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Progressive Muscle Relaxation as an Intervention to Reduce Manic Symptoms

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PROGRESSIVE MUSCLE RELAXATION AS AN INTERVENTION TO REDUCE MANIC SYMPTOMS

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Introduction: Bipolar disorder is a serious mental illness, but medications and psychosocial approaches designed to treat it leave significant room for improvement. This study investigated Progressive Muscle Relaxation (PMR), a treatment originally designed to reduce anxiety, as a way to reduce manic symptoms.

Methods: Participants with bipolar I disorder (n = 44) were assigned via stratified randomization to complete PMR or a control condition (self-focused calming). Participants underwent a positive mood induction procedure, and completed several measures of manic symptoms at Session 1 and Session 2 (several weeks later).

Results: Among those who experienced a successful positive mood induction, PMR and the control condition generally resulted in similar reductions in high-arousal positive affect. Participants who practiced PMR between the two sessions tended to experience greater reductions in positive affect at Session 2 compared to those who did not practice.

Discussion: The relative parity of the PMR and control conditions suggests that people with bipolar I disorder have effective strategies for regulating positive emotions. Rather than teaching additional strategies, it may be more fruitful to develop methods for helping people with bipolar disorder to implement the strategies that work for them.

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Chapter 1: Introduction

Bipolar I disorder is a serious mental health problem that is believed to affect about one percent of the population (Judd & Akiskal, 2003; Kessler et al., 1994, 1997, 2005; Narrow et al., 2002; Regier et al., 1993; Weissman et al., 1996). The disorder is related to alarmingly high rates of problems across a number of domains, including health care costs, disability, medical comorbidity, hospitalization, and suicide risk (Andlin-Sobocki & Wittchen, 2005; Baldessarini & Tondo, 2003; Kupfer, 2005; Peele, Xu, & Kupfer, 2003). In addition to the concrete costs and prevalence mentioned above, however, bipolar disorder has far-reaching effects for those who have the disorder, as well as their friends and family members in the form of damaged relationships and lost career opportunities.

Despite bipolar disorder's capacity to wreak havoc in the lives of its sufferers, current treatments for this devastating condition leave many people symptomatic and unable to maintain stable functioning. The current study was designed to address this issue by teaching Progressive Muscle Relaxation (PMR), a method for reducing anxiety, to participants with bipolar disorder. I will begin by reviewing literature on the treatment of bipolar disorder, including both medications and the psychosocial treatments that have been designed to supplement them. I will then review several bodies of literature linking mania with anxiety, with arousal as a key bridge between them. I will note two important deficits that are present in bipolar disorder, namely insight and executive functioning, and explore the ways that these deficits can sabotage the effective treatment of mania. I will

then discuss PMR as a potential strategy for preventing mania that may address arousal while circumventing these deficits.

Treatment Manuals versus Interventions

At the outset, it is important to note that this dissertation is guided by a specific model of treatment development. Although the psychotherapy field has been dominated by studies comparing extensive treatment manuals to control conditions (the Empirically Supported Treatment [EST] movement; see DeRubeis & Crits-Christoph, 1998), this approach has been criticized on several fronts. Westen and others (Rosen & Davison, 2003; Westen, Novotny, & Thompson-Brenner, 2004a, 2004b) have pointed out that manuals themselves typically contain dozens of facets, and traditional treatment studies do little to differentiate helpful from unhelpful components. Because of the imprecision and error variance involved in these studies, many have argued for testing smaller components of therapy, labeled as intervention strategies. By testing these more basic strategies, it has been hoped that researchers might begin to more precisely consider which strategies fit for which clients at which time (Berking et al., 2008; Persons, 2006; Miklowitz & Scott, 2009; Rosen & Davison, 2006). Hence, although this dissertation focuses on treatment development, the goal is to test a single intervention strategy.

Existing Treatments for Bipolar Disorder

The treatment of bipolar disorder through psychopharmacological means has often been traced back to lithium, approved for use in the treatment of mania in 1970 (Mitchell & Hadzi-Pavlovic, 2000). Since then, numerous other drugs have shown some effectiveness in treating bipolar disorder. Adjunctive psychosocial treatments have been

developed to further improve the functioning of those for whom drugs are only partially successful. Drug and psychosocial treatments will be considered separately below, with special attention paid to effects for depression versus mania. Throughout these sections, the term "bipolar disorder" will refer specifically to bipolar I disorder (marked by a history of manic or mixed episodes) unless otherwise stated.

Pharmacological Treatments

Two broad categories have been used to define treatments for bipolar disorder: those meant to help people recover from a current episode (acute treatments), and those meant to help prevent relapse (maintenance treatments). Each category will be considered separately.

Addressing acute mania. Mood stabilizers are considered one of the front-line treatments for bipolar disorder (American Psychiatric Association, 2002). Lithium falls into this category; it may benefit up to 80 percent of people with bipolar disorder (Nivoli, Murru, & Vieta, 2010; Prien & Potter, 1990). Two large randomized controlled trials have demonstrated that lithium is nearly twice as likely as placebo to lead to treatment response within three to four weeks among patients who were acutely manic. In these studies, response was defined as a 50% reduction in scores on the Young Mania Rating Scale (Bowden et al., 1994; Paulsson & Huizar, 2003; for the Young Mania Rating Scale see Young, Biggs, Ziegler & Meyer, 1978). Lithium can be accompanied by serious side effects, and the potential for lithium toxicity necessitates frequent blood tests. Despite these concerns and the introduction of other medications useful for the treatment of mania, lithium continues to be a first line treatment recommendation for acute mania

(American Psychiatric Assocation, 2002) because it is the medication with the largest base of evidence in the treatment of bipolar disorder (Storosum et al., 2007; Thase & Denko, 2008).

In addition to lithium, several other drugs may help reduce current manic symptoms. These include anticonvulsants such as divalproex sodium (also known by its trade name, Depakote), which is also considered a "first-line" treatment for acute mania by the American Psychiatric Association (2002). Depakote's extended-release formulation has recently demonstrated its efficacy at reducing manic symptoms in a randomized controlled trial of 377 patients with mania (Bowden et al., 2006). In addition to Depakote, carbamazepine (Tegretol) is an anticonvulsant medication that has recently received FDA approval as an anti-manic agent (Weisler et al., 2005). Anticonvulsant medications may be especially helpful for people who experience mixed manic episodes with depressive features (Gelenberg & Pies, 2003).

In addition to mood stabilizers and anticonvulsants, atypical antipsychotics have been used in the treatment of acute mania (Fountoulakis, Vieta, & Schmidt, 2010; Tohen et al., 1999). One prominent example is olanzapine (Zyprexa), which may be particularly useful for severe cases (American Psychiatric Association, 2002) or episodes featuring agitated or psychotic features (Patel, Crismon, & Pondrom, 2005).

A recent meta-analysis led to the conclusion that mood stabilizers (including lithium), carbamazepine, and atypical antipsychotics all result in similar reductions in acute manic symptoms (Smith, Cornelius, Warnock, Tacchi, & Taylor, 2007). Results suggest that about half of patients in the midst of an acute manic episode may experience

clinical response (defined as 50% reduction in Young Mania Rating Scale scores) within a few weeks of starting an anti-manic drug.

Relapse prevention. As reviewed above, several drugs have established efficacy in reducing acute manic symptoms. The prevention of recurrence is an equally important treatment goal; a large body of literature addresses this issue of maintenance or relapse prevention.

With rare exceptions, all medications used for maintenance treatment in bipolar disorder also have established acute anti-manic properties. For instance, lithium has consistently been used as a first-line drug to prevent manic relapse (American Psychiatric Association, 2002). Unfortunately, the median time to relapse while on lithium has been estimated to be about one year even when blood serum levels are kept in the therapeutic range (Keller et al., 1992). Other authors have found slightly more encouraging results: conclusions from a recent meta-analysis suggested that manic relapse rates on lithium are about 15% during follow-up periods of one to two years, compared to about 25% for those on a placebo (Geddes et al., 2004). Other reviews have also concluded that lithium may reduce relapse by as much as half over placebo treatments (e.g. Sachs & Thase, 2000; Smith, Cornelius, Warnock, Bell, & Young, 2007). Thus, estimates of precise rates of relapse while taking lithium vary, but outcomes from even relatively encouraging trials and reviews suggest that significant numbers of people will experience manic relapse despite lithium treatment. Even among patients for whom lithium is successful in preventing mania, rates of discontinuation are high (Johnson & McFarland, 1996; Maj et al., 1998), limiting its usefulness as a maintenance treatment.

APA treatment guidelines advise considering other medications if lithium proves ineffective or if its side effects are intolerable. Among these other approaches, several anticonvulsant medications are also used in the maintenance phase of bipolar disorder. Results in this domain suggest significant room for improvement: based on a recent review, Smith, Warnock, Tacchi, and Taylor (2007) concluded that Depakote is not statistically better than placebo at preventing relapse over a twelve- to eighteen-month follow-up period. Results from other reviews suggest that carbamazepine is no better than treatment with lithium alone (Cookson & Elliott, 2006).

Atypical antipsychotics are also used for bipolar maintenance. Some researchers have concluded that olanzapine may perform somewhat better than lithium in terms of preventing manic relapse, but acknowledge that methodological issues temper those results (Dando & Tohen, 2006). For instance, several of the trials found to favor olanzapine featured an enriched sample that had already demonstrated a clinical response to that drug (e.g. Tohen et al., 2005; Tohen et al., 2006). A recent trial found that risperidone (Risperdal) may delay recurrence of manic episodes (Quiroz et al, 2010).

Other antipsychotics await rigorous testing in the maintenance phase of bipolar disorder (Hellewell, 2006). A study within the STEP-BD study (details below; also see Ketter et al., 2010) concluded that quetiapine may be useful in preventing manic relapse after a depressive episode, but that lack of a control group makes concrete conclusions difficult to reach.

Summary of pharmacological treatments. In sum, several medications have established themselves as efficacious and effective treatments for bipolar disorder, in that they are statistically differentiable from placebo. Many patients with acute mania will

experience some level of relief from anti-manic agents. Even among those who achieve remission, however, relapse appears to be the norm rather than the exception. This represents a dire mental health situation. In the face of this difficulty, NIMH and other agencies have funded a series of studies to determine if psychosocial treatments, administered as adjuncts to medication, can help prevent the development of manic episodes among those with bipolar disorder. A discussion of this literature follows.

Psychosocial Treatments

Almost every psychosocial treatment trial to date has focused on persons who have not been manic at the start of the trial. These treatments generally aim to prevent the recurrence of manic or depressed symptoms, and are meant to be implemented in the context of ongoing psychopharmacology with one or more of the agents described above. Major treatment approaches are summarized in the following sections.

Psychoeducation. Psychoeducation – teaching people with bipolar disorder about their illness – has been studied in isolation, and also been incorporated into almost all other psychological treatments. Perry and colleagues (1999), in one of the earliest trials investigating psychoeducation as a stand-alone treatment, conducted seven to twelve individual psychoeducation sessions focused on recognition of early symptoms and appropriate treatment-seeking. Participants had suffered from an episode of mania or depression within the previous twelve months. That study found that psychoeducation led to longer periods without manic relapse (65 weeks, versus 17 weeks for the control group) and improved social/occupational functioning compared to treatment as usual. In a larger study, Colom and colleagues (2003) conducted a randomized trial that involved

either 21 sessions of group-based psychoeducation or 21 unstructured group meetings for patients who had not experienced an episode for at least six months. Study results suggested that group-based psychoeducation increased periods of wellness and reduced the lengths of hospitalizations over a two-year follow-up period. It is noteworthy that treatment effects for psychoeducation versus the control condition were not statistically significant in reducing the incidence of manic episodes (although this may have reflected power issues in the context of a small number of episodes, as results did approach statistical significance in that direction). These authors also concluded that psychoeducation can significantly reduce the incidence of hypomania. Furthermore, similar levels of medication use between the treatment and control groups suggested that medication compliance alone was not sufficient to explain the positive effects of psychoeducation. A sizeable follow-up study (Colom et al., 2009) revealed that group psychoeducation led to separate reductions in manic, hypomanic, and mixed episodes during five-year follow-up compared to a medication-only control condition.

Cognitive Behavioral Therapy. Many studies have investigated cognitive-behavioral therapy (CBT) for bipolar disorder. CBT typically includes cognitive restructuring (i.e., helping the patient to think differently about their illness and stressors) as well as problem-solving and communication skills. In an early trial targeting bipolar disorder, Lam and colleagues (2003) randomized patients to routine psychiatric care plus CBT versus a control group that received routine psychiatric care. The CBT manual employed in this study featured heavy emphasis on psychoeducation as well as the importance of engaging in calming activities when confronted with manic symptoms.

Participants had a history of multiple recent episodes, but were not currently depressed or manic. The results favored the CBT group in several domains, including number of days in manic or depressed episodes, hospitalizations for these episodes, and social functioning. At a two-year follow-up (Lam, Hayward, Watkins, Wright, & Sham, 2005), CBT continued to show an advantage in relapse rates, mood ratings, and social functioning. More than half of the CBT group experienced a relapse during the one-year course of the study, however. Of those in the CBT group, seventeen percent experienced a manic episode during the first year of follow-up, compared to 31% in the control group. During the second year, CBT was not statistically differentiable from the control group in terms of preventing manic relapses; about 50% of participants in either group experienced a manic relapse by the end of two years post-treatment. CBT's ability to prevent manic relapse, then, may be relatively short-lived without more intensive interventions to sustain these effects (Lam et al., 2003, 2005).

