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## Transdiagnostic Treatment of Bipolar Disorder and Comorbid Anxiety with the Unified Protocol: A Clinical Replication Series

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### Abstract

Bipolar disorder (BD) is a chronic, debilitating disorder with recurrent manic and depressive episodes. Over 75% of bipolar patients have a current or lifetime diagnosis of a comorbid anxiety disorder. Comorbid anxiety in BD is associated with greater illness severity, greater functional impairment, and poorer illness-related outcomes. Effectively treating comorbid anxiety in individuals with BD has been recognized as one of the biggest unmet needs in the field of bipolar disorder. Recently, the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) was developed to be applicable to the full range of anxiety and mood disorders, based upon converging evidence from genetics, cognitive and affective neuroscience, and behavioral research suggesting common, core emotion-related pathology. Here, we present a preliminary evaluation of the efficacy of the UP for the treatment of BD with comorbid anxiety, in a clinical replication series consisting of three cases.

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Bipolar disorder (BD) is a debilitating disorder associated with intense emotional experiences that manifest in recurrent manic or hypomanic episodes and, oftentimes, chronic depressive episodes. In the most recent large-scale epidemiological survey, rates of BD in the U.S. were estimated at 2.6% of the population, with 83% of these cases classified as “severe” (Kessler, Chiu, Demler & Walters, 2005). The negative impact of BD on functioning and well-being is notable: BD is associated with considerably higher rates of unemployment than the general population (Kogan et al., 2004), significantly impaired psychosocial functioning (Suppes et al., 2001), higher rates of attempted suicide relative to any other Axis I disorder (Chen & Dilsaver, 1996), and high rates of health care utilization (Kessler et al., 2005). Thus, BD has a substantial and significant impact on social, interpersonal, and economic well-being.

Whereas BD was traditionally thought of as a disorder that follows an episodic course, with both symptomatic and functional recovery occurring between mood episodes, more recent conceptualizations recognize BD as a much more chronic and disabling disorder. Clinical and epidemiological evidence suggests BD to be characterized by persistent, residual mood symptoms that occur between mood episodes (Kessler et al., 2006; Fagiolini et al., 2005; Trede et al., 2005), and the presence of interepisode symptoms dramatically increases the

risk of subsequent mood episodes (Perlis et al., 2006). Further, interepisode symptoms may be significantly exacerbated by the presence of comorbid pathology, as BD rarely occurs in isolation. The National Comorbidity Survey replication (NCS-R; Merikangas et al., 2007) documented that 92% of patients with BD have had another lifetime co-occurring Axis I disorder, with greater than 70% meeting criteria for three or more comorbid disorders, most frequently anxiety disorders. Greater than 75% of BD patients surveyed in the NCS-R had a lifetime diagnosis of a comorbid anxiety disorder (Merikangas et al., 2007). Similarly, in the large-scale, multi-site Systematic Treatment Enhancement Program for Bipolar Disorder trial (STEP-BD; Simon et al., 2004), over one-third of patients presented with a current, co-occurring anxiety disorder. The presence of both current and lifetime comorbid anxiety has been identified as an independent marker of greater BD severity, and is associated with earlier illness onset, greater chronicity, reduced treatment response, greater functional impairment, and increased suicidality relative to BD without comorbid anxiety (Otto et al., 2006; Simon et al., 2004). Therefore, the presence of comorbid anxiety disorders in the context of BD represents a crucial treatment target for improving illness course and outcomes.

Adequately addressing comorbid anxiety in the context of BD represents one of the most significant current challenges to the successful treatment of BD. To date, pharmacotherapy has been the foundation of treatment for BD; however, pharmacotherapy for the treatment of comorbid anxiety in BD is faced with significant barriers to success. Specifically, both selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines, which represent the first-line pharmacological treatments for anxiety, may be contraindicated in the context of BD. SSRIs have been found to interact with mood stabilizers, aggravate side effects, and even trigger mania (El-Mallakh & Hollifield, 2008; Freeman et al., 2002; Sasson et al., 2003). Benzodiazepines likewise are less than ideal in the treatment of BD, as they have been shown to induce dependency (Chouinard, 2004). This potential for addiction is particularly problematic in a population already at increased risk of developing substance dependency (Brunette et al., 2003; Goodwin & Jamison, 2007).

In light of these limitations of pharmacotherapy, psychosocial treatments of BD and comorbid anxiety may be a viable treatment alternative. Cognitive-behavioral therapy (CBT) is one of the most effective treatments for primary anxiety disorders, and has also demonstrated efficacy in the treatment of BD (Ball et al., 2006; Lam et al., 2003; Lam, Hayward, Watkins, Wright & Sham, 2005; Reilly-Harrington et al., 2007; Scott et al., 2006; Sylvia et al., 2011; Zaretsky et al., 2008). However, very few controlled studies of CBT that specifically target comorbid anxiety in BD have been conducted. In addition, the few existing studies that have examined psychosocial treatment for comorbid anxiety in BD have been limited by targeting only one specific anxiety disorder, or approach the treatment of anxiety as independent from the treatment of BD-related residual symptoms (for a recent review, see Provencher, Hawke, & Thienot, 2011). This may not adequately address the presence of multiple, comorbid anxiety symptoms that frequently co-occur with residual mood symptoms in BD. In addition, treating comorbid anxiety as a separate illness from BD does not address the potential interaction between anxiety symptoms and residual mood symptoms, or their potential impact on episode relapse.

