequately trained in implementing evidence-based treatments for anxiety, as well. Psychotherapy, a first-line treatment for anxiety symptoms, becomes particularly important among children comorbid for bipolar disorders, as SSRIs may trigger or worsen manic symptoms (Kowatch et al., 2005). Clinicians who work with children with mood disorders need flexibility in implementing evidence-based treatments as they incorporate the multiple comorbidities often present in this population.

The current findings also call for further research on anxiety comorbidity among children with mood disorders. Future studies should continue to examine the effect of anxiety comorbidity and anxiety symptoms on children with mood disorders. The findings of the current study and previous research appear particularly mixed regarding the interplay of anxiety and manic symptoms. Some studies suggest anxiety symptoms are associated with higher levels of manic symptoms, but the findings of the current study suggest no significant associations between manic and anxiety symptoms. This could, in part, be due to the overall severity and multiple comorbidities present in the current sample or the operational definition of manic symptom severity. It is important to determine if particular anxiety symptoms can be a marker for a future BPD diagnosis and aid in early identification.
Future research should also assess the effect of anxiety comorbidity on suicidality, a significant and dangerous problem among children with mood disorders. The MF-PEP participants had overall low levels of suicidality, so analyses had low power. If anxiety is a marker for suicidality among children with mood disorders, anxiety can be identified as a risk factor and have important preventative implications.

Finally, future research should continue to assess the effect of comorbidity on treatments for children with mood and anxiety disorders. The results of the current study indicate comorbidity presents in most children with mood disorders and may lead to differential treatment effects. Researchers should also consider the specific mechanisms through which anxiety impacts treatment outcome. Similarly, treatment guidelines for the treatment of childhood mood disorders should continue to be updated as researchers learn more about comorbidities, including anxiety. Newman and colleagues (1998) state, “Although comorbid cases may require long-term multimodal treatments which are expensive, the cost to the individual and society of ignoring such regimens may ultimately be far more expensive” (p. 310).
References


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Appendix A

Children’s Global Assessment Scale Ratings

100-91 Superior functioning in all areas (at home, at school, and with peers); involved in a wide range of activities and has many interests (e.g., has hobbies or participates in extracurricular activities or belongs to an organized group such as Scouts, etc); likeable, confident; “everyday” worries never get out of hand; doing well in school; no symptoms.

90-81 Good functioning in all areas; secure in family, school, and with peers; there may be transient difficulties and everyday worries that occasionally get out of hand (e.g., mild anxiety associated with an important examination, occasionally “blowups” with siblings, parents, or peers)

80-71 No more than slight impairment in functioning at home, at school, or with peers; some disturbance of behavior or emotional distress may be present in response to life stresses (e.g. parent separations, deaths, birth of a sibling), but these are brief, and interference with functioning is transient; such children are only minimally disturbing to others and are not considered deviant by those who know them

70-61 Some difficulty in a single area, but generally functioning pretty well (e.g. sporadic or isolated antisocial acts, such as occasional hooky or petty theft; consistent minor difficulties with school work; mood changes or brief duration; fears and anxieties that do not lead to gross avoidance behavior; self-doubts); has some meaningful interpersonal relationships; most people who do not know the child well would not consider him or her deviant, but those who do know him or her well might express concern

60-51 Variable functioning with sporadic difficulties or symptoms in several but not all social areas; disturbance would be apparent to those who encounter the child in a dysfunctional setting or time but not to those who see the child in other settings

50-41 Moderate degree of interference in functioning in most social areas or severe impairment of functioning in one area, such as might result from, for example, suicidal preoccupations and ruminations, school refusal and other forms of anxiety, obsessive rituals, major conversion symptoms, frequent anxiety attacks, poor or inappropriate social skills, frequent episodes of
aggressive or other antisocial behavior, with some preservation of meaningful social relationships

40-31 Major impairment in functioning in several areas and unable to function in one of these areas, i.e. disturbed at home, at school, with peers, or in society at large, e.g. persistent aggression without clear instigation; markedly withdrawn and isolated behavior due to either mood or thought disturbance, suicidal attempts with clear lethal intent; such children are likely to require special school and/or hospitalization or withdrawal from school but this is not a sufficient criterion for inclusion in this category)

30-21 Unable to function in almost all areas; e.g. stays at home, in ward, or in bed all day without taking part in social activities or severe impairment in reality testing or serious impairment in communications (e.g. sometimes incoherent or inappropriate)

20-11 Needs considerable supervision to prevent hurting others or self (e.g. frequently violent, repeated suicide attempts) or to maintain personal hygiene or gross impairment in all forms of communication, e.g. severe abnormalities in verbal and gestural communication, marked social aloofness, stupor

10-1 Needs constant supervision (24-h care) due to severely aggressive or self-destructive behavior or gross impairment in reality testing, communication, cognition, affect, or personal hygiene
## Appendix B

Content of MF-PEP Parent and Child Sessions.

<table>
<thead>
<tr>
<th>Session</th>
<th>Parent Group</th>
<th>Child Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Childhood mood disorders and their symptoms</td>
<td>Childhood mood disorders and their symptoms</td>
</tr>
<tr>
<td>2</td>
<td>Medications: Monitoring effectiveness and side effects, names and classes of medications</td>
<td>Medications: symptoms and the medications that target them; “Naming the Enemy”</td>
</tr>
<tr>
<td>3</td>
<td>“Systems of Care:” Mental health and educational services</td>
<td>“Tool Kit” to manage symptoms and emotions</td>
</tr>
<tr>
<td>4</td>
<td>Learn about negative family cycle; Review first half of the program</td>
<td>Learn about the connection between thoughts, feelings, and actions; Thinking-Feeling-Doing</td>
</tr>
<tr>
<td>5</td>
<td>Develop problem-solving and coping skills</td>
<td>Develop problem-solving skills “Stop-Think-Plan-Do-Check”</td>
</tr>
<tr>
<td>6</td>
<td>Improve verbal and nonverbal communication coping skills</td>
<td>Improve nonverbal communication skills</td>
</tr>
<tr>
<td>7</td>
<td>Symptom Management</td>
<td>Improve verbal communication skills</td>
</tr>
<tr>
<td>8</td>
<td>Review second half of the program; graduate</td>
<td>Review and graduate</td>
</tr>
</tbody>
</table>