Although findings of the Lam study suggested at least some effect of CBT, other trials, using other CBT manuals, have not obtained effects. Findings from the largest trial of CBT for bipolar disorder to date (total n = 253, or whom 127 received CBT) indicated predominantly negative results (Scott et al., 2006). About 40% of participants (all of whom were initially not manic) receiving CBT had experienced another manic episode during the 18-month follow-up period, compared to 35% of controls. Further analyses suggested that CBT was less useful for patients with more prior mood episodes (Scott et al., 2006; Scott, Colom, & Vieta, 2007). This suggests that CBT may be the least effective for the patients who would appear to need it the most, although it may simply emphasize the difficulties of treating highly symptomatic patients. In addition to these

large studies, a number of smaller trials of CBT have been conducted. One recent trial conducted in Spain (Isasi, Echeburúa, Limiñana, & González-Pinto, 2010) found that a combination of CBT, psychoeducation, and relaxation, conducted over 20 sessions in a group format along with medication management, outperformed medication management alone. These results held for manic symptoms (as measured by the Young Mania Rating Scale) at post-treatment and one-year follow-up. Several other small trials have apparently lacked adequate power to detect effects on their own, but some researchers have conducted meta-analyses to pool results. Meta-analyses and reviews of CBT treatments have come to conclusions similar to the Lam trial presented above: CBT appears to result in about a 50% reduction in the number of people who relapse when compared to psychopharmacology alone (Beynon, Soares-Weiser, Woolacott, Duffy, & Geddes, 2008; Miklowitz, 2008; Otto, Reilly-Harrington, & Sachs, 2003; Scott, 2006; Scott, Colom, & Vieta, 2007; Zaretsky, Rizvi, & Parikh, 2007). Many studies do not report results separately for manic and depressive relapses, though. Two recent reviews with attention to manic versus depressive outcomes suggest that outcome data are particularly poor for manic episodes (Miklowitz, 2008; Scott, 2006).

Several CBT treatments have incorporated various facets beyond the core components of cognitive restructuring, psychoeducation, and problem-solving alluded to above. For example, Johnson and Fulford (2009) have developed a CBT manual with a focus on goal attainment and confidence. Mindfulness techniques have also been taught as part of larger CBT protocols (e.g. Weber et al., 2010). Many of these types of treatments have not yet been subjected to rigorous randomized controlled trials, and it can

be difficult to determine whether positive outcomes are attributable to the CBT shell or the specific modifications.

Taken together, the CBT treatment outcome studies paint a sobering picture. It seems clear that CBT does have some beneficial effects for people with bipolar disorder, leading to improved social functioning and fewer days in episodes than medication alone. This success is counterbalanced, however, by evidence that CBT may work less well in preventing mania than in preventing depression, and that rates of relapse after CBT remain quite high. At least one recent trial (Isasi et al., 2010) suggests that CBT (when combined with psychoeducation, relaxation, and medication management) can reduce manic symptoms. The literature more broadly, however, suggests that CBT's effects on mania appear to be limited to one year post-treatment (Lam et al., 2005) or patients with relatively fewer past episodes (Scott et al., 2006).

Interpersonal and Social Rhythm Therapy. Another well-known treatment for bipolar disorder is Interpersonal and Social Rhythm Therapy (IPSRT; Frank, 1999; Frank et al., 2005). This treatment encourages more stable social rhythms (e.g. sleep/wake time, meal times), and also addresses common interpersonal situations faced by people with bipolar disorder. In one study, Frank and colleagues (2005) enrolled participants who were recovering from acute mania or depression in a crossover design to differentiate the effects of acute and preventive IPSRT treatment. Acute treatment continued until participants evidenced only minimal symptoms for four weeks, whereas preventive treatment continued for two years. Participants were randomized to IPSRT or intensive clinical management (ICM) in each phase, yielding four treatment conditions: IPSRT in the preliminary phase and in the preventive phase; ICM in the preliminary and preventive

phase; IPSRT during the preliminary phase and then ICM for the preventive phase; and ICM in the preliminary phase and IPSRT during the preventive phase. The study found that acute IPSRT was associated with more regular social rhythms and longer well periods when compared to ICM, but findings did not generalize to the prevention phase. That is, IPSRT offered during the preventive phase did not offer benefits compared to ICM. IPSRT therefore does not appear useful compared to ICM when administered for a longer period of time (Frank et al., 2005). Overall, IPSRT has been associated with significant reductions in depressive symptoms, but may be less useful in reducing manic symptoms (Frank, 1999).

Family Focused Therapy. Other treatments are oriented toward the greater family context in which bipolar disorder often occurs. Family Focused Therapy (FFT; Miklowitz & Goldstein, 1997) was created based on evidence that family environments high in expressed emotion – that is, high levels of criticism, hostility, and emotional overinvolvement – predict faster relapse for several disorders, including bipolar disorder (Butzlaff & Hooley, 1998). The treatment is conducted with the patient and his or her family (spouse, parents, or siblings) in three modules. The first module involves psychoeducation about bipolar disorder, including its etiology and factors related to its course (e.g. medication adherence, detecting initial symptoms). The second module focuses on improving the family members' ability to communicate with one another, and the third involves problem-solving skills training. Together, the three modules require approximately 21 sessions to complete over a 9-month period.

One study compared FFT to a less intensive crisis management control condition among participants who had recently recovered from a manic or depressed episode

(Miklowitz et al., 2003). Over a two-year period, families randomized to FFT demonstrated greater stabilization of mood symptoms. Further analysis revealed, however, that the effects were only statistically significant for the prevention of depressive episodes. In addition, the relatively low intensity of the control condition left open the possibility that the observed treatment effects for FFT were due simply to its more frequent sessions.

Another study compared FFT to an equally intensive individual treatment, thus ruling out simple treatment frequency effects (Rea et al., 2003). This study enrolled participants who had been on an inpatient unit for a recent manic episode. The study found FFT to predict significantly lower rates of relapse and hospitalization. Treatment effects for FFT versus the comparison treatment only emerged, however, one year after treatment. This suggests that patients may gain full benefit from FFT only after their families have a chance to internalize or develop skills over time. In addition, this study did not report outcomes for mania and depression separately, instead collapsing both types of relapse into one outcome. Despite several studies of FFT, then, no study has provided evidence that FFT helps prevent mania. This finding is perhaps tied to evidence that family conflict specifically predicts depressive, but not manic, symptoms in bipolar disorder (Gitlin, Swendsen, Heller, & Hammen, 1995)

Other psychosocial interventions. I mentioned above that the bipolar treatment literature is dominated by treatment manuals, which themselves typically consist of dozens of interventions administered over several sessions. There are some noteworthy exceptions to this trend, however. For instance, the role of sleep has been investigated with some extraordinarily detailed case studies (e.g. Totterdell & Kellett, 2008; Wirz-

Justice et al., 1999; Wehr et al., 1998). More well-controlled studies targeting sleep, however, have met with limited success (e.g. Shen, 2008).

Comparisons of different psychosocial treatments. To date, relatively few studies have considered whether one psychosocial treatment provides an advantage compared to others. At least one study has suggested that cognitive therapy does not provide a benefit as compared to psychoeducation (Zaretsky, Lancee, Parikh, & Miller, 2003).

The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD; Miklowitz et al., 2007a, 2007b; Parikh, LeBlanc, & Ovanessian, 2010) was the first large trial to carefully compare several psychosocial treatments for bipolar disorder, and has included several sub-studies of various pharmacological interventions as well. Outcome criteria for that set of studies have included relapse prevention and quality of life. One STEP-BD study enrolled 293 participants with bipolar I or II disorder who were suffering from an acute depressive episode; evidence may therefore be more relevant for evaluating effects on depression rather than mania. The treatment arm included CBT (n = 75), IPSRT (n = 62), and FFT (n = 26), and the control condition featured "collaborative care" (CC, consisting of three sessions of psychoeducation; n = 130). All participants were provided with medication management (itself the subject of separate outcome analyses). Follow-up continued for twelve months after study entry.

Outcomes from STEP-BD suggest that the intensive treatments outperformed CC in terms of time to recovery from depression and months of clinical wellness (two or fewer symptoms of mania or depression; Miklowitz et al., 2007b). Even so, more than one-third of the participants randomized to CBT, IPSRT, and FFT had not achieved recovery (much less maintained wellness for any significant period) at the end of the

study year. Results so far have generally not investigated outcomes in terms of manic and depressive relapse separately. No statistically significant differences were found among CBT, IPSRT, and FFT.

Overall Summary of Bipolar Treatment

In sum, pharmacological treatments appear to feature significant room for improvement in terms of mania prevention, leading researchers to attempt to fill this gap via adjunctive psychosocial treatments. The literature reviewed above suggests that bipolar disorder is somewhat amenable to psychosocial treatments in the context of ongoing psychopharmacology. There is much work to be done, however: relapse appears to be the norm rather than the exception for those patients fortunate enough to achieve remission. Some of the largest trials (e.g. STEP-BD) were conducted in the context of depression rather than mania. In the few studies to examine relapses for both mania and depression separately (e.g. Colom et al., 2003; Frank, 1999; Lam et al., 2003, 2005; Miklowitz et al., 2003), treatment benefits generally appear to be more robust for the depressive rather than the manic pole of the illness. Psychoeducation (Colom et al., 2009) or CBT with self-calming and psychoeducational components (Lam, 2005), appear to be notable exceptions, in that they have demonstrated robust effects on mania prevention in at least one well-designed study each.

Beyond the gaps in the treatment outcome studies, little research has looked carefully at the particular components that are most helpful in preventing or reducing manic symptoms. Available evidence in trials that do demonstrate effects on mania suggest that medication adherence is a major mechanism behind some current results

(Miklowitz et al., 2003). Regarding mechanisms, some recent treatment development work has been conducted (cf. Johnson & Fulford, 2009), but no randomized controlled trial supports the idea that interventions effectively target mania above and beyond the role of psychoeducation. Other researchers have more carefully investigated the role of sleep in stabilizing patients with bipolar disorder, including some remarkably intensive case studies (e.g. Wehr et al., 1998). Larger controlled trials specifically targeting sleep, however, have met with mixed results (Shen et al., 2008). Thus, the field has not yet adequately addressed the issue of preventing the recurrence of manic episodes among those who suffer from bipolar disorder, and what evidence that exists appears to provide little concrete data regarding mechanisms (Scott et al., 2006). The discussion will now turn to one novel approach to thinking about a potential component of mania: arousal.

Treating Mania: Arousal as a Mechanism to Consider

The research reviewed above has revealed that few psychosocial treatments adequately address manic symptoms. This section will consider arousal as an important component of manic symptoms that has received minimal attention in existing treatments for bipolar disorder. Arousal is a well-recognized dimension in considering emotions (Clark & Watson, 1991); intriguingly, arousal can seemingly potentiate the effects of both negative and positive affective states. In common circumplex models, arousal combined with negative affect produces anxiety and fear, whereas arousal combined with positive affect may be more closely tied to elation and excitement, states that are frequently observed during mania (Watson et al., 1995a, 1995b; Watson & Tellegen, 1985).

The picture is more subtle than this, however. Mania is predominantly experienced as a euphoric state, but can also manifest as an unpleasant, irritable one (American Psychiatric Association, 2000). Rather than valence, then, several authors have concluded that the issue of avoidance versus approach is what separates anxiety from mania. Anxiety is concerned with avoiding unwanted scenarios, while mania appears to be tied up with the pursuit of valued approach-relevant goals (Depue & Iacono, 1989; Johnson, Ruggero, & Carver, 2005). Thus anxiety is thought to be tied to high levels of avoidance or an overactive Behavioral Inhibition System (BIS), while mania is thought to be tied to high levels of engagement or an overactive Behavioral Activation System (BAS; Carver & White, 1994; Gray, 1981, 1994). People with bipolar disorder are highly sensitive to cues of reward (see Johnson, 2005; Urošević, Abramson, Harmon-Jones, & Alloy, 2008; Johnson, Fulford, & Eisner, 2009). Some authors have specifically connected this increased BAS sensitivity to asymmetrical resting frontal cortical activity (Harmon-Jones & Allen, 1997). According to this model, irritability as a manic symptom arises when pursuit of one's goals is thwarted. Arousal could therefore be seen as an indicator of high engagement in the pursuit of approach goals. Arousal in the context of bipolar disorder (specifically, elation or irritability) appears specifically tied to approach rather than avoidance. A key question, then, is to determine whether the psychophysiological profile of anxiety (which has been amenable to change by PMR and similar techniques) is at all similar to those of elation and irritability. Such similarities would suggest that PMR could be helpful in reducing the arousal states of mania, just as it has been helpful in reducing the arousal state of anxiety. Some rather preliminary research suggests that approach and avoidance (which, as above, are tied closely to mania

and anxiety, respectively) share strikingly similar physiological profiles, including skin conductance response, heart rate, and late positive event-related potentials in the central-parietal area (Löw, Lang, Smith, & Bradley, 2008), despite some areas in which they demonstrate clear differences (Bradley, 2000).

Beyond physiological profiles, the syndromes of anxiety and mania appear to share some additional overlap, one example of which is diagnostic comorbidity. Researchers conducting the National Comorbidity Survey found that a 12-month bipolar disorder diagnosis had very high tetrachoric correlations (between .39 and .52) with each of several categories of anxiety disorders (Kessler et al., 2005). Indeed, correlations between manic symptoms and anxious symptoms were higher than those between manic and depressive symptoms. Other authors have concluded that the lifetime comorbidity between bipolar disorder and anxiety disorders may be close to 90% (Kessler et al., 1997; Merikangas et al., 2007). Hence, the comorbidity rates of anxiety and mania suggest that it might be fruitful to consider models of arousal in regard to bipolar disorder.

In addition to comorbidity, mania and anxiety also seem to share a core set of symptoms that are related to arousal. For instance, sleep disturbance has been considered a "hallmark" manic symptom (Hirschfeld, Lewis, & Vornik, 2003; Sierra et al., 2007; Wehr, Sack, & Rosenthal., 1987), and is also a key symptom of generalized anxiety disorder. Indeed, of the nine symptoms of mania listed in the DSM criteria, more than half can be conceptualized as symptoms of arousal, including decreased need for sleep, elevated or expansive mood, increased talkativeness, and increases in goal-directed activity. One of the major self-report measures of mania, the Internal State Scale (ISS; Bauer et al., 1991; Bauer, Vojta, Kinosian, Altshuler, & Glick, 2000), provides a positive

screen for bipolar disorder via a subscale labeled "Activation." This subscale consists entirely of items measuring arousal, including overactivity, restlessness, and racing thoughts.