Advances in CBT have suggested that a transdiagnostic approach to treatment, targeting common core processes across disorders, offers both an efficacious and parsimonious solution to the treatment of co-occurring disorders. Recently, the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP; Barlow et al., 2010) was developed to be applicable to the combined treatment of the full range of anxiety and mood disorders. In line with the recent NIMH Research Domain Criteria initiative (RDoC; Insel et al., 2010), the UP was developed based upon evidence from genetics, cognitive and affective

neuroscience, behavioral, and physiological data that converge upon core deficits appearing across bipolar mood and anxiety disorders. Specifically, individuals with these disorders demonstrate a biological and psychological vulnerability towards more intensified affectivity than healthy controls, and exhibit a tendency to view affective experiences as aversive, uncontrollable and unpredictable (Green, Cahill, Malhi, 2007; Phillips, Ladouceur & Drevets, 2008; Wessa & Linke, 2009; Wilamowska et al., 2010). This is coupled with maladaptive and inefficient attempts to control and regulate emotional experiences (Green et al., 2011; Gruber, Eidelman, Johnson, Smith, & Harvey, 2011; Johnson, McKenzie, & McMurrich, 2009; Mennin, Holaway, Fresco, Moore, & Heimberg, 2007). Thus, the UP was developed to target specifically key aspects in core emotional processing that appear to drive symptoms across disorders, such as emphasizing the interaction between internal physiological cues and behavioral action tendencies, as well as the effect of narrowed cognitive appraisals and biases on response patterns. An emphasis is placed upon increased objective and present-focused awareness of cognitive, behavioral, and visceral affective cues that serve to intensify experiences and drive maladaptive behavioral response tendencies, and the replacement of maladaptive patterns of responding with more adaptive responses through extinction learning, by way of targeted emotion exposures.

Currently, the UP consists of eight modules, with five of these modules forming the core components of treatment (see Barlow et al., 2010). Following a brief module emphasizing the clarification of treatment goals and motivational enhancement for treatment engagement (Module 1), patients are introduced to the adaptive nature and function of emotions, with a particular emphasis on the adaptive function of both negative and positive emotions (Module 2). Emotional processing is introduced as comprising the interaction between three primary domains: physiological responses or “feeling states,” specific thought and attentional processes, and behavioral response patterns. Patients are shown how emotional experiences contribute to the formation of learned associations between specific internal and external cues and patterns of responding within these three domains, and how specific emotions drive specific behavioral responses.

Following this psychoeducation module, patients are shown skills for increasing their ability to access present-focused, mindful, objective awareness of their own patterns of emotional processing (Module 3). They are given a daily, present-focused awareness exercise intended to help condition the association between a deep inhalation and a shift in attention to sights, sounds, and sensations occurring in the present moment, thereby “interrupting” their automatic patterns of responding and allowing objective distance to observe their responses within the three interacting domains of thoughts, feelings, and behaviors. Using this increased awareness, patients then are given skills to help explore the contribution of each of these three domains to emotion experiences; specifically, the contribution of maladaptive automatic appraisals (Module 4), emotion-driven (EDBs) and avoidance behaviors (Module 5), and physiological or interoceptive cues (Module 6). In Module 4, patients begin to identify specific thought patterns and beliefs that influence emotional responses, and are given strategies to increase cognitive flexibility. In Module 5, patients identify maladaptive EDBs and behavioral avoidance patterns, and practice engaging in opposite behaviors, a long-standing strategy to modify emotions (Barlow 1988). In Module 6, patients participate in interoceptive exposures designed to isolate physiological sensations from their emotional context and increase the patient’s awareness and tolerance of specific somatic cues. Finally, in Module 7, patients are given the opportunity to practice and integrate these skills through emotion exposures, with the goal of replacing maladaptive learned associations with new, adaptive associations. Module 8 provides psychoeducation for relapse prevention.

Given the demonstrated efficacy of the UP in the treatment of a range of co-occurring anxiety and unipolar mood disorders (see Ellard et al., 2010; Farchione et al., in press), the

UP was applied clinically to a selection of cases of BD with comorbid anxiety disorders. It was theorized that, 1) because of the emphasis in the UP on directly addressing emotional processing occurring across disorders; 2) because of the specific difficulties managing intense emotional experiences that occur in patients with BD; and 3) because of the contribution of interepisode pathology on subsequent episodic relapse and the significant negative impact of anxiety on BD illness and course, the UP might be a uniquely efficacious treatment approach for this population. In an initial evaluation of this notion, we present below a description of three cases of BD with comorbid anxiety treated with 15 sessions of the UP. Two cases completed all UP treatment modules within the 15 sessions, and are described in full below. One additional case did not complete all modules within the 15-session limit, and is presented in brief, highlighting the challenges of delivering the UP in a time-limited way in this population. All patients were receiving concurrent psychiatric treatment and were on stable doses of mood stabilizers. Prior to beginning treatment with the UP, patients received an initial diagnostic assessment using the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998), a brief structured diagnostic interview for the assessment of DSM-IV Axis I and ICD-10 psychiatric disorders. Severity of manic, depressive, and anxiety-related symptoms were assessed at pre- and post-treatment using a combination of well established clinician-administered and self-report measures, which included: the Hamilton Depression Rating Scale (HAM-D-17; Hamilton, 1960); the Montgomery Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979); the Young Mania Rating Scale (YMRS; Young et al., 1978); the Clinical Global Impression Severity (CGI-S) and Improvement (CGI-I) Scales (Guy, 1976); the Beck Depression Inventory (BD-II; Beck, Steer & Brown, 1996); and the Beck Anxiety Inventory (BAI; Beck, Epstein, Steer, & Brown, 1988). In addition, all patients completed weekly monitoring ratings of mood, sleep, and medication compliance to track mood episodes. Specific, potentially identifying details in each case have been altered to protect patient confidentiality. Outcomes data are presented in Table 1.