Beyond evidence that arousal is a core feature of manic symptoms, it can also be a harbinger of onset. Early studies that tracked hourly activity and symptoms found that increases in activity were an excellent predictor of impending manic shifts (e.g. Klein, Lavie, Meiraz, Sadeh, & Lenox, 1992; Wehr et al., 1982). Thus a body of literature supports the idea that arousal symptoms are prominent features of mania.

These phenomenological similarities in arousal-related states have led some researchers to posit that anxiety and mania may be related to a similar set of psychobiological vulnerabilities (for examples see Chen & Dilsaver, 1995a, 1995b; Holmes et al., 2008). For instance, results from several studies suggest elevated norepinephrine activity in both bipolar disorder and various anxiety disorders; furthermore, such activity in bipolar disorder appears to be higher during manic than depressed or euthymic periods (for a review see Freeman, Freeman, & McElroy, 2002). Elevated norepinephrine activity seems to be related to a heightened sense of arousal, independent of affective valence (Berridge, 2007). In addition, antidepressants with norepinephrine reuptake inhibiting properties (e.g. tricyclics) appear more likely to trigger manic symptoms than do other antidepressants (for a review see Gijsman et al., 2004). That is, excess norepinephrine activity may be causally related to increased manic symptoms.

Norepinephrine-related increases in arousal may therefore provide an important link between mania and anxiety conditions. If this is the case, then treatments initially

designed for addressing anxiety, to the extent that they reduce arousal and norepinephrine levels, may also be effective at directly reducing manic symptoms. Treatments to reduce anxiety are associated with changes in norepinephrine functioning (e.g. Antoni et al., 2000). Although not the focus of this study, such treatments could also provide the benefit of reducing the high rates of anxiety among those with bipolar disorder. Anxiety treatments are relatively advanced, but there are unique challenges in addressing anxiety within the context of bipolar disorder. When comorbid bipolar disorder is not present, antidepressant medications are among the most recommended treatments for anxiety disorders. Efficacy rates are similar or better than those for the traditional anxiolytic treatment of benzodiazapenes (Roy-Byrne & Cowley, 2007), side effects are less pronounced, and addictive properties are of minimal concern (especially for selective serotonin reuptake inhibitors; see Nutt, 2003). The use of antidepressants may be contraindicated in the context of bipolar disorder, however, due to the risk of inducing mania (Ghaemi, 2006; Goldberg et al., 2007; Holmes, Geddes, Colom, & Goodwin, 2008; Truman et al., 2007). Furthermore, several analyses from STEP-BD recently concluded that adding an antidepressant to a mood stabilizer is no more useful in managing bipolar depression than a mood stabilizer alone (Goldberg et al., 2007; Sachs et al., 2007). The use of benzodiazepines carries the risk of addiction (Ashton, 1997), which is especially concerning given the documented comorbidity between bipolar disorder and substance abuse (Kessler et al., 2005).

The research reviewed above suggests that mania and anxiety differ on at least one important dimension: mania appears to reflect an overactive BAS, while anxiety appears to reflect an overactive BIS. Despite this difference, the literature also points to

some fundamental connections between mania and anxiety. These connections, including physiological arousal, symptom overlap, and diagnostic comorbidity, suggest that treatments developed for anxiety may be useful in treating mania. Medication treatments for anxiety, however, are controversial in the context of bipolar disorder due to the risk of inducing mania (in the case of antidepressants) and the risk of dependence (in the case of benzodiazepines). Thus, a psychosocial intervention that could address physical arousal in mania may be beneficial. To be clear, the current intervention might not address all features of mania; instead, it is believed that addressing one set of manic symptoms might have significant advantages.

No researchers have yet explicitly tested the role of arousal reduction as an intervention strategy for mania. It is worth noting, though that many of the approaches that people with bipolar disorder endorse using to reduce their initial manic symptoms (prodromal symptoms; Molnar, Feeney, & Fava, 1988) are likely to reduce arousal. These include scaling back excessive behavior, taking extra time to rest/sleep, seeking medical attention, and engaging in calming activities (Lam, Wong, & Sham, 2001). Several recently-developed treatment programs have also included relaxation strategies for managing bipolar disorder (e.g. Isasi et al., 2010; Johnson & Fulford, 2009). The goal of this study is to more explicitly test a single approach that is well-validated as a way to reduce arousal.

Barriers to Treating Mania

Beyond the need to consider more specific mechanisms in mania, the difficulties in addressing manic symptoms using psychosocial treatments might also reflect a set of

barriers that make treatment more difficult in the context of mania. It is widely believed that there are issues that make mania particularly resistant to treatment, above and beyond the relative inattention that has been paid to arousal. The following sections will therefore consider deficits in insight and executive functioning as two such barriers. It will conclude with a synthesis of research on these domains, and discuss the implications for mania prevention.

Insight

Insight – a person's awareness and understanding of their psychiatric symptoms – appears intact in bipolar depression or euthymia, but declines as manic symptoms become more and more severe (for review, see Ghaemi & Rosenquist, 2004). In fact, over 90% of people with bipolar disorder can reliably name their personal mania prodromes (i.e. signs of impending mania) when they are euthymic (Lam et al., 1997, 2001, 2005; Molnar, Feeney & Fava, 1988; Smith & Tarrier, 1992). Insight (or lack thereof) will only be relevant for certain mania prevention strategies. One can categorize methods to prevent/reduce manic symptoms into one of two broad categories. First, some strategies are implemented more or less continuously and do not depend on the emergence of prodromal symptoms. For instance, maintaining an effective dosage of a mood stabilizer or consistently getting enough sleep might fall under this domain, as they do not necessarily rely on the patient's insight into their current mood state. In contrast, other treatment approaches are only meant to be implemented when the patient begins to notice some type of change in his or her emotional state, cognition, or behavior. For instance, many treatment approaches encourage patients to reduce their engagement in

goal-directed activity when they find themselves becoming "sped-up" (e.g. Johnson & Fulford, 2009). Implementing this latter type of strategy requires a basic level of insight into the onset of one's manic symptoms: without such insight, the patient will not know when a particular strategy is called for.

Thus, it may be important to consider training people to use strategies that can be executed and internalized easily during well periods. To borrow a quote from children's author Norton Juster: "Practice does not make perfect; practice makes permanent…" If skills are practiced enough during euthymia, it is possible that they may "carry over" into the initial stages of mania, reducing the chances of a full-blown manic episode. That is, low insight levels do not represent an insurmountable barrier to carefully crafted psychosocial approaches. A related body of research has investigated the role of executive functioning in insight as well as in bipolar disorder more generally; studies on this construct are reviewed below.

Executive Functioning

Executive functioning is generally conceptualized as a broad set of cognitive abilities related to planning, rule acquisition, abstract thinking, and initiating and inhibiting behaviors. A host of studies suggest that people with bipolar disorder have impaired executive functioning during mania (e.g. Albus et al., 1996; Dixon, Kravariti, Frith, Murray & McGuire, 2004; Murphy et al., 1999). Some have argued that deficits in executive functioning might interfere with insight. Other studies go further in demonstrating that these deficits are present to a lesser degree even during euthymic periods (for reviews see Arts, Jabben, Krabbendam, & van Os, 2008; Robinson et al.,

2006). It thus appears that people with bipolar disorder have impaired executive functioning at baseline, but that these deficits become more severe as a manic episode develops (Dixon et al., 2004). Furthermore, these deficits seem to be present early in the course of illness, rather than merely developing after years of mood episodes. As was mentioned above, however, patients can still detect their manic symptoms despite these deficits (Arts et al., 2008; Lam et al., 1997, 2001, 2005; Molnar, Feeney & Fava, 1988; Smith & Tarrier, 1992).

The pattern of executive function deficits reviewed above suggests several considerations in designing treatments that are more easily and reliably implemented. Research on prodromal symptoms suggests, for instance, that some coping strategies are associated with better outcomes than others (e.g. Lam & Wong, 1997; Lam, Wong & Sham, 2001). Examples of useful coping strategies include: reducing excessive behavior, taking extra time to rest/sleep, seeking medical attention, and engaging in calming activities. Little work has been done to investigate the precise mechanisms by which these useful strategies led to reduced manic symptoms. It is worth noting, however, that each of them appears to feature an explicit behavioral component. Such strategies may require less executive function compared to more complex cognitive interventions that depend on the ability of a person to monitor and challenge their own cognitive states.

Summary of Barriers to Treatment

Insight and executive functioning are both impaired among those with bipolar disorder. These deficits are most pronounced when manic symptoms are most severe, but are present to a lesser extent during the prodromal phase and even during euthymic mood

states (Ghaemi & Rosenquist, 2004; Robinson et al., 2006). Some people with bipolar disorder demonstrate maladaptive coping responses in the face of prodromal symptoms, but others use strategies that are associated with better functioning (Lam, Wong, & Sham, 2001). These findings may have several important implications for interventions targeting mania. Any intervention for reducing or preventing full-blown manic symptoms will need to be simple and direct enough to be implemented despite impaired insight and planning abilities. Such a strategy would ideally be easily rehearsed during euthymic periods to allow relatively automatic implementation when symptomatic. Although no research has directly examined this, effective treatment manuals often suggest behavioral strategies to supplement cognitive interventions, particularly in the focus on manic relapse (Colom & Vieta, 2003; Lam et al., 2005). In addition, strategies that have an immediate impact on symptoms despite varying levels of cognitive impairment would likely be most helpful. Based on this research, as well as the literature on arousal reviewed earlier, the next section will discuss one such treatment that could be successfully applied in the context of bipolar disorder.

Progressive Muscle Relaxation

Progressive Muscle Relaxation (PMR; Bernstein & Borkovec, 1973) is a treatment methodology that may fit the criteria described above. It is a simple, direct, easy-to-use strategy that has led to reductions in anxiety in a variety of medical and psychological conditions (for reviews see Gould, Otto, Pollack, & Yap, 1997; Jorm et al., 2004; Renfroe, 1988) despite some non-replications (e.g. Craske, Brown, & Barlow, 1991; Lolak, Connors, Sheridan, & Wise, 2008). PMR has been successfully integrated

into more comprehensive interventions for various conditions (Antoni, Ironson, & Schneiderman, 2007; Johnson & Fulford, 2009). In addition, and of crucial importance for this study, PMR can be taught in just one session (Őst, Ferebee, & Furmark, 1997; Rausch, Gramling, & Auerbach, 2006).

Beyond the pragmatic issues, PMR is well-documented as a way to reduce arousal. It is noteworthy that PMR has established particular efficacy with panic disorder and GAD (Conrad & Roth, 2007; Gould et al., 1997; Jorm et al., 2004), two of the anxiety disorders with the highest comorbidity with bipolar disorder (Doughty, Wells, Joyce, Olds, & Walsh, 2004; Kessler et al., 1997; MacKinnon et al., 2002). It has also established an ability to reduce somatic arousal (Ghoncheh & Smith, 2004) and sleep disturbance, key symptoms of mania (Gustafson, 1992; Viens et al., 2003). If PMR can have these same effects in the context of bipolar disorder, then it could prove to be a powerful tool for scaling back manic symptoms before a full-blown episode occurs.

PMR originated with Jacobson (1938). This method involves the patient systematically tensing, and then relaxing, groups of muscles in sequence until the entire body has achieved a state of relaxation. Initially this process involved 30 muscle groups and took several sessions to train. Since then others have developed more abbreviated versions with 16 or even fewer muscle groups that have nonetheless demonstrated similar treatment gains (e.g. Bernstein & Borkovec, 1973). It is theorized that anxiety is part of a more general stress activation response, and that reducing muscle tension leads to lower perceived stress and better overall health.

Drawing on the barriers to treatment in bipolar disorder, I have suggested that the "ideal" intervention for preventing mania might be easily and routinely implemented to

counter difficulties from insight and low executive functioning, and would provide immediate benefit when used. PMR appears to meet all of these criteria. It has been successfully taught to a variety of populations in as little as one group-based session, underscoring its relative simplicity. Its effects on anxiety are well-documented, and most patients describe the effects as pleasurable. If successfully implemented, it results in a feeling of calm and relaxation that is immediately apparent. This study investigated whether this technique can be taught in one session to people with bipolar disorder. Outcome measures included manic symptoms immediately post-intervention as well as at five-week follow-up.

Statement of the Problem

The literature reviewed above has demonstrated that people with bipolar disorder often continue to experience distressing symptoms despite treatment. This appears to be true for both the manic and depressive phase of the illness. Current psychosocial treatments, however, appear particularly limited in the prevention of mania. Several different issues might have interfered with progress in this field. Recent reviews have suggested that more work is needed to identify specific mechanisms involved in mania, and to develop interventions that more specifically target these mechanisms. Some striking conceptual similarities between mania and anxiety suggest that arousal may be a promising mechanism to target in order to prevent mania and improve existing treatments. Finally, bipolar disorder often features diminished insight and executive functioning, particularly as manic symptoms increase. These issues suggest that simple, routine interventions that do not require high levels of insight or executive function might

be particularly useful. As a first step in treatment development, this study tested an innovative approach to regulating manic symptoms among people with bipolar disorder: PMR (Bornstein & Borkovec, 1973; Antoni, Schneiderman, & Ironson, 2007).

Bipolar disorder is an episodic illness, but even those with a relatively severe course only experience significant manic symptoms a small portion of the time (Judd et al., 2003). Beyond measuring manic symptom changes during the first session and at five-week follow-up, a brief analog procedure was used to induce a state of high arousal positive affect (further details are provided below in the Methods section).

Considerable debate exists in the field of psychology regarding the best ways to test, package, and disseminate treatments for various disorders. At one extreme, treatments could be conceptualized as packages or manuals that are generally self-contained and provide the necessary therapeutic steps to treat a given mental illness. On the other hand, a meaningful approach to clinical research might be to investigate specific intervention strategies that can be easily integrated into treatment (Franklin, DeRubeis, & Westen, 2006; Westen, Novotny, & Thompson-Brenner, 2004a, 2004b). It is in this latter spirit that the proposed study has been designed. This study's results have implications for the use of PMR as a part of treatment aimed at preventing manic relapse.

The current study, then, is innovative in several ways. Most previous studies of psychosocial approaches to prevent mania have involved multifaceted interventions. This study, in contrast, featured a relatively specific approach (PMR), a technique that has demonstrated an ability to reduce anxiety and arousal, but that has not yet been tested in bipolar disorder. In addition to its ability to reduce anxiety, PMR may be useful in bipolar disorder despite several barriers related to mania, including impaired insight and

executive functioning. The positive mood induction (also seldom seen in previous studies) was used to create an analog for prodromal manic symptoms, allowing this study to relatively quickly test PMR's ability to help people with bipolar disorder reduce such symptoms. This study therefore represents an important addition to the literature on preventing manic relapse in bipolar disorder.

Hypotheses

Hypotheses of this study were as follows.

(1) After a positive mood induction, people with bipolar disorder would experience an immediate reduction in manic symptoms after implementing PMR.

(2) This reduction in manic symptoms after implementing PMR would be statistically greater than that shown by a control group that has a chance to implement their own self-calming strategy.

(3) After a five-week follow-up period, participants trained in PMR would again experience a greater reduction in manic symptoms after the positive mood induction and a PMR rehearsal than would the control group after a positive mood induction and a self-calming strategy.

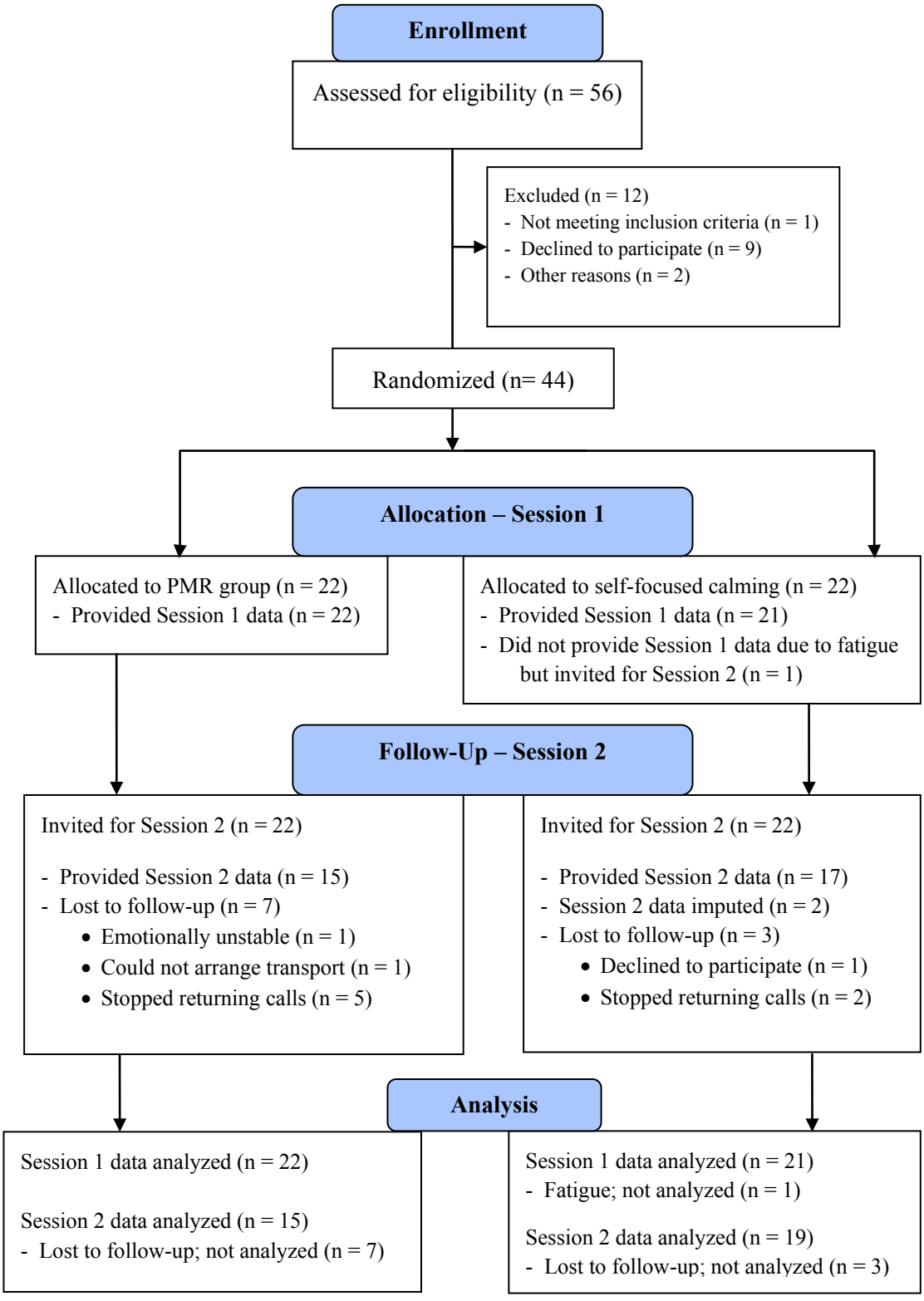
Chapter 2: Methods

This study was conducted at the University of Miami in Coral Gables, Florida. All procedures were approved by the University of Miami Institutional Review Board. A CONSORT flowchart of participant enrollment can be found in Figure 1 (Schulz, Altman, & Moher, 2010).

Participants

Participants had all completed previous studies through Dr. Sheri Johnson's lab at the University of Miami. Recruitment for that study had involved community postings, advertisements on the Miami public transportation system, and Craigslist. The current study's inclusion criteria were: participants between the ages of 18 and 65, with a diagnosis of bipolar I disorder according to the Structured Clinical Interview for the DSM-IV (SCID; First & Gibbon, 2004; see Measures below for more details). Additional inclusion criteria were: participants who had been speaking English since age 10 or earlier, and were without any self-reported history of a neurological disorder such as Alzheimer's or Huntington's disease. Participants needed to be able to understand the study procedures and give informed consent, and so participants with severe cognitive deficits were not enrolled.

Figure 1. CONSORT diagram of study enrollment (Schulz, Altman, & Moher, 2010).



Furthermore, enrolling participants with current, active substance abuse issues could introduce significant confounds (e.g. related to executive functioning; Scheurich, 2005), as well as complicating diagnostic assessment. As such, this study excluded participants who had met criteria for alcohol or substance abuse or dependence within the past six months. The six month limit was chosen to ensure that participants did not demonstrate drug- or alcohol-related cognitive deficits during the study, while also maximizing the number of potential participants.

As originally conceptualized, I aimed to rule out participants with severe depressive symptoms during the first session. Recruitment pressures, however, resulted in a broadening of the study entry criteria to enroll participants regardless of depressive symptoms at Session 1. Four participants with Session 1 data reported high levels of depressive symptoms at Session 1 (MASQ Anhedonic Depression subscale score greater than 90). In general, parallel analyses suggested that inclusion of these participants in the final dataset fundamentally changed neither the statistical significance of outcomes nor effect sizes. Exceptions will be noted in the Results section where applicable.

Interventions

Participants were randomized to either PMR or a control intervention, using stratification procedures to ensure matching on key variables. Both the experimental and control groups received a brief introduction to the study, and the experimental group also received training in PMR. In lieu of relaxation training, the control group was given an opportunity to implement their own emotion regulation strategy. Both groups had the opportunity to use these strategies after they had gone through a positive mood induction,

a procedure designed to cause an elevated mood and an initial level of manic symptoms. More detail on these interventions follows.

Introduction to the Study

All participants received a brief introduction to orient them to the study with the following wording: "Many people with bipolar disorder can find themselves caught up in new goals, activities, or relationships. This can cause a spiral of increasing excitement, confidence, and engagement. If left unchecked, these feelings can lead to a full-blown manic episode. The process can also feature a sense of physical arousal or tension. A goal of today's session is to think about useful tools for preventing manic symptoms."

Progressive Muscle Relaxation

The experimental condition involved a brief (about 20-minute) training on PMR, based on existing manuals (Bornstein & Borkovec, 1973; Antoni, Ironson, & Schneiderman, 2007). This training briefly described the rationale behind PMR (including potential applications for bipolar disorder) and included step-by-step training to tighten and relax sixteen muscle groups. The earliest manifestations of PMR featured more distinct muscle groups, but this study targeted sixteen muscle groups because that number has been used successfully in popular manuals (e.g. Antoni, Ironson, & Schneiderman, 2007).

Control Condition: Self-Focused Calming

Participants in the control group were given the opportunity to implement their own emotion regulation strategy based on their own experience. As reported above, a body of literature has demonstrated that people with bipolar disorder can report effective

strategies for reducing manic symptoms (e.g. Lam et al., 2001). Participants were given up to 30 minutes to use any strategy they chose. After they had the opportunity to use their own strategy, a very brief questionnaire assessed what strategy they used and their satisfaction with that strategy. The amount of time they took to engage in self-focused calming was recorded for use as a covariate.

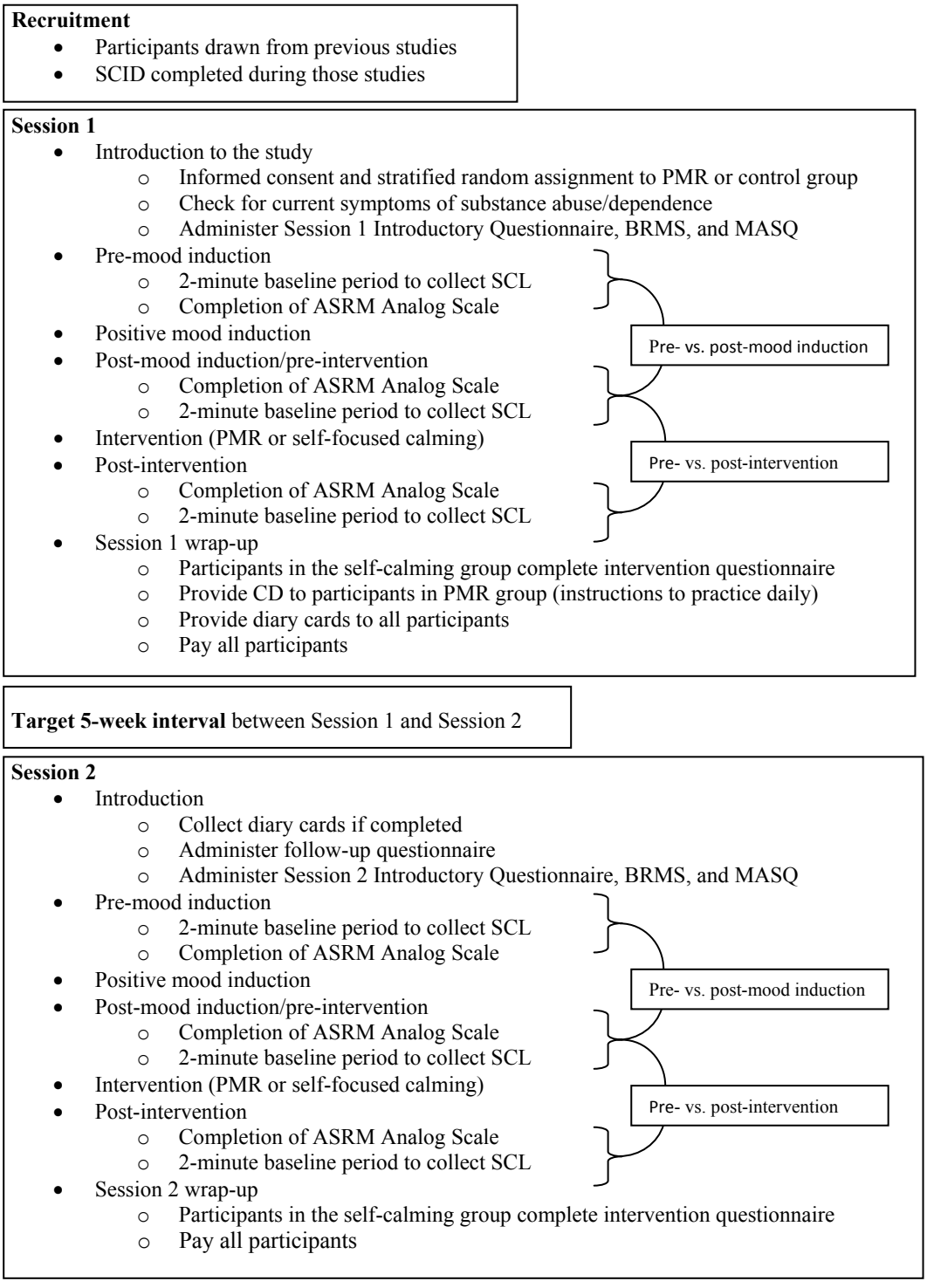
Procedure

A step-by-step chart outlining all of the study procedures can be found in Figure 2. Details on measures can be found in the "Measures" section below. Participants were instructed over the phone to avoid excessive caffeine or nicotine intake during the six hours before their scheduled appointments, as these substances have well-known effects on arousal.

Stratified Randomization

Participants were stratified on key variables that might be expected to correlate with outcomes. These included current mood stabilizing medication, current psychosocial treatment, history of an anxiety disorder diagnosis, history of a substance abuse diagnosis, and gender. The first eight participants were assigned randomly to the PMR or control condition, and remaining participants were assigned based on this stratification scheme. Based on PMR's history of application to anxiety, balancing the groups on comorbid anxiety diagnoses was considered the highest priority for stratification.

Figure 2. Flowchart of study procedures



Session 1

All Participants completed written informed consent procedures. Participants then completed a brief demographic questionnaire, including two items assessing the participant's level of motivation to reduce highly positive and highly irritable/frustrated moods. After the demographic questionnaire, all participants completed the Bech-Rafaelsen Mania Scale and the Mood and Anxiety Symptom Questionnaire, and then received the introduction to the study described above.