## Case 1

S.D. was a 62-year old, married, Caucasian male presenting for psychosocial treatment for the first time. He was under the care of a psychiatrist, and was being treated with lithium (1500mg) as a mood stabilizer and Seroquel (20mg) for sleep. S.D. was a retired firefighter, and at the time of treatment was helping his son and daughter-in-law with the care of his first grandchild. He was seeking help managing his moods; in particular, controlling episodes of anger, which had caused significant difficulties in his relationships with his wife and family over the years. Most notably, his anger outbursts had caused a prolonged rift in his relationship with his son, which he was only now starting to mend. He was fearful of losing control of his emotions and subsequently damaging his relationship with his family once again.

S.D. reported he had always been considered “moody,” but never sought treatment until the late 1980s after the urging of his primary care physician. He described a long-standing pattern of vacillations between “feeling like Superman” and debilitating episodes of depression that often left him unable to get out of bed. Over the years, his mood symptoms had caused interference not only in family relationships, but also in his relationships with employers and friends. He described his life as a series of “chaotic events,” and often felt out of control of his behaviors. He started treatment with lithium in his mid 40s, which he found helpful for controlling episodes of mania, but he still found it difficult to control his occasional outbursts of irritability and anger, and experienced recurrent episodes of depression. He was particularly fearful of these episodes of depression, and was anxious about their potential for recurrence.

In addition to his mood symptoms, S.D. reported struggles with anxiety and substance dependence. He reported a lifetime history of PTSD, initially triggered by physical abuse at the hands of his father, and exacerbated after combat exposure during the Vietnam War. He reported several current symptoms of PTSD, including nightmares and flashbacks, a sense of numbness and avoidance of thoughts or feelings related to the traumas, difficulty sleeping, and exaggerated startle. S.D. also reported a history of substance dependence in partial remission, primarily cocaine and alcohol, which had peaked during his early 40s, but continued to cause interference in his life. He entered treatment for addiction in his mid 40s, and had struggled to maintain sobriety since. He denied using substances at the frequency and amount he used to, refraining from his previous “bingeing” behaviors, but reported he occasionally gives in to cravings, finding it difficult to completely abstain.

The initial sessions with S.D. focused on conducting a thorough diagnostic assessment and orienting him to treatment. Based upon this assessment, S.D. met criteria for bipolar I disorder, PTSD, and substance abuse. His initial symptom assessment scores indicated moderate levels of depression and anxiety, low levels of manic symptoms, and moderate illness severity (see Table 1). A discussion of S.D.’s readiness for change and engagement in treatment was conducted by exploring S.D.’s goals for treatment and the pros and cons of changing versus staying the same (UP Module 1). S.D. reported his recent role as grandfather and the new responsibility of caring for his grandson were strong motivators for treatment and change. He felt his son and daughter-in-law entrusting him with the care of his grandchild, giving him the opportunity to prove himself as reliable and helpful, was providing him an opportunity to “make up for his past failures” and “be a better person,” thus regaining his family’s trust and respect. Therefore, finding new, adaptive ways of coping that allowed him to function as a trusted and reliable member of his family became a concrete goal for treatment.

S.D. was willing to try CBT, but was particularly wary of engaging in psychotherapy, as he had always been taught that talking about feelings and emotions was for “sissies.” As such, the first session focused on exploring the adaptive function and nature of emotions, introducing S.D. to non-judgmental awareness and acceptance of emotions as important aspects of everyday functioning (UP Module 2). S.D. responded very well to discussing emotions from the perspective of their adaptive function and nature, and found it easier to relate to discussing his own experiences within this framework. The specific, adaptive function of negative emotions such as anger and sadness was introduced, with an emphasis on distinguishing between initial, adaptively triggered emotions and maladaptive reactions to these emotions. S.D. was able to see why the full range of emotions are at their core adaptive and necessary, and why an exploration of his reactions to emotional experiences might be useful for understanding where his own emotional experiences become maladaptive.

An example of a recent outburst of anger was used to demonstrate for S.D. how an initial emotional experience might evolve from an adaptive response to a maladaptive response, helping him to map out the antecedents or triggers, responses to the triggers, and consequences of these responses. S.D. recalled an incident of “road rage,” during which a near accident with another driver caused him to yell, scream, and punch his steering wheel while his infant grandson was in the backseat. He reported nearly getting out of his car and engaging the other driver, and avoided a physical fight only after some considerable restraint. S.D. was able to identify the near accident as the emotional trigger, and was able to identify an initial reaction of fear. The physiological response associated with this initial fear reaction was explored and discussed in terms of the adaptive function; specifically, the increased heart rate, flushing, and muscle tension S.D. experienced were identified as part of an adaptive “fight or flight” response. S.D.’s subsequent reaction to this trigger was then



explored. He identified that derogatory thoughts towards the other driver, feelings of anger, and behaviors of yelling and punching the steering wheel all followed his initial fear reaction. The short-term consequence of this response was discussed, and the reinforcing nature of this response was emphasized. In particular, S.D. identified that this response gave him some relief initially by allowing him to vent his anger and feel more in control of the situation. However, S.D. was also able to identify the long-term consequence of this response; specifically, his negative feelings for yelling in front of his grandson and nearly endangering him by engaging in a physical fight. He also identified feelings of frustration and depression developing soon after the event, resulting from a general sense of being out of control and self-loathing about his behavior.