Positive Mood Induction

After introduction to the study, all participants completed a brief mood measure including the ASRM and Nervous scales (described below). This was followed by a two-minute baseline period to collect Skin Conductance Level (SCL) data, and then a positive mood induction aimed at creating a high-arousal positive affect state. Specifically, participants were instructed to think in detail about a dream coming true, while upbeat music played in the background. This type of approach has been shown to induce feelings of happiness that are similar to, but not as intense as, a manic state (Mayer, Allen, & Beauregard, 1995). Music alone has shown reliable mood-enhancing effects (Clark & Teasdale, 1985; Krumhansl, 1997). The literature for guided imagery alone is less developed, but the combination of music and imagery appears to be particularly powerful (see Gilet, 2008 for a review). Westermann and colleagues (1996) concluded that positive mood inductions have generally demonstrated modest effect sizes (Cohen's $d = 0.4$), and induce an elevated mood for anywhere between 50% and 100% of participants

(depending on the specific mood induction procedure and how this elevation is defined and measured).

Previous studies conducted at the University of Miami have found this mood induction procedure to lead to increased ratings of happiness among non-affectively ill controls as well as participants with bipolar disorder. After about five minutes of the positive mood induction, participants repeated the mood measure. Participants were given the opportunity to repeat the positive mood induction if they reported only a minimal improvement in their mood.

Participants in the experimental group were then trained in PMR, while those in the control group were instructed to use whatever emotion regulation technique they believe would have calming effects for them (see "Interventions" section above). For the remainder of this dissertation, the term "intervention" will refer to either PMR or self-focused calming; in addition, the terms "self-focused calming" will be synonymous with "control condition" or "control group." After completion of the intervention, participants completed the mood measure a third time, allowing calculation of change pre- to post-intervention. Then, participants were debriefed and instructed regarding follow-up procedures. Those in the PMR group were given a CD with instructions for completing PMR at home on a daily basis if possible. Instructions noted that daily practice for five weeks is recommended in order to master the technique. The CD itself contained a 13-minute audio track, following the script for PMR covering the same 16 muscle groups as were covered in the session. All participants were instructed to complete daily Diary Cards, and were paid $20 for completing Session 1.

Follow-up period. The follow-up period was intended to last for five weeks. Due to scheduling conflicts, missed phone calls, and the like, some participants were unable to complete Session 2 until several months after Session 1, and thus time between sessions was considered as a covariate in analyses. Participants were encouraged to bring their completed Diary Cards with them to Session 2. To minimize attrition, however, they were invited to attend Session 2 whether they had completed any Diary Cards or not.

Session 2

As shown in Figure 2, the procedure for Session 2 generally mirrored that for Session 1, with a few exceptions. At Session 2, participants completed a brief Follow-up Questionnaire to supplement the information from the Diary Cards. Unlike Session 1, participants in the PMR group were given up to 30 minutes to complete PMR with a CD (rather than in person with the experimenter). The control group was once again given up to 30 minutes to implement their own self-calming strategy. At the end of the session, participants were debriefed and paid an additional $20.

Measures

This study included self-report, interviewer-administered, and psychophysiological assessments. The measures selected for this study have generally demonstrated their utility in numerous studies.

Introductory Questionnaire

Each session involved administration of a brief custom introductory questionnaire. This questionnaire assessed basic demographics, as well as information about caffeine intake, medications, and engagement in treatment. Two additional items

asked the participant to rate their motivation to reduce overly happy or overly irritable/frustrated moods on 1-10 Likert scales.

Structured Clinical Interview for the DSM-IV (SCID)

All diagnoses were made with the Structured Clinical Interview for the DSM-IV (SCID; First & Gibbon, 2004). The SCID is a semi-structured interview designed specifically to yield diagnoses based on DSM-IV criteria. This study involved administration of the mood, psychosis, anxiety, and substance abuse modules, allowing definitive diagnoses of bipolar I disorder, as well as potential rule-outs based on current substance abuse. Secondary analyses investigated whether the presence of an anxiety diagnosis was related to differential effects of PMR. The SCID was administered by Christopher Miller or other clinical psychology doctoral students specializing in bipolar research, all of whom completed extensive training before conducting interviews. Ongoing reliability checks were conducted for at least ten percent of participants, revealing adequate intra-class correlations for major depressive episodes (.93), mania (.86), and psychosis (.74).

Bech Rafaelsen Mania Scale (BRMS)

The Bech Rafaelsen Mania Scale (BRMS; Bech et al., 1979) is a brief clinician-rated interview that assesses common symptoms of bipolar disorder over the previous week. It features eleven total items, each rated on a five-point scale. It has achieved excellent internal consistency and inter-rater reliability, as well as strong correlations with more exhaustive measures of manic symptoms (Bech, 1988; Bech, Bolwig, Kramp, & Rafaelsen, 1979; Licht & Jensen, 1997). It has been widely used in treatment and basic

research (e.g. Bech, 2002; Johnson et al., 2008; Malkoff-Schwartz et al., 1998). Scores on the BRMS reliably differentiate placebo and treatment groups, as well as detect changes in symptoms associated with treatment (Bech, 2002). To enhance reliability, our group uses structured interview probes and detailed anchors for each rating scale. The BRMS was administered once at Session 1 and again at Session 2 by Christopher Miller. Several sessions were recorded, and agreement was established with other doctoral students specializing in bipolar research and Dr. Johnson in ongoing reliability meetings. Intra-class correlation for the BRMS was .84 based on 14 cases, indicating adequate reliability.

Mood Measure – Altman Self-Rating Mania Scale (ASRM)

As the BRMS covers a one-week interview, the Altman Self-Rating Mania Scale (ASRM; Altman, Hedeker, Peterson, & Davis, 1997, 2001) was used to assess changes in manic symptoms within each session. The ASRM has been used for this purpose in several studies (e.g. Bopp et al., 2010; Johnson & Fulford, 2009). It features five items tapping common manic symptoms including happiness, self-confidence, sleep, talkativeness, and over-activity. Three adjustments to this measure were required for this study, however. First, the item tapping sleep was removed, as changes in sleep patterns would be impossible within a laboratory session. Second, the item tapping "being more active" was worded as "excited," as changes in activity level (e.g. socially, sexually) would also be unlikely during the session. Third, the scoring rubric was changed from a wordy five-option multiple-choice format to a one to seven Likert scale ranging from "not at all" to "extremely." This change was made due to time pressure within the session, as the effects of mood induction procedures can fade within just a few minutes

(e.g. Frost & Green, 1982). The result was a very brief, 4-item measure that nonetheless correlated modestly with the BRMS at both Session 1 (r = .33, p = .03) and Session 2 (r = .50, p = .003). Larger correlations would not necessarily be expected given the focus of the BRMS is on the past week while the focus of this ASRM scale is "right now." This scale was administered three times at each session; alpha reliability at Session 1 was .80, .84, and .74 at the three administrations, and reliability at Session 2 was .87, .84, and .81.

Mood Measure – Nervous

Items drawn from several other scales were also administered at the same time as the ASRM described above (before the mood induction, prior to the intervention, and after the intervention). In total, the twelve items typically took less than a minute to rate. Items were drawn from the Positive and Negative Affect Schedule (PANAS; Watson & Clark, 1994; Watson, Clark, & Tellegen, 1988; Watson & Tellegen, 1985), the Affect Valuation Inventory (AVI; Tsai, Knutson, & Fung, 2006), and a brief mood grid for assessing valence/arousal (Jefferies, Smilek, Eich, & Enns, 2008). Two items in particular constituted a very brief measure of for anxiety: a Likert scale for "nervous" and a reverse-coded Likert scale for "relaxed."Throughout this document, the term "Nervous Measure" will refer to the combination of these two items. This scale was administered three times at each session; alpha reliability at Session 1 was .79, .64, and .56 at the three administrations, and reliability at Session 2 was .16, .86, and .43. I have no particular explanation for the low reliability during the first administration of Session 2.

Mood and Anxiety Symptom Questionnaire (MASQ)

The MASQ (Watson & Clark, 1991; Watson et al., 1995a, 1995b) is a 62-item scale designed to assess symptoms commonly occurring in mood and anxiety disorders. Each item consists of a feeling or sensation, which the participant rates on a five-point scale ranging from "not at all" to "extremely." The MASQ consists of several subscales: three general (general distress: depression, general distress: anxiety, and general distress: mixed) and two specific (somatic anxiety and anhedonic depression). The three general scales feature significant overlap with one another, reflecting one overarching anxious/depressive factor, while the two specific scales are expected to be relatively unrelated, supporting an overall tripartite model of emotion (Clark & Watson, 1991). The general factor contains items tapping overall feelings of arousal (e.g. on edge, keyed up, high-strung), while the anxious arousal factors features mostly somatic symptoms (e.g. feeling dizzy, racing heart, shortness of breath). The MASQ was administered once at Session 1 and again at Session 2. Alpha reliability for the Somatic Anxiety subscale was at .83 at Session 1 and .88 at Session 2. Alpha reliability for the General Distress – Anxiety subscale was .80 at Session 1 and .85 at Session 2.

Diary Cards

The current study aimed to determine whether participants implement PMR on their own during the five-week follow-up period. Daily Diary Cards were distributed at the end of the first session, with very brief questions tapping mood to be completed daily by all participants. Those in the PMR group were instructed to fill out Diary Cards after completing PMR each day if possible. To minimize attrition based on embarrassment at

not completing the diary cards, participants were encouraged to return for Session 2 regardless of whether they completed any of the cards. Participants were reminded to bring cards to session 2 when that appointment was scheduled. Nonetheless, only five participants returned for Session 2 with the diary cards, and so these data were not included in analyses.

Follow-up Questionnaire

A custom questionnaire was administered at session 2 to determine whether participants found PMR or their own self-focused calming strategy to be helpful during the intervening weeks. This questionnaire included closed-ended (e.g. "On about how many days during the past five weeks did you use PMR?") and open-ended questions (e.g. "Did you find PMR to be helpful? If not, why not?"). Participants in the control condition completed a parallel questionnaire with questions that asked about their own self-focused calming strategy rather than PMR.

Skin Conductance Level

Relying on self-reports of emotions alone may be particularly questionable in the context of a mood induction, as some mood induction procedures appear to be sensitive to demand characteristics (e.g. Clark, 1983; Gerrards-Hesse, Spies, & Hesse, 1994). To address these issues, skin conductance level (SCL) was used to supplement the self-report and clinician-administered scales described above (Figner & Murphy, 2011). It has long been established that SCL reflects activation of the sympathetic nervous system, including both cholingergic and adrenergic activity (Dawson, Schell, & Filion, 2000).

SCL has been shown to have modest correlations with self-reported arousal (Schilling & Poppen, 1983).

For this study, participants were first asked to go to the bathroom and wash their hands using a gentle, non-alcohol based soap provided by the researcher, as alcohol-based soaps can lead to an artificially muted SCL due to dryness. Participants' fingertips (the distal phalanges of the index and middle fingers of their non-dominant hand) were then gently abraded with fine steel wool, and participants were instructed to rub a few drops of an abrading Mavidon "lemon prep" skin preparation into their fingertips. After wiping their fingers clean with a tissue, each of the two fingers was applied with a one square centimeter disposable silver/silver chloride (Ag/AgCl) electrode, with an additional drop of Biopac 101-isotonic recording electrical gel to ensure a good electrical connection between the electrode and the skin. Leads were then attached to both electrodes, and participants were provided with a foam block to allow them to comfortably rest their hand and minimize movement artifacts.

A Biopac system was used to collect SCL data at 200Hz. A small current (5 microsiemens) was applied to the leads, which was too small to be felt by the participants. A series of triggers (timed with the start and end of the various tasks administered during the study) provided landmarks for data analysis. The SCL data collection for some participants was unsuccessful; reasons for this included equipment malfunction, improper triggering, and electrodes becoming disconnected during the course of the session.

Analysis Overview

Before examining hypotheses, a series of preliminary analyses were conducted. Analyses investigated the success of the stratification scheme, using independent samples *t*-tests to compare the PMR and control groups on stratification variables. Then, *t*-tests compared those who did versus did not complete Session 2. The success of the mood induction was investigated – dichotomous analyses considered the percentage of people who achieved a certain threshold for their mood, and continuous analyses considered the degree of change in mood. The continuous analyses of mood induction success at Session 1 used a repeated measures ANOVA focused on the ASRM, with pre-mood induction versus post-mood induction serving as a within-subjects variable to indicate change in manic symptoms over the course of the mood induction. PMR versus control group (i.e. treatment assignment) served as a between-subjects variable. To look at mood induction success at Session 2, I added another within-subjects factor (session number) to this repeated measures ANOVA. Of note, this ANOVA included tests of mood induction success at Session 1, but a considerably smaller sample size based on listwise deletion of those participants who did not complete Session 2. This general framework – a repeated measures ANOVA for Session 1, and a second ANOVA that included session number as an additional within subjects factor – was used at several points throughout the study.

Further investigation examined the correlates of mood induction success, using partial correlations between post-mood induction ASRM scores and relevant variables, controlling for pre-mood induction ASRM scores. The first hypothesis for this study was that, on average, participants would experience a reduction in manic symptoms immediately after they implemented PMR. The second hypothesis was that persons in the

PMR group would experience a greater reduction in manic symptoms than those in the control group at Session 1. For both hypotheses, the primary outcome was the ASRM, with pre-intervention versus post-intervention as a within-subjects variable and treatment assignment as a between-subjects variable. For the first hypothesis, a significant interaction term would indicate a need for post-hoc analyses (i.e. paired sample *t*-tests for the PMR and control groups).

The third hypothesis was that those trained in PMR would demonstrate a greater decrease in manic symptoms than the control group at Session 2. For this analysis, two indices of manic symptoms were considered: the ASRM self-report measure was given before and after PMR in each session, and the BRMS interview measure was administered once each session as a measure of manic symptoms over the past week. To examine the ASRM as a dependent variable, repeated measures ANOVA was used with pre- versus post-intervention as a within-subjects variable, treatment assignment as a between-subjects variable, and session number as an additional within-subjects factor. A significant pre- versus post-intervention by treatment assignment interaction was hypothesized. For the BRMS, a repeated measures ANOVA was conducted with session number as a within-subjects variable and treatment assignment as a between-subjects variable. A significant session by treatment assignment interaction was hypothesized, reflecting differential patterns of change over the course of the study for the PMR and control groups.

Chapter 3: Results

Data were collected between May of 2009 and the July of 2010. All analyses were conducted using SPSS Version 17 and 19.

Data Check and Cleaning

Preliminary analyses ensured that all relevant study variables were approximately normally distributed. Continuous variables were flagged if they had skewness or kurtosis above one and statistically significant Kolmogorov-Smirnov tests indicating non-normal distributions (Massey et al., 1951). The number of manic episodes experienced per year was non-normally distributed; specifically, this variable demonstrated noticeable right-skew (skewness = 1.36, Kolmogorov-Smirnov = .236, $p < .001$). A square-root transformation reduced the skewness to 0.76 (although the Kolmogorov-Smirnov statistic remained significant with a value of .203, $p < .001$). For analyses using the number of manic episodes per year, parallel analyses were conducted using the square-root transformed variable. No results were fundamentally different, however, and so the non-transformed variable was retained. Missing values within internally consistent subscales were imputed using mean imputation (less than 5% of the data on any item).

Characteristics of the Sample

Characteristics of the final sample (n = 44) can be found in Table 1. About 80% of the sample described themselves as White, 16% as Black, 2% as Asian, and 2% as other or mixed race. In addition to these racial categories, 25% described themselves as Hispanic. Additional data related to illness characteristics can be found in Table 2, along with parallel data from epidemiological and large-sample studies. The sample for the current study generally appeared similar to these samples, with a few exceptions. The

current sample was less likely to be taking a mood stabilizing medication than enrollees in the STEP-BD Study (57% versus 89%; Ghaemi et al., 2006), although an additional 18% of my sample reported taking an antidepressant or antipsychotic medication. Likewise, the current sample appeared to have a lower rate of comorbid anxiety disorder diagnoses than has been reported (68% versus 93%; Kessler et al., 1997).

Success of Stratification and Comparability of Groups

Preliminary analyses checked if stratified randomization created well-matched PMR and control groups. Variables used for stratification included age, gender, anxiety disorder history, substance abuse history, current mood stabilizing medication use (yes/no), and current psychosocial treatment. Independent samples *t*-tests demonstrated that stratification was successful ($p > .20$ for all of these variables). Additional *t*-tests investigated whether PMR and control groups differed on any other potentially relevant illness-related characteristics; see the bottom half of Table 1. Once again, no significant group differences were revealed ($p > .10$ for each domain), suggesting that the PMR and control groups were fundamentally similar across a range of potentially important variables at the beginning of the study. In short, stratification was successful.

Table 1. Characteristics of the PMR and control groups

Variable	PMR group (n = 22)	Control group (n = 22)	*p*
Variables used for stratification			
Age	35 ± 11	37 ± 15	.71
Percent female	68%	64%	.76
Anxiety disorder diagnosis	68%	68%	1.00
Substance abuse diagnosis history	64%	68%	.76
Current mood stabilizer use	45%	64%	.24
Current psychosocial treatment	68%	55%	.37
Other variables			
Percent endorsing minority status	41%	36%	.76
Age of mania onset	22 ± 10	22 ± 8	.81
BRMS at Session 1	8.2 ± 6.5	5.4 ± 5.1	.12
MASQ Anhedonic Depression	59 ± 19	64 ± 16	.37
MASQ Somatic Anxiety	40 ± 11	39 ± 12	.73
History of psychotic mood episodes	59%	59%	1.00
Number of manic episodes	11 ± 11	11 ± 12	.95
Number of depressed episodes	14 ± 12	15 ± 12	.88

Table 2. Comparison of this sample to epidemiological samples of bipolar I disorder

Variable	This sample	Other sample	Source
Mood stabilizer	57%	89%	Ghaemi et al., 2006
Comorbid anxiety diagnosis	68%	93%	Kessler et al., 1997*
Comorbid substance	66%	60%	Merikangas et al., 2007
abuse/dependence diagnosis		71%	Kessler et al., 1997
Have experienced a major depressive episode	93%	80%	Kessler et al., 1997
Have experienced psychotic symptoms while in mood episodes	59%	50%	Perälä et al., 2007
Age of manic onset	22 $\pm$ 9	21 + 2	Bland et al., 1988

* Note: regarding comorbid anxiety diagnoses, the differences between my sample and that from Kessler and colleagues (1997) appeared to be driven mostly by comorbid specific phobia diagnoses (9% versus 66%, respectively).

Attrition and Imputation

Analyses of attrition and missing data had two goals: first, to determine predictors of missingness, and second, to determine whether to impute data for missing scale scores. One participant appeared extremely tired during Session 1 (e.g. he fell asleep at several points during the session); thus, his Session 1 data were not used in analyses. The participant reported he had not been sleeping due to significant mood dysregulation in the weeks prior to our session. Based on the apparently illness-related nature of his fatigue, this participant's data were not imputed.

Figure 1 above provides a flowchart of participant enrollment and attrition (i.e. which participants did not return for Session 2 of the study). Of the 43 participants with valid Session 1 data, 12 did not come back for the follow-up session. Of those who did not complete Session 2, one reported being too emotionally unstable to continue with the study, one could no longer arrange transportation, one reported no longer being interested in the study, and seven stopped returning calls. Two additional participants appeared to miss Session 2 for reasons unrelated to their mental health status: one participant had surgery for a long-standing medical condition, and another participant moved away from Miami after completing Session 1. This latter participant did not appear to be moving for impulsive or illness-related reasons (i.e. the move was planned well in advance for education-related reasons). Data for these two participants were therefore considered to be missing completely at random, and they were not included in analyses of attrition.

To determine correlates of attrition, a total of 19 independent samples *t*-tests compared those participants who returned for Session 2 to those who did not. Variables included illness/comorbidity variables (comorbid anxiety symptoms, a history of

substance abuse, a history of psychotic mood episodes, Global Assessment of Functioning scores), demographics (age, gender, ethnicity), initial mood state (BRMS score and MASQ subscales at Session 1), illness course (episodes per year, age of onset), and treatment variables (current mood stabilizer prescription, antipsychotic prescription, antidepressant prescription, psychosocial treatment). Where Levene's tests were significant ($p < .05$), *t*-values and degrees of freedom were adjusted for heterogeneity of variance between those who did and did not complete Session 2. These analyses revealed several significant tests: compared to those who did not complete Session 2, those who completed Session 2 were, on average, about eight years older, $t(23) = 2.10$, $p = .05$, had mania onset that was about nine years later, $t(40) = 2.78$, $p = .01$), had about a third as many manic episodes per year, $t(11) = 2.58$, $p = .03$), and were more likely to report taking antipsychotic medications, $t(25) = 2.37$, $p = .03$. Overall, those who attrited appeared to have a more severe course of illness and less involvement in medication treatment.

Thus, missingness at Session 2 was generally not at random. Based on this, only the two participants whose Session 2 data were missing completely at random had data imputed using the "multiple imputation" function in SPSS Version 19.0. Thus, after imputation, my sample featured 43 participants with valid Session 1 data (22 in the PMR group and 21 in the control group) and 34 participants with valid Session 2 data (15 in the PMR group and 19 in the control group).

Alternative Strategies Used by the Control Group

Participants in the control group reported their own strategies for self-calming at Session 1 and Session 2; see Table 3. A diverse array of strategies was reported, on average 4.3 times per week. The most commonly used approach at session 1 and session 2 was breathing exercises.

Table 3. Endorsement of self-calming strategies in the control group

	Session 1	Session 2
Breathing exercises	8	5
Going for a walk	5	2
Imagery	3	4
Meditation	3	2
Napping	2	2
Cognitive techniques (e.g. focusing on difficulties to reduce overly happy mood)	3	2
Prayer	1	1
Stretching	1	1
Writing (e.g. in a journal)	0	2
Other relaxation techniques	2	0

Success of the Positive Mood Induction

As described above, this study used a positive mood induction to elevate mood during each session. Preliminary analyses determined whether this procedure was successful in inducing a positive mood according the ASRM. Table 4 contains scores for each group at each administration. Dichotomous and continuous analyses were conducted to examine the effectiveness of the mood induction at each time point. For dichotomous analyses, successful mood induction was defined as either (1) improving by at least three points out of the potential 28 points on the ASRM, or (2) achieving a post-induction total score on this subscale of 20 or above (reflecting an average score of 5 or higher out of 7 for each item, with a 1 indicating "not at all" and a 7 indicating "extremely"). Based on this rubric, 25 participants (58%) experienced a successful positive mood induction at Session 1. The PMR and self-focused calming groups were equally likely to experience a successful positive mood induction at session 1, $\chi^2(1) = 0.24$, $p = .63$). Of the eighteen participants for whom the Session 1 mood induction was not successful, ten were from the PMR group while eight were from the control group; six experienced a successful positive mood induction at the second session (three from each of the PMR and control groups). The goal of the study was to test whether PMR would reduce positive mood. To test this, analyses of primary outcomes focused on this subset of participants.

Table 4. Mean ASRM analog scores for PMR and control groups at Session 1 and Session 2

Session 1, among the entire sample						
	PMR (n = 22)		Control (n = 21)			
Administration	Mean	SD	Mean	SD	Cohen's *d*	*p*
Pre-mood induction	15.5	4.5	14.6	5.5	-0.18	.55
Pre-intervention	17.9	5.1	16.6	6.2	-0.23	.47
Post-intervention	18.1	3.9	14.7	4.9	-0.77	.01
Session 1, among participants who experienced a successful mood induction						
	PMR (n = 12)		Control (n = 13)			
Administration	Mean	SD	Mean	SD	Cohen's *d*	*p*
Pre-mood induction	16.0	5.4	16.4	6.0	0.07	.87
Pre-intervention	21.3	3.6	20.1	4.2	-0.32	.43
Post-intervention	19.6	3.9	15.9	4.2	-0.91	.03
Session 2						
	PMR (n = 15)		Control (n = 19)			
Administration	Mean	SD	Mean	SD	Cohen's *d*	*p*
Pre-mood induction	16.6	4.7	14.2	6.1	-0.44	.21
Pre-intervention	18.6	4.1	16.2	5.6	-0.49	.16
Post-intervention	18.5	3.6	14.7	4.5	-0.93	.01

At Session 2, 22 participants (65%) experienced a successful positive mood induction, with an associated effect size of 0.38. Of the 12 participants who did not, five were from the PMR group and seven were from the control group. One possibility is that the mood regulation training administered interfered with the effectiveness of the mood induction at Session 2. Given the possibility that the treatment program reduced the mood induction effects, participants who failed to achieve a high mood in response to the Session 2 mood induction were not excluded from analyses. The success of the mood induction at Session 1 was related at the trend level to success of mood induction at Session 2, $\chi^2(1) = 2.83$, $p = .09$, suggesting some modest consistency in who had a mood shift post-induction across the two sessions.

Beyond analyses of mood induction success as a dichotomous variable, continuous analyses were conducted as continuous analyses typically have greater power than dichotomous ones (Cohen, 1983; Ragland, 1992). The effect size for the mood induction based on this continuous definition was modest overall (Cohen's $d = 0.42$). Repeated measures ANOVAs were conducted with ASRM scores post-mood induction as a dependent variable. The first ANOVA focused on Session 1 alone. Independent variables included pre- versus post-mood induction as a within-subjects variable, and treatment assignment (PMR versus control group) as a between-subjects variable. This ANOVA revealed a significant main effect for pre- versus post-mood induction, $F(1,41) = 13.25$, $p = .001$, suggesting that participants overall experienced a significant increase on the ASRM during the mood induction. The main effect for treatment assignment, $F(1,41) = 0.53$, $p = .47$, and the interaction between pre- versus post-mood induction and treatment assignment, $F(1,41) = 0.08$, $p = .78$, did not approach statistical significance,

suggesting that the increase in ASRM scores during the mood induction did not significantly differ between the PMR and control groups.

A second analysis included data from both Session 1 and Session 2, and investigated whether the mood induction resulted in a different pattern of emotion change at Session 2. This ANOVA included session number as an additional within-subjects factor, as well as all relevant interaction terms. As with the ANOVA described above, the main effect for pre- versus post-mood induction was highly significant, $F(1,31) = 16.14$, $p < .001$, and the interaction between treatment assignment and pre- versus post-mood induction was not statistically significant. The main effects for treatment assignment and session number were also nonsignificant, as were all of the additional interaction terms (all $F < 3.00$, $p > .10$). Taken together, these results suggested that (a) the positive mood induction was associated with significant increases in ASRM scores at both sessions, and (b) the change in ASRM over the course of the mood induction was similar at Session 1 and Session 2, and (c) the mood induction was not differentially successful for the PMR versus the control groups.

Skin conductance data for both sessions can be found in Table 5. A similar repeated measures ANOVA aimed to evaluate the success of the positive mood induction using SCL as the dependent variable. For Session 1, pre- versus post-mood induction served as a within-subjects variable, and treatment assignment served as a between-subjects variable. This analysis revealed a significant main effect for pre- versus post-mood induction. These findings indicated higher arousal after the Session 1 mood induction than before, $F(1,35) = 6.24$, $p = .02$. No other main effects or interaction effects were significant in this analysis (all $F < 1.00$, $p > .50$), again suggesting similar

trajectories of change between the PMR and the control group for SCL at Session 1. Due to difficulties with missing SCL data, session 2 data were examined separately from session 1 data, using a parallel repeated measures ANOVA. SCL did not differ before and after the mood induction procedure at Session 2, main effect $F(1,26) = 1.86$, $p = .18$. The magnitude of the change in SCL over the course of the mood induction was similar at both sessions, however, suggesting that this nonsignificant result for Session 2 may have reflected power issues.