This experience was further explored using the three-component model of emotion, allowing S.D. to explore how the interaction of his thoughts, feelings and behaviors that followed the initial emotional trigger may have escalated the experience. A particular emphasis was placed upon the relationship between increased autonomic activity and his emotion-driven behaviors (EDBs), such as the verbal behavior of yelling and physical behavior of punching the steering wheel, as well as the negative thoughts towards the other driver. The tendency for adaptive emotional responses to be paired with and followed by maladaptive automatic responses (EDBs) was also discussed. Through this exploration, S.D. was able to map out where the adaptive response of fear, triggered by an immediate threat to his well-being, crossed over to a maladaptive response with negative consequences. S.D. found it particularly helpful to view his experiences in this way, and quickly recognized his dismissal of emotions as “weak” did not take into account their adaptive purpose or help him to explore where his own reactions to these emotions were becoming problematic.

S.D.’s first homework assignment was to begin monitoring the antecedents, responses, and consequences (ARCs) of emotional experiences in situations that came up between sessions, as well as to begin taking daily observations of his mood (elevated, depressed, or normal), hours of sleep each night, and medication use. Early on in treatment, S.D. noted he was quickly becoming more aware of both his negative thoughts and his emotion driven behaviors. He also reported some difficulty remembering to complete homework, and noted difficulties with organization more generally. Some time was spent brainstorming the ideal time of day to complete his homework assignments to ensure success, as well as a location to keep his session materials so they are readily accessible. S.D. decided to keep his session materials with his medications, and would complete assignments in the evening at the same time he takes his medication. He also enlisted the help of his wife, who added reminders for him to complete his session homework alongside her daily reminders for him to take his medication. This plan worked well for S.D., and increased his homework compliance.

Once S.D. had a firm understanding of the framework of the ARC of emotions for understanding his experiences, he was given tools to increase his ability to objectively observe his experiences (UP Module 3). Specifically, in-session mindfulness exercises were conducted that encouraged S.D. to observe sensory experiences happening externally to him in the present moment, such as sounds, temperature, and tactile sensations, and to observe the three components of emotions (thoughts, physical sensations, and behaviors) as they were occurring in the present moment. S.D. was shown how to begin to condition his breath to help him adapt a stance of present-focused awareness, by pairing a deep inhalation with focused attention on a sensory cue (a sound, smell, or tactile sensation). S.D. responded very positively to these exercises, stating they gave him a sense of calm and a sense he could regain control of his reactions. He began practicing daily mindfulness exercises by pairing a deep breath with an awareness of something in his surroundings. He quickly adapted this skill to situations when he felt intense emotions or a sense of being out of control. To help him cope with intense or overwhelming emotional experiences, S.D. was encouraged to give

himself a mindful “time out,” exiting the situation he was in and using mindful awareness strategies to bring himself back to the present moment and observe his emotional reactions. S.D. found this very helpful for preventing the engagement in impulsive EDBs. He described several situations in which he excused himself to his room, took a deep breath, focused his attention on a sound, and was able to ride out intense emotions. He reported this helped him to think before he acted on his emotions, and prevented him from “doing something stupid,” like shouting at his wife.

The next several sessions were spent on closer examination of the role of each of the three domains of emotional experiences (physical sensations, thoughts, and behaviors), beginning with the role of negative automatic appraisals (UP Module 4). S.D. was able to identify several maladaptive automatic appraisals, which were primarily focused on self-loathing statements or anger directed at others, the source of which S.D. identified as similar statements made to him by his father and other significant role models throughout his life. Particular attention was paid to how these negative statements influenced and intensified his experiences, and homework focused on identifying patterns between certain emotions and physical sensations and automatic negative appraisals. The identification of certain common themes and “thinking traps” was emphasized through homework assignments and in-session exploration of recent emotional experiences. S.D. found the concept of thinking traps very useful, helping him to gain objective distance from his experiences, and he adopted his own term to help him label when he caught himself engaging in negative automatic thinking. S.D. learned skills for generating and considering alternate or “equally possible” appraisals, thereby increasing his cognitive flexibility. Throughout, S.D. began to gain a better understanding of the association between certain mood states, and in particular physical sensations associated with mood states, and the corresponding patterns of negative thought.

Notably, at this time in treatment S.D. experienced a depressive episode, which followed a bout with the flu. S.D. came to session viewing the return of his depressive symptoms as a failure, and reporting a sense of hopelessness. This provided an opportunity for S.D. to explore how his physical sensations (heaviness and fatigue from the flu) had triggered negative automatic appraisals and catastrophic thoughts about the implications of his depressed mood. He was also able to identify certain behaviors associated with the thoughts, such as withdrawing from family and friends. He was able to identify how these negative appraisals served to worsen his mood and increase his sense of heaviness and amotivation. S.D. was encouraged to use this experience and experiences like these as an opportunity to explore mood triggers and his reactions to these triggers, using present-focused awareness skills to help identify the associations between thoughts, feelings and behaviors, and identify maladaptive patterns of responding.

This experience also provided an opportunity to explore more closely the role of behaviors in S.D.’s emotional experiences (UP Module 5). In particular, S.D. was encouraged to monitor and record his emotion driven behaviors (EDBs) associated with certain feeling states or automatic thoughts, such as an urge to withdraw and stay in bed in response to his depressed mood, and was introduced to the concept of acting opposite to this urge, such as getting up and going for a walk with his wife instead of staying in bed. This was initially difficult for S.D., but he was able to utilize both mindfulness skills and a review of his pros and cons for change (UP Module 1) to help motivate him to engage in behaviors opposite to his EDBs. S.D. found the discussion of EDBs and avoidance behaviors to be particularly helpful for understanding his substance use. He was able to recognizing how certain cues or feeling states were closely paired with urges to use. S.D. again utilized present-focused awareness to note these associations and gain distance in order to “ride out” his cravings. S.D. also explored EDBs in relation to triggered anger. He reported an incident in which he lashed out at his wife, and was able to use present-focused awareness to both calm himself