Table 5. Skin conductance data at session 1 and session 2

Session 1					
	PMR (n = 20)		Control (n = 17)		
Administration	Mean	SD	Mean	SD	*p*
Pre-mood induction	4.86	2.63	4.38	2.30	.56
Pre-intervention	5.87	3.63	4.90	3.56	.42
Post-intervention	7.21	2.78	7.14	3.56	.95
Session 2					
	PMR (n = 11)		Control (n = 14)		
Administration	Mean	SD	Mean	SD	*p*
Pre-mood induction	4.30	2.49	3.80	2.96	.65
Pre-intervention	4.52	3.14	4.88	4.43	.82
Post-intervention	5.34	2.76	6.64	3.91	.36

Analyses were also conducted to examine which participants experienced a more versus less successful positive mood induction. That is, what variables were associated with the amount of change in ASRM scores during the course of the mood induction? Candidate variables for these analyses included illness/comorbidity variables (comorbid anxiety symptoms, a history of substance abuse, a history of psychotic mood episodes, Global Assessment of Functioning scores), demographics (age, gender, ethnicity), initial mood state (BRMS score and MASQ subscales at Session 1), illness course (episodes per year age of onset), treatment variables (current mood stabilizer prescription, antipsychotic prescription, antidepressant prescription, psychosocial treatment), motivation to reduce overly happy or overly irritable/frustrated moods, and use of caffeine/nicotine during the day of the session (coffee, soda, cigarettes). For potential predictors that were continuous, partial correlations were conducted (partialing out pre-mood induction ASRM analog scores). For potential predictors that were dichotomous, repeated measures ANOVAs were conducted. None of these variables significantly predicted mood induction success at either Session 1 or Session 2, with one exception: motivation to reduce happy moods was negatively correlated with mood induction success at Session 1, partial $r(40) = -.34$, $p = .03$. This result was not replicated at Session 2, however.

Investigation of Potential Confounds

A series of analyses determined if any background demographic variables predicted outcomes at Session 1 (and should therefore be considered as covariates). Variables included illness/comorbidity characteristics (comorbid anxiety diagnoses, history of substance abuse, history of psychotic mood episodes, Global Assessment of

Functioning scores), demographics (age, gender, ethnicity), illness course (episodes per year, age of onset), treatment variables (current mood stabilizer prescription, antipsychotic prescription, antidepressant prescription, psychosocial treatment), and use of caffeine/nicotine during the day of the session (coffee, soda, cigarettes). I also included the amount of time taken to complete the intervention (whether PMR or self-focused calming) as a potential covariate. As with the tests of mood induction success presented above, continuous variables were investigated via partial correlations (controlling for post-mood induction mood), and dichotomous variables were investigated via repeated measures ANOVA. None of these variables were significantly related to ASRM scores at Session 1.

I also investigated variables that were related to BRMS scores at Session 1 (using the same variables listed above). Unlike the ASRM, the BRMS was only administered once at each session, meaning that simple correlations and *t*-tests sufficed to determine what variables were related to the BRMS at study entry. Note that these analyses were conducted to characterize the predictors of the BRMS in my sample, rather than to provide variables to control for in subsequent analyses. Several significant findings emerged: those with an anxiety disorder diagnosis, $t(41) = 2.25$, $p = .03$, those who were not taking an antidepressant medication, $t(40) = 2.09$, $p = .04$, and those who were enrolled in psychosocial treatment, $t(41) = 2.70$, $p = .01$ tended to have higher BRMS scores entering the study.

Tests of Primary Hypotheses

The first hypothesis was that implementation of PMR would be associated with an immediate reduction in manic symptoms among those with bipolar disorder after a positive mood induction at Session 1 and Session 2. The second hypothesis was that any reduction in manic symptoms would be greater for the PMR group than for the control group at Session 1. A repeated measures ANOVA was relevant for both of these hypotheses, with the ASRM at Session 1 as the primary outcome, treatment assignment as the between-subjects factor and pre- versus post-intervention as the within-subjects factor. This analysis focused on the 25 participants who experienced a successful positive mood induction. There was no significant effect of treatment, $F(1,31) = 3.42$, $p = .08$, nor treatment by pre- versus post-intervention interaction, $F(1,23) = 2.13$, $p = .16$, but there was a significant main effect of pre- versus post-intervention, $F(1,23) = 12.38$, $p = .002$. This suggested that, among this subsample, the intervention (PMR or self-focused calming) was associated with a significant reduction in ASRM scores at Session 1, although neither the PMR nor the control condition appeared to outperform the other. Examination of means suggested that the magnitude of reduction in the ASRM over the course of the intervention appeared to be higher for the control group (Cohen's $d = 1.00$) than the PMR group (Cohen's $d = 0.47$).

A similar repeated measures ANOVA investigated whether the intervention led to change in SCL. A significant main effect for pre- versus post-intervention, $F(1,16) = 9.04$, $p = .01$ suggested that participants who underwent a successful positive mood induction experienced an increase, rather than a decrease, in SCL over the course of the intervention at Session 1 (whether PMR or self-focused calming). [a] No other main effects

or interaction effects were significant. Results were fundamentally similar at Session 2, as the main effect for pre- versus post-intervention suggested an increase rather than a decrease in SCL over the course of the intervention, $F(1,23) = 6.59$, $p = .02$.

The third hypothesis was that the PMR group would also demonstrate a greater reduction in manic symptoms than the control group at Session 2. This was examined using two parallel repeated measures ANOVAs of ASRM and BRMS scores among the 20 participants who experienced a positive mood induction at Session 1 and also had data for Session 2. For the first set of analyses, ASRM scores served as the outcome variable, and independent variables included pre- versus post-intervention and session number as within-subjects variables, and treatment assignment as a between-subjects variable. This ANOVA revealed a significant main effect for pre- versus post-intervention, $F(1,18) = 4.97$, $p = .04$, a significant main effect for treatment assignment, $F(1,18) = 5.62$, $p = .03$, and a trend-level interaction between treatment assignment and pre- versus post-intervention, $F(1,18) = 3.37$, $p = .08$. All other effects were nonsignificant ($F < 2.0$, $p > .20$). Based on these significant effects, post-hoc analyses collapsed across sessions. Focusing once again on participants who experienced a successful positive mood induction (and also provided data at both sessions), paired sample *t*-tests revealed a significant reduction in the ASRM for the control group, $t(22) = 4.46$, $p < .001$) but not the PMR group, $t(17) = 0.56$, $p = .59$.

I also investigated the third hypothesis using Session 2 BRMS scores as an outcome measure (see Table 9). A repeated measures ANOVA was conducted with treatment as a between-subjects factor, and Session 1 versus Session 2 as a within-subjects factor. The main effect for treatment assignment achieved statistical significance,

$F(1,31) = 5.27$, $p = .03$. The main effect for session number was nonsignificant, $F(1,31) = 1.66$, $p = .21$, as was the interaction between treatment assignment and session number, $F(1,31) = 2.46$, $p = .13$. This pattern suggested that the control group overall had lower BRMS scores than the PMR group collapsed across Session 1 (before any intervention) and Session 2, but that trajectories of change in BRMS scores over the course of the study did not significantly differ between the PMR and control groups. Moreover, there was no significant decline in BRMS scores from session 1 to session 2.

On average, participants entered the study in a relatively euthymic state as measured by the BRMS (mean $\pm$ SD = 6.9 $\pm$ 5.9), well below the cutoff of fifteen for even "minimal" manic symptoms (Bech et al., 1979). This raised the possibility that the null results reported for the BRMS above may have simply been based on low initial scores. A repeated measures ANOVA for the BRMS (parallel to the one presented above) was conducted among those participants (n = 14) whose initial BRMS scores were seven or greater. In this case, the main effect for session number was significant, $F(1,12) = 10.2$, $p = .01$. The main effect for treatment assignment was nonsignificant, as was the interaction between treatment assignment and session number. These results suggested an overall pattern of reduction in BRMS scores over the course of the study, but that neither the PMR nor the control group outperformed the other.

Table 9. BRMS for PMR and control groups at both sessions

	PMR		Control			
Administration	Mean	SD	Mean	SD	Cohen's *d*	*p*

Session 1	8.2 (n = 22)	6.5	5.4 (n = 21)	5.0	-0.49	.12
Session 2	7.8 (n = 15)	5.0	3.6 (n = 19)	3.4	-1.05	.01

Additional Variables Related to Primary Outcomes at Session 2

Analyses were conducted to examine predictors of the ASRM after completing the intervention (PMR or self-focused calming) at Session 2. In addition to many of the variables identified in the previous sections (illness/comorbidity variables, demographics, illness course, treatment variables, motivation to avoid overly happy and irritable/frustrated moods, and use of caffeine/nicotine), I included the number of days between Session 1 and Session 2 as a potential predictors of outcomes. Independent samples *t*-tests were used for dichotomous variables, and partial correlations (partialing out the variance explained by ASRM at Session 2 before completion of the intervention) were used for continuous variables. At Session 2, a history of a substance abuse diagnosis was associated with a higher post-intervention ASRM score, indicating higher arousal, $F(1,30) = 7.16$, $p = .01$. No other variables emerged as significant predictors of Session 2 ASRM for the sample as a whole.

Predictors of Outcomes for the PMR Group

The analyses immediately above looked at predictors of outcomes for the sample as a whole (including those in both the PMR and control groups). An additional set of analyses investigated what factors were associated with ASRM and BRMS scores within the PMR group specifically. Partial correlations were conducted for continuous variables (controlling for pre-intervention ASRM or Session 1 BRMS scores), and independent

samples *t*-tests were used for dichotomous variables. Candidate variables included illness/comorbidity variables (comorbid anxiety symptoms, a history of substance abuse, a history of psychotic mood episodes, Global Assessment of Functioning scores), demographics (age, gender, ethnicity), illness course (episodes per year, age of onset), treatment variables (current mood stabilizer prescription, antipsychotic prescription, antidepressant prescription, psychosocial treatment), days between Session 1 and Session 2, self-reported motivation to avoid overly happy or irritable/frustrated moods, and self-reported practice of PMR between the sessions. These analyses revealed that PMR practice was significantly negatively correlated with the ASRM after completing PMR at Session 2, after controlling for pre-PMR ASRM, partial r (12) = -.61, p = .02. That is, those who reported relatively more PMR practice during the weeks between Session 1 and Session 2 tended to experience a greater reduction on the ASRM after using PMR during Session 2. The two participants who practiced PMR daily experienced reductions of two and six points on the ASRM at Session 2, corresponding to effect sizes of 0.29 and 1.35.

As stated above, neither the PMR nor the control group demonstrated robust effects on BRMS scores. Parallel analyses among those with more elevated BRMS scores at study entry, however, suggested a reduction in the BRMS over the course of the study. Given this finding, the partial correlation between PMR practice and BRMS scores at Session 2 (controlling for Session 1 BRMS) was calculated for this subset of participants (n = 7). Results were statistically nonsignificant despite the magnitude of the correlation, the latter of which suggested that PMR practice was associated with a reduction in BRMS scores at Session 2, partial r(3) = -.75, p = .14.

Research on PMR in the context of other disorders has raised the question of whether practice itself, versus the perceived efficacy of PMR, is truly responsible for positive outcomes (e.g. see Antoni et al., 2006). In order to investigate this possibility, I conducted an additional partial correlation focused on the ASRM. In addition to controlling for pre-PMR ASRM at Session 2, I also controlled for the amount of change in the ASRM associated with PMR use at Session 1. The result from this partial correlation was statistically significant for the ASRM, $r(11) = -.60$, $p = .03$. Among those with initially elevated BRMS scores, additionally controlling for the effects of PMR at Session 1 revealed a very strong relationship between PMR practice and Session 2 BRMS scores, partial $r(2) = -.95$, $p = .05$.

Use of PMR between Session 1 and Session 2

The results described above generally did not favor the PMR group when compared to the control group in terms of reduction in manic symptoms. Those who engaged in relatively more PMR practice outside the sessions, however, tended to experience a greater reduction in the ASRM at Session 2. On average, participants in the PMR group who returned for Session 2 reported using PMR 1.9 times per week (n = 15). If those who did not attend Session 2 (n = 7) were included (under the assumption that they did not practice PMR at all), this weekly practice rate was reduced to 1.3 times per week.

Some participants reported that they found PMR to be helpful during the time between Session 1 and Session 2 (8 of 15 returning PMR participants rated it as at least a "5" on a 1-7 scale with a "1" indicating "not helpful at all" and a "7" indicating "very

helpful"). With only one exception, these eight participants were the only participants who reported using PMR at least weekly. Among those who did report using PMR outside of the sessions, only two reported using it daily (the recommended frequency for mastering the technique). Qualitatively, participants provided a variety of reasons for their dislike of the technique and lack of implementation, with little overlap between participants. Two participants noted that they simply did not feel like doing it, without further elaboration. Each of the following reasons was endorsed by a participant: being too distracted, preferring face-to-face administration (rather than the CD provided at the end of Session 1), finding it annoying, forgetting to practice, and being overwhelmed with other stressors. Quantitatively, correlations explored the relationship between PMR use and illness/comorbidity variables (comorbid anxiety diagnosis, a history of substance abuse, a history of psychotic mood episodes, Global Assessment of Functioning scores), demographics (age, gender, ethnicity), initial mood state (BRMS score and MASQ subscales at Session 1), illness course (episodes per year age of onset), treatment variables (current mood stabilizer prescription, antipsychotic prescription, antidepressant prescription, psychosocial treatment), motivation to avoid overly happy or overly irritable/frustrated moods, and use of caffeine/nicotine during the day of the session (coffee, soda, cigarettes). These analyses revealed two statistically significant relationships. High scores on the Somatic Anxiety subscale of the MASQ at Session 1 were positively correlated with PMR use between sessions, $r(15) = .67$, $p = .01$. In contrast, antipsychotic medication use at Session 1 was negatively correlated with PMR use between sessions, $r(15) = -.68$, $p = .01$.

Effects of PMR on Anxiety

Additional analyses examined the usefulness of PMR in reducing anxiety symptoms. Anxiety was measured in two ways: first, the Nervous Measure provided within-session ratings of anxiety in the moment, while the MASQ Somatic Anxiety and General Anxiety subscales (completed once per session) assessed anxiety over the previous week. At Session 1, the initial Nervous Measure administration (before the positive mood induction or intervention) was strongly correlated with both the Somatic Anxiety, $r(43) = .44$, $p = .003$, and the General Anxiety, $r(43) = .64$, $p < .001$, MASQ subscales. These correlations were not significant at Session 2, however.