and connect his behavior with feelings of fatigue and frustration due to an unrelated incident. He reported feeling very encouraged by his ability to use the skills from session to both calm himself and put his behaviors into context, and as a consequence he was able to apologize to his wife, rather than engage in his usual behavior of rumination, which would typically serve to worsen his mood, increase his irritability, and cause him to lash out again. S.D. also explored the engagement of opposite behaviors during episodes of depression. Specifically, S.D. identified several pleasant activities he enjoyed such as working on his house and garden, and worked towards engaging in these pleasant activities when he felt depressed, rather than giving in to his EDB to retreat into his bedroom. Throughout, S.D. worked to become more aware of how his physical sensations or physical state (fatigue, tension, arousal) contributed to both his negative automatic appraisals and his EDBs (UP Module 6).

The final phase of treatment was focused on utilizing the skills S.D. had learned thus far through emotion exposure tasks (UP Module 7). Specifically, for S.D., exposures were designed around his response to strong cues to engage in substance use, such as speaking to certain friends over the phone or experiencing an elevated mood state, as well as confronting situations in which he might become irritable or angry. In addition, S.D. designed several positive emotion exposures aimed at increasing his engagement in pleasant and rewarding activities, such as taking walks with his wife, having dinner with family and friends, and working in his garden. In addition, S.D. began to explore common themes arising in his automatic appraisals, and began to identify core beliefs of being worthless, incompetent, vulnerable, weak, and unlovable, all of which he connected to his past traumatic experiences. He began to compare these beliefs about himself with his current experiences, and became increasingly able to identify positive examples of his competence, value, and self-worth as evidence against these core beliefs.

At the time of treatment termination, S.D. reported noticing a significant improvement in his ability to cope with his mood and emotions, and noted a very positive effect on his relationships with significant others, including his son. He evidenced a significant improvement in his post-treatment assessment scores, all of which fell within the normal range after the 15 sessions, and was rated as mildly ill and very much improved on the CGI-S and CGI-I respectively (see Table 1). At the time of termination, S.D. expressed that, with his new skills for managing emotions and mood, he felt ready to explore further CBT, and in particular was interested in pursuing exposure therapy for his past traumas. He expressed an interest in reconnecting with the Veterans Administration (VA) service to provide continued support and further treatment for his trauma. This was a significant change for S.D., as he had previously distanced himself from the services offered through the VA, considering seeking help as a sign of weakness. He was put into contact with the local V.A., and at the time of termination was transitioning to continued treatment through the VA.

## Case 2

B.L. was a 23 year old, single, Caucasian female referred for psychosocial treatment by her psychiatrist. She was receiving pharmacotherapy, and was on stable doses of lamotrigine (150mg) and sertraline (75mg). B.L. reported a long-standing struggle with mood swings, anxiety, and substance dependence, and at the time of intake was experiencing frequent distressing nightmares and an increase in suicidal ideation. She reported three previous suicide attempts over the past two years, the most recent occurring eight months prior to her intake interview. She reported the first of these attempts had been impulsive, and the other two had been premeditated. She also reported being under the influence of drugs and alcohol at the time of each attempt, and experiencing a feeling of disappointment when the attempts were unsuccessful. Following her most recent attempt, she voluntarily entered a detox



program, and at the time of her intake assessment had successfully maintained sobriety for the six months since leaving the program. She reported still struggling with urges to use, particularly during her mood swings.

B.L. reported a psychosocial history marked by instability and a lack of social supports. She was raised solely by her mother and was frequently left on her own growing up. Her mother's work caused them to relocate frequently, and she attended several different schools before high school. She was often the target of bullying at school, had difficulty maintaining friendships, and recalled the friendships she did have frequently ended in "bitter fallout." Throughout high school and her first two years of college, she was able to maintain a few close friendships; however, these friendships were punctuated by substance abuse, and she reported she had recently lost several of these friends upon becoming sober.

B.L. reported a life-long struggle with mood difficulties and anxiety. She recalled several incidences of severe depression, beginning in childhood. She was hospitalized at age 14 following the death of her aunt, whom she referred to as the only other person in her life she was close to. She fell into a severe depression following her aunt's passing, refusing to eat and dropping down to 72 pounds. She reported several past manic episodes, which often resulted in her putting herself in dangerous or risky situations, using substances, and engaging in risky sexual behavior. In addition to her struggles with mood symptoms, B.L. reported two incidents of sexual abuse, one in her junior year of high school, and another in her freshman year in college. She experienced frequent intrusive thoughts and nightmares following these events, along with feelings of numbness, avoidance, inability to recall important aspects of the events, difficulty sleeping, hypervigilance, and exaggerated startle. B.L. also reported experiencing frequent panic attacks; anxiety and avoidance of social situations; and compulsive washing and arranging behaviors. B.L.'s struggles with mood symptoms, anxiety, and substance use had caused her to drop out of college after two years, and were making it difficult for her to maintain steady employment. She reported often feeling "out of control," and was particularly fearful of relapsing into substance use and falling into a worsening depression. She had received talk therapy in the past, but had never received CBT, and was anxious to try "anything that will get my life under control."

At the start of treatment, a thorough diagnostic assessment and psychosocial history was conducted. Based upon this assessment, B.L. met criteria for bipolar I disorder, most recent episode depressed; panic disorder with agoraphobia, social phobia, obsessive compulsive disorder, PTSD, and substance dependence in partial remission. Her scores on symptom measures indicated severe depression, severe anxiety symptoms, moderate manic symptoms, and marked illness severity (see Table 1). Because of B.L.'s previous suicide attempts and fluctuating suicidal ideation, the initial treatment session focused on exploring triggers for suicidality, identifying current protective factors that could help to prevent further attempts, and the delineation of a safety plan. B.L. was able to list her mother, her close friend, and her desire to go back to school as factors that were keeping her from acting on any suicidal thoughts. B.L.'s goals for treatment and readiness for change were also discussed (UP Module 1). B.L. listed maintaining sobriety and finishing her college degree as two primary treatment goals. She also wished to learn better ways of coping with her mood swings and distress, and how to prevent "becoming derailed" by her emotions. B.L. stated that starting treatment was helping her to feel more hopeful about her future, and she expressed a commitment to engage in treatment.

B.L. arrived at her first treatment session in a great deal of distress after experiencing a strong urge to use substances, which caused her to doubt her ability to remain sober. She had come across paperwork related to her detox program the night before, which triggered both cravings to use, as well as negative thoughts about her self worth and her ability to remain

abstinent from substance use. This experience provided an opportunity to introduce the adaptive function of emotions, the interaction of thoughts, feelings and behaviors, and in particular the ability for strong emotions to trigger learned associations between these three domains (UP Module 2). The adaptive nature of this ability was first introduced, emphasizing how having the ability to quickly associate situations and contexts with consequences was inherently useful, enabling us to quickly recognize and move away from danger, or quickly move towards something that is rewarding and self-preservative, without having to waste precious energy or time deliberating upon the rewarding properties of the stimulus or situation. However, the consequence of failing to update associations based upon current contexts was also discussed; in particular, when the learned association is no longer applicable to the current context, such as when a previously threatening situation becomes non-threatening.

In B.L.'s case, the name and logo of a detox program had become associated with the experience of strong cravings and thoughts of self-doubt as to her ability to overcome her cravings. Simply viewing the logo and materials triggered these associated thoughts and experiences, and caused B.L. to act according to these triggered experiences. However, it was pointed out that the associated thoughts of low self-worth and self-doubt were not congruent with the current context in which she had successfully completed a detox program and maintained sobriety for six months, and in this sense were more congruent with a past context than the current one. B.L. was able to map out her subsequent reactions to this triggered negative emotional experience, noting her thoughts, physiological feelings, and behavioral responses. She reported ruminating about her failures, and watching a "depressing" movie, which served to perpetuate her low mood. She was able to see that acting in response to these "outdated" contexts failed to take into account her more recent positive achievements, and had kept her "stuck" in a negative mood state. B.L. noted how self-doubt was closely associated with feelings of fear and sadness and thoughts of hopelessness, which tended to increase urges to use, thereby perpetuating a negative cycle of responding. By viewing this experience as a process, B.L. was shown how becoming aware of this process, breaking it down and evaluating the match between old associations and the current context, could provide her with greater control and influence on the ultimate outcomes of her experiences.

Using this as a starting point, B.L. began to observe other emotional situations and record the associated thoughts, feelings and behaviors. B.L. was given present-focused awareness exercises to help practice observing her experiences as they unfold, and allowing her to "ride out" cravings and feelings of distress (UP Module 3). B.L. struggled initially with these exercises, finding it hard not to engage in avoidance behaviors, but found the daily present-focused exercises particularly helpful. Using present-focused awareness, she was able to begin decoupling her automatic thoughts and behaviors in response to feelings of depression, anxiety, distress, or physiological cravings to use, and was increasingly able to successfully refrain from acting on these feelings. Specifically, she began to observe how certain mood and physiological states were associated with certain thought and behavior patterns. B.L. worked on identifying how these thoughts and behaviors served to intensify her feelings of distress, and practiced determining whether her patterns of responding were "leftover" associations, or if they fit the current context. B.L. began to successfully use present-focused awareness to refrain from rumination and worry during periods of low mood, and was able to "sit" with her feelings of depression. She noted her mood returned to normal in a much shorter period of time, and was very encouraged by this experience. She also noted that by observing her experiences in this way, her mood did not dip quite so low, and did not seem to trigger full episodes of depression.

As B.L. became more adept at noticing and recording her emotional experiences, the next few sessions focused on a closer examination of her automatic appraisals and associated emotion driven behaviors (UP Modules 4 and 5). B.L. provided several examples of negative automatic thoughts, and began to notice how certain physiological and mood states tended to trigger similar thought patterns. For example, when B.L. was feeling more depressed or fatigued, her thoughts became focused on low self-worth and a sense of hopelessness, which resulted in a tendency to isolate herself and listen to sad music or watch sad movies. She recognized how these behaviors led her to ruminate and worry more, and tended to exacerbate her distress. She also noted that feelings of contentment were often followed by feelings of guilt. For example, she would frequently ruminate and worry about her mother's struggles with depression, which she appraised as "all [her] fault." In this way, a feeling of contentment was often quickly followed by a feeling of anxiety. She also began to recognize how low mood states caused her to easily dismiss or ignore her strengths and abilities.

When her mood was elevated, or she felt more autonomically aroused, she noted her thoughts became more reckless and resigned. She described thoughts as having a common theme of "who cares" or "what does it matter" during these episodes, which tended to drive an urge to engage in self-destructive behaviors and increase her urges to use substances. She noted an increase in impulsive and risky behaviors during these mood states, and would find herself "tempting fate," such as going for a walk alone late at night in an unsafe neighborhood. She noted that her suicidal thoughts would also increase following this pattern. B.L. was introduced to the concept of cognitive errors and thinking traps, with particular attention to how these errors tended to be associated with certain behaviors and physiological states. In particular, B.L. began to recognize a tendency to engage in all-or-nothing catastrophic thinking, and would often interpret interactions with others as overly negative or judgmental. She would frequently discount positive events or achievements, easily dismissing them or attributing them to something outside her influence. B.L. recognized the bi-directional effect these types of thoughts had on her mood and behaviors and subsequent thoughts.