Parallel repeated-measures ANOVA were conducted with the in-the-moment Nervous Measure as the primary outcome. Treatment assignment served as a between-subjects factor, and session number and pre- versus post-intervention served as within-subjects factors. Results revealed nonsignificant effects for session number and all interactions of session number with other variables. A significant main effect for pre- versus post-intervention emerged, $F(1,31) = 11.69$, $p = .002$, as did a significant pre- versus post-intervention by treatment assignment interaction, $F(1,31) = 6.57$, $p = .02$. Based on this pattern of results, post-hoc analyses (consisting of paired sample *t*-tests comparing pre-intervention to post-intervention scores for the PMR and control groups) revealed that the PMR group, but not the control group, experienced a significant reduction in anxiety over the course of the intervention. The effects of PMR on anxiety held for both Session 1, paired sample $t(21) = 3.51$, $p = .002$, and Session 2, paired sample $t(14) = 2.50$, $p = .02$.

In addition, a parallel repeated measures ANOVA was computed with the MASQ Somatic Anxiety subscale as a dependent variable. Analyses revealed no significant effects for session number, $F(1,31) = 1.24$, $p = .27$, or treatment assignment, $F(1,31) = 1.70$, $p = .20$. Contrary to hypotheses, the session by treatment assignment interaction revealed no statistically significant changes in scores on this subscale, $F(1,31) = 0.50$, $p = .49$. [b]

Chapter 4: Discussion

This study investigated the usefulness of PMR for reducing manic symptoms among those with bipolar I disorder. Among participants who experienced a successful positive mood induction at Session 1, the PMR condition led to a small reduction in high-arousal positive affect as measured by the ASRM. The control condition, in which participants used their own emotion regulation strategy, appeared to work equally well (or even better) at reducing positive affect at Session 1. Findings for Session 2 generally mirrored those for Session 1, in that the PMR group did not appear to fare better than the control group.

The BRMS was administered once at each session, and neither the PMR nor the control group evidenced statistically reliable change in manic symptoms on that measure over the course of the study. This finding may have reflected the fact that few participants had elevated BRMS scores to begin with, leaving little room for improvement. A focus on those participants with at least moderate elevation on the BRMS at Session 1 suggested that both PMR and the self-focused calming condition resulted in reduced manic symptoms at Session 2, although regression to the mean may have contributed to this finding.

At Session 2, those participants who had practiced PMR more on their own experienced a greater reduction in positive affect after PMR use than did participants who reported less frequent practice. Participants who were initially elevated on the BRMS also appeared to benefit from PMR practice. Research on PMR has raised the question of whether PMR practice itself, or simply the perceived efficacy of the PMR technique, is most predictive of the improved health outcomes associated with PMR (e.g. Antoni et al.,

2006). In the current study, the link between PMR practice and PMR usefulness at Session 2 remained relatively unaffected by controlling for PMR's effects at Session 1, suggesting that practice, specifically, may have been helpful above and beyond perceived efficacy. In fact, the correlation between PMR practice and Session 2 BRMS scores (partialing out the effects of PMR's effectiveness and BRMS scores at Session 1) exceeded -.90! Despite this strong relationship between practice and reduction in high-arousal positive affect at Session 2, only two of the 22 participants in the PMR group practiced PMR daily (the recommended amount to develop mastery). On average, PMR practice occurred about twice a week among those who returned for Session 2. If one were to make the assumption that those who did not return for Session 2 also did not practice PMR, then this would reduce average practice to about 1.3 times per week. This is broadly in line with some studies of PMR (e.g. Agee, Danoff-Burg, & Grant, 2009), although more intensive interventions have resulted in higher levels of practice (e.g. Antoni et al., 1991).

The qualitative reasons provided for the lack of practice in this study varied widely from person to person, ranging from "I didn't feel like it" to "I had too much going on." Quantitative analyses revealed that participants who entered the study with high levels of anxiety practiced more, and that participants who were currently prescribed an antipsychotic practiced less. The correlation between anxiety and practice makes intuitive sense, as PMR was described in this study as a treatment "originally designed to reduce anxiety." The latter finding may reflect the fact that many antipsychotics have mood-dampening properties (based on their well-known effects on dopamine pathways, see Ito et al., 2009), such that people taking them had little positive affect to regulate.

This suggests that people with bipolar disorder may require more intensive interventions to encourage practice and internalization of PMR skills. This finding is not limited to PMR, however: several trials have revealed that even multiple-session interventions can fail to significantly improve medication adherence in bipolar disorder (e.g. Miklowitz et al., 2000; Perry et al., 1999). Problems with adherence are not limited to medications, but instead appear to apply to psychosocial treatments as well (see Sajatovic, Davies, & Hrouda, 2004). Indeed, issues of treatment adherence and completion of homework are of central importance with bipolar disorder as well as mental health conditions more generally (Persons, Davidson, & Tompkins, 2001; Velligan et al., 2010).

Are there ways to improve treatment adherence in bipolar disorder? Psychoeducation that directly addresses attitudes and knowledge about medications have been found to improve adherence to psychopharmacology (Gaudiano, Weinstock, & Miller, 2008). This type of psychoeducation appears to be most effective if it is a direct focus of several sessions of treatment. Johnson and Fulford (2008) found that patients who believed that they were afflicted with bipolar disorder for non-biological reasons were less likely to adhere to prescribed medications. This suggests, however tentatively, that a mismatch between belief and mechanism (i.e., a lack of alignment between a patient's beliefs regarding the source of their symptoms and the mechanism of a proposed treatment) may predict poorer adherence. Turning to the broader treatment outcomes literature suggests that patients' expectancies regarding the utility of assigned homework is an important predictor of adherence (Westra, Dozois, & Marcus, 2007). Furthermore, some authors have emphasized the importance of assigning homework within the context

of treatment as a collaborative effort (Kazantzis & Daniel, 2009). Perhaps spending more time describing the rationale for PMR in the context of bipolar disorder would have led to more consistent practice.

Participants in this study demonstrated the capacity to apply their own strategies for self-calming in the lab. This raises what may be a fundamental issue: given that people with bipolar disorder already appear to have useful tools for reducing high-arousal positive affect, is teaching additional skills a useful treatment goal? In the introduction to this study, I described PMR's potential usefulness as being derived from its targeting of arousal, its capacity to be learned and practiced while euthymic, and its immediate and recognizable effects. Many of the strategies endorsed by people in the control group, however, appear to meet these very same criteria (e.g. engaging in meditation or breathing exercises). Why would participants be expected to practice PMR consistently if they already have a set of self-calming tools at their disposal? This study joins a growing body of research in demonstrating that people with bipolar disorder have the capacity to engage in regulatory strategies when they find themselves experiencing positive affect. Previous studies with this population have found success for both cognitive strategies (Gruber, Harvey, & Johnson, 2009) and behavioral strategies (Lam & Wong, 1997, 2005) when implemented. It remains possible that it is more difficult for people to implement these strategies outside of the controlled laboratory setting. Speculatively, they may be less likely to implement these strategies as early signs of hypomania unfold and sensitivity to threat diminishes. Thus, a pivotal treatment goal may not be to teach yet more emotion regulation strategies, but to encourage people to implement the emotion regulation strategies that they already have at critical moments.

How can we increase the use of such strategies among people with bipolar disorder? For over two decades, clinicians have attempted to address this issue by teaching self-monitoring skills for identifying early prodromal symptoms (e.g. Chor, Mercier, & Halper, 1988). Indeed, close inspection reveals that nearly all of the major treatment manuals for bipolar disorder involve self-monitoring components, in the hopes that increased awareness of symptoms will help motivate patients to implement emotion regulation skills when they begin becoming manic. The provision of self-monitoring skills can have a constellation of other benefits, including increased patient investment in treatment and a corresponding reduction in costs. Self-monitoring therefore fits well with a collaborative care model, further emphasizing the importance of patients being actively involved with their treatment (Bauer et al., 2006a, 2006b).

Despite these potential benefits, surprisingly little research has assessed the provision and use of self-monitoring skills (Miller, Johnson, & Eisner, 2009). The NIMH prospective Life-Chart Method has been subject to some empirical study (NIMH-LCM-p; Denicoff et al., 2000, 2002), and allows the tracking of rapid mood fluctuations. Some recent self-monitoring work has begun to utilize electronic platforms for ease of mobility, use, and interpretation (Bauer et al., 2008; Schärer et al., 2002). This preliminary research suggests that further refinement of self-monitoring tools will be an important research goal over the coming years.

The findings presented above should be considered in the context of several important limitations. The aim of the study was to test PMR among participants who had experienced an elevation in high-arousal positive affect after completing a positive mood induction. The effects of the positive mood induction – namely, a moderate effect size

(Cohen's d = .42) and success rate (about 60%) – were generally in line with other positive mood inductions in the literature (Westermann et al., 1996). Not surprisingly, participants who endorsed a high amount of motivation to reduce or eliminate overly happy moods were less affected by the positive mood induction procedure at Session 1. This fits with an emerging literature suggesting that some people with bipolar disorder tend to dampen or minimize positive emotional experiences. A measure to assess this tendency, the Responses to Positive Affect Questionnaire (RPA) has recently been developed (Feldman, Joormann, & Johnson, 2008). Although not administered as part of this dissertation protocol, this scale was nonetheless completed by many of my participants as part of a separate study. As expected, the Dampening subscale was negatively correlated with success of the positive mood induction. Thus, participants who are highly motivated to avoid positive moods and those who engage in strategies to dampen positive moods when they occur may be particularly resistant to positive mood induction procedures.

At Session 1, 25 of the 44 participants enrolled in the study experienced a successful positive mood induction. Recruitment pressures and feasibility did not allow the enrollment of more participants, and so this smaller sample raises questions of statistical power. This subsample was large enough to detect changes as a result of the intervention (PMR and self-focused calming). Power to detect significant interaction effects, however, was low, meaning that differential change in positive affect due to the PMR versus control condition was unlikely to be detected. The effect sizes at Session 1 associated with the PMR condition (Cohen's d = 0.47) and the control condition (Cohen's d = 1.00) suggested that a larger sample may have favored the control group.

Another limitation to consider is the lack of a no-treatment control group. The current design, pitting PMR against participants' own regulatory strategies, left open the possibility that observed treatment effects may have simply reflected a "wearing off" of the effects of the mood induction. Positive mood induction effects tend to last longer for bipolar than non-bipolar comparison groups, however (Farmer et al., 2006). Furthermore, the fact that PMR practice correlated strongly with the reduction in positive affect at Session 2 suggested that something other than a naturalistic return to baseline occurred. Nonetheless, inclusion of a no-treatment control group would have strengthened the current study.

Another potential limitation of the current study was the relative brevity of the PMR intervention itself (20 minutes of training/practice at Session 1). It is possible that a longer intervention could have demonstrated more robust effects. At least one other study has found that PMR can reduce anxiety in a single 30-minute group administration (Rausch, Gramling, & Auerbach, 2006). In the current study, PMR was associated with a statistically significant reduction in self-reported anxiety at both sessions. Furthermore, this reduction in anxiety was statistically differentiable from the control condition (which did not experience any appreciable reduction in anxiety while engaging in self-calming). These effects for anxiety suggested that participants were sufficiently engaged by the PMR training to benefit from it within the session despite its brevity.

It was also disappointing that SCL results were inconsistent with initial hypotheses. This was not necessarily surprising, however, given that PMR relies on systematic tensing and relaxing of muscles, which would be expected to raise SCL

regardless of calming effects. The lack of psychophysiological validation leaves open the possibility that response bias contributed to the study's results.

Despite these limitations, this study also has significant strengths. To this writer's knowledge it was the first to compare two strategies for reducing high-arousal positive affect among those with bipolar disorder. Furthermore, its focus on particular intervention strategies (PMR and self-focused calming) suggested that people with bipolar disorder have their own useful strategies for regulating positive emotions: in contrast, studies that focus on larger treatment manuals may be unable to provide detailed information about which components are helpful. It is also unique in investigating the relationship between PMR practice and outcomes for both in-the-moment mood and manic symptoms outside of the study sessions. The finding that even a brief PMR training can lead to in-the-moment reductions in anxiety among those with bipolar disorder is noteworthy given the high comorbidity between bipolar and anxiety disorders.

Overall Summary

The primary hypothesis driving this study was that manic symptoms could be reduced with a treatment approach originally designed to target anxiety. To arrive at this hypothesis, I reviewed a large body of literature describing the connections between mania and anxiety (e.g. diagnostic comorbidity, high arousal). I found that PMR did not demonstrate superiority to the control condition (self-focused calming) among participants who underwent a successful positive mood induction. Participants who had engaged in relatively more PMR practice on their own were able to use PMR more effectively at Session 2.

Overall, the control group was able to use a variety of calming strategies that appeared at least as useful as PMR for reducing high-arousal positive affect during the sessions. This study therefore joins a growing body of literature in suggesting that people with bipolar disorder have access to effective emotion regulation strategies. Thus, instead of teaching patients more emotion regulation skills, a more effective approach may be to increase the frequency with which they use the emotion regulation skills they already have at critical moments as symptoms emerge. Providing self-monitoring tools (especially on electronic platforms such as smartphones) may be one way to accomplish this goal; ideally, future research will more fully explore the usefulness of such tools.

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Notes

[a] One likely explanation for this finding within the PMR group is that PMR (requiring tensing and then releasing one's muscles) led to exertion and sweating despite its possible calming effects. For the control group, participants who chose self-focused calming strategies of being outdoors in the heat of Miami (e.g. going for a walk) might have been responsible for this increase. Independent samples *t*-tests compared such participants to others in the control group whose strategies did not involve being outside (e.g. deep breathing, imagery); no statistically significant differences were revealed at Session 1, $t(15) = 0.7$, $p = .49$, or Session 2, $t(11) = 1.3$, $p = .22$.

[b] Parallel analyses focused on the MASQ General Distress: Anxiety subscale, and found fundamentally similar results to those for the MASQ Somatic Anxiety subscale.