About midway through treatment, B.L. reported she had experienced rapid mood swings between sessions, beginning with feelings of depression and switching to a manic episode. She noted an increase in suicidal ideation and impulsivity that accompanied these mood swings, including one night of relapse into substance use. After fully assessing her current level of suicidal intent and reviewing her safety plan, these recent mood swings were mapped onto the three component model of emotions, exploring triggers for her mood symptoms and the accompanying thoughts, feelings and behaviors in response to these triggers. B.L. was able to identify several triggers, including changes in medication, recent travel and sleep disruption, and memories of past traumatic events triggered by a change in seasons. By mapping out specific experiences in "real time," B.L. explored how the interaction of specific physiological and feeling states, thoughts and memories, and behaviors had served to exacerbate and worsen her symptoms. B.L. found this exercise particularly helpful, noting she had previously felt helpless in the face of her mood swings, but could now see specific triggers that preceded them and aspects of her experiences during these mood episodes she was able to alter or control, such as her thoughts and behaviors in response.

These experiences were also used to introduce B.L. to the last two important components of emotional experiences: EDBs and physiological sensations (UP Modules 5 and 6). B.L. explored her EDBs associated with specific mood states and thought patterns. Particular attention was paid to her tendency to engage in self-destructive or "self-punishing" behaviors in response to the visceral cues that accompanied both low and elevated mood.

B.L. also identified her tendency to engage in compulsive and avoidance-related behaviors in response to anxiety-related interoceptive cues, such as avoiding crowded places and social interactions, or engaging in excessive washing, ordering and arranging. B.L. made a list of alternate behaviors, with a specific focus on identifying positive or self-care related behaviors that could function to replace her self-destructive and avoidance behaviors. For example, when she experiences a low mood, B.L. identified working on artwork or going to a movie with a friend as opposite behaviors to sitting alone listening to sad music. She identified running, going to the gym, or going for a walk with a friend as alternate behaviors when she experiences an elevated or autonomically aroused state. She also practiced refraining from washing or arranging when feeling anxious, instead allowing herself to sit with the anxiety without engaging in the compulsive response, and challenged her negative automatic appraisals regarding social situations by entering situations rather than avoiding them. Throughout, B.L. found using her breath to anchor her, observing her thoughts, feelings and behaviors in an objective way, and turning her attention to the present context to be particularly helpful in allowing her to refrain from engaging in emotion-driven behaviors and instead chose more adaptive behaviors.

The subsequent sessions were focused on increasing B.L.'s awareness of the interoceptive cues that accompanied mood and anxiety states, and decoupling physiological states from their automatic, associated learned responses (UP Module 6). B.L. engaged in several interoceptive exercises designed to mimic feelings of anxiety, panic, arousal, and low mood. These included running in place, spinning in circles, breathing through a thin tube, hyperventilating, hand staring, sitting in a slumped posture while frowning, and wearing heavy clothing. B.L. was initially apprehensive about engaging in interoceptive exposures that mimicked anxiety and panic symptoms. However, after repeating exposures in session several times in a row, she was able to see how her distress diminished, and more readily engaged in exposure practice at home. Through these exercises, B.L. became more aware of the role of physiological and somatic states in her overall mood and emotional responses, and was able to identify the association between specific somatic, interoceptive cues and specific patterns of thoughts and behaviors. By recognizing this connection, B.L. became more adept at breaking these associations by labeling her somatic sensations, identifying the associated automatic thoughts, and replacing associated emotion driven behaviors with opposite actions. For example, when B.L. felt more autonomically aroused and anxious, she was able to respond to this arousal by going for a run. When she felt psychomotor slowing, fatigue, or heaviness, she was able to respond compassionately, labeling her feelings as a transient low mood, and engaging in self-care such as meditating, calling a friend, or taking a leisurely walk with her mother.

The final phase of treatment with B.L. focused on practicing skills learned throughout treatment through emotion exposures, and helping her to move towards her education and career goals (UP Module 7). B.L. particularly struggled with engagement in positive activities, which often triggered feelings of guilt or a sense of being vulnerable to the "other shoe dropping." Therefore, emotion exposures were designed around increasing her engagement in positive events, such as working on her art and spending time with friends. B.L. also struggled with associations between having an active social life and using substances. Exposures were designed around engagement in social activities that supported her goal of abstinence and the use of treatment skills to help break associations between certain social situations (e.g. social gatherings) and self-destructive behaviors. B.L. also engaged in situational exposures designed to target anxiety about panic attacks, such as riding on subways and going to crowded movie theaters. B.L. also completed writing assignments exploring her positive hopes for the future, and helping her to clarify her long-term life goals.

B.L. responded very well to treatment, and reported greater confidence in managing her moods by treatment termination. She evidenced significant improvement in her symptoms after the 15 sessions, falling within the normal to borderline range on all symptom measures, and was rated as mildly ill and very much improved on the CGI-S and CGI-I respectively (see Table 1). By the time of treatment termination, she had re-enrolled in college, was actively pursuing the completion of her degree, and was feeling very positive about her future. She had developed strong relationships with friends who were supporting her goal of maintaining abstinence. She was also engaging in regular exercise and continuing to work on art. She planned to continue engaging in bi-weekly CBT sessions to help solidify and consolidate the skills she had learned over these initial 15 sessions.

### Case 3– Challenges to Treatment Delivery

We have presented above two cases successfully treated with the UP. However, it is important to also note that vulnerability to recurrent manic or depressed episodes, the potential for increased suicidality, or the presence of other psychosocial stressors in this patient population may represent a challenge to successful treatment. Severe mood episodes may necessitate a focus on mood stabilization rather than the delivery of treatment components as intended. The increased risk of vulnerability to environmental or situational stressors also may have a direct or indirect relationship with symptom severity, and may necessitate interventions aimed at crisis management. Because the UP is a skills-based intervention that relies upon engagement in treatment and practice between sessions to maximize treatment results, these interruptions in treatment delivery can potentially limit overall outcomes in settings where treatment is not able to be flexibly applied (e.g. over a flexible number of sessions).

For example, Case 3 (N.G.) was a 51 year old, Caucasian male who met diagnostic criteria for bipolar I disorder, social phobia, GAD, and ADHD, and was experiencing severe levels of depression, moderate anxiety, mild mania, and mild illness severity at the start of treatment (see Table 1). N.G. was engaged through the early stages of treatment and reported an initial improvement in symptoms, but suffered two severe setbacks around the time of session 10 – the death of a close friend and the loss of an expected promotion at work. He experienced a significant relapse of his depression following these losses, and the remaining treatment sessions were spent helping N.G. manage his grief and problem-solve next steps in his job and career. Subsequently, N.G. did not complete all treatment modules, and his mood symptoms had not stabilized by session 15 (see Table 1). However, N.G. did report during his final session that he felt he had benefitted from treatment thus far, and was interested in continuing CBT. Thus, N.G. was given referrals upon termination to help him pursue further treatment and offer continued support for his grief.

### Conclusion

We have presented here clinical case examples illustrating the application of the UP, a transdiagnostic treatment for emotional disorders, to patients with BD and comorbid anxiety disorders. Both BD and anxiety disorders are characterized by intense emotional experiences with a significant impact on functioning. The UP was developed to specifically target maladaptive emotional processing that occurs across disorders, and to allow patients to gain control over their reactions to intense emotions. In this way, the goal of treatment is not to eliminate intense or uncomfortable emotions, but rather to give patients the skills necessary to manage their reactions to these experiences in real time, thereby preventing the escalation, exacerbation, or intensification of these experiences, and facilitating the selection of more adaptive behavioral and cognitive responses. Because of the tendency for intense affectivity to drive functional impairment in BD and the contribution of comorbid anxiety to severity



and course of BD, it was theorized that the UP, an emotion-focused transdiagnostic treatment, might be in a unique position to address mood and anxiety symptoms in this population.

Overall, treatment with the UP was well received these cases. Feedback from these patients suggested that gaining a more objective understanding of how the interaction of physiological, cognitive, and behavioral responses influenced their experiences, and how they might alter these responses, was particularly helpful for managing their symptoms and overall mood. Specifically, gaining the understanding that, whereas they might not have control over triggered emotions or fluctuations in mood, they did have control in how they reacted to these experiences, gave them a sense of mastery and efficacy in making cognitive and behavioral choices. All three patients found the present-focused awareness skills to be particularly helpful towards gaining a greater awareness of these maladaptive reactions and interrupting cycles of maladaptive responding.

It is notable that, in these particular cases, the protocol was delivered within the boundaries of a 15-session limit imposed by this pilot trial. The improvement in symptoms and functioning in these cases (see Table 1) suggests significant gains can be made in adopting more adaptive emotion regulation skills over the course of brief treatment. However, all three patients requested continued care to help consolidate skills and continue with exposure practice, and it is not known whether gains made across these initial 15 sessions were maintained over the long term or the long-term effect on episode relapse. In addition, one patient (Case 3), experienced significant losses towards the end of treatment, and was subsequently unable to complete all of the UP modules. Therefore, given the overall severity of this population, and the potential for the management of added psychosocial stressors to interrupt treatment delivery, it is not yet known what optimum number of treatment sessions would be required in order to achieve and maintain treatment gains. Therefore, although the results of these cases are promising, future, more systematic longitudinal and randomized controlled studies are needed to formally evaluate the efficacy of the UP for the successful treatment of BD with comorbid anxiety both acutely and long term.

In summary, treatment with the UP, a transdiagnostic, emotion-focused CBT treatment, appears to be a promising approach to the treatment of BD with comorbid anxiety disorders. The outcomes of the cases presented here suggest the UP is both a feasible and acceptable treatment approach in this population. However, future, controlled studies will be needed to formally assess both the short- and long-term efficacy of the UP in managing symptoms and preventing further episodes, as well as to evaluate specific moderators and mediators of treatment in this difficult-to-treat population. If the UP proves efficacious, this may offer a viable option towards meeting the crucial need for treatments that address the significant impact of anxiety comorbidity in BD.

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**Table 1**

Pre- and Post-Treatment Outcome Scores

Comorbid Diagnoses	Case 1		Case 2		Case 3	
	PTSD, Substance Dependence		PDA, Soc, OCD, PTSD, Substance Dependence		Soc, GAD, ADHD	
	Pre	Post	Pre	Post	Pre	Post
BDI	21	11	50	0	22	14
BAI	25	10	50	15	19	18
HAM-D	12	6	22	6	16	17
MADRS	10	3	31	3	18	18
YMRS	2	1	14	2	3	2
CGI-S	4	3	5	3	3	4
CGI-I	---	1	---	1	---	3

Note: ADHD = attention deficit hyperactivity disorder; OCD = obsessive-compulsive disorder; GAD = generalized anxiety disorder; PDA = panic disorder with agoraphobia; PTSD = post-traumatic stress disorder; Soc = social phobia.