

# Leveraging Mobile Technology to Improve the Treatment of Comorbid Bipolar and Substance Use Disorders

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## Introduction

Co-occurring substance abuse in bipolar disorder is a prevalent and costly problem. Bipolar disorder a leading cause of disability worldwide [1], with up to 60% of these individuals possessing a history of a comorbid substance use disorder (SUD) [2]. Furthermore, research indicates that individuals with SUDs have a 5-8 times greater risk of bipolar disorder compared to the general population [2,3]. Comorbid bipolar and substance use disorders (BP-SUD) are associated with a higher frequency of mood episodes, greater persistence of mood symptoms, increased relapse risk, greater psychiatric comorbidity, greater disability, higher mortality, increased violence, more hospitalizations, higher suicide risk, and poorer functioning compared with non-comorbid patients, as well as higher treatment costs [4-11].

Treatment non adherence is among the highest in patients with BP-SUD compared with other clinical populations. Research indicates that up to 60% of bipolar patients are treatment non adherent [12,13]. For example, a study of 168 patients with bipolar disorder followed over 18 months found that 25% discontinued medications altogether, an additional 33% who remained on medications were non adherent to them, and 25% were non adherent to psychosocial treatments [14]. Research suggests that numerous factors are associated with non-adherence, including illness insight, medication side effects, treatment beliefs, patient-doctor alliance, symptom severity, and substance use [12,13,15,16]. In fact, comorbid alcohol and/or drug use is perhaps the most important predictor of non-adherence in bipolar disorder [13,17,18]. For example, Keck et al. [19] followed 134 bipolar patients post-hospitalization and found that patients with comorbid SUDs (33%) were less likely to be adherent to medications compared to those without SUDs (58%).

Ecologically-valid predictors of adherence are needed to guide interventions for BP-SUD. Little is known about the relative contribution of adherence predictors when combined, and even less is known about how these barriers might fluctuate in the patient's natural environment. Prior studies have been mostly cross-sectional or retrospective in nature [12,13,15,16]. This is problematic because memory bias may influence self-reporting [20]. Also, many adherence barriers fluctuate according to environmental circumstances (e.g., interpersonal stressors, drug cues), making them difficult to assess out of context [21,22]. Furthermore, psychiatric symptoms and their expression are predictive of non-adherence, including situationally-varying emotional states, substance misuse, and mood symptoms [23, 24]. Recently, "readiness to change" based on the Transtheoretical Model of Behavior Change [25] has shown promise in predicting non adherence in non-bipolar/non-SUD samples. More specifically, Genberg et al. [26] showed that HIV positive patients in earlier stages of change (contemplation, preparation) had significantly lower adherence to antiretroviral therapy compared to those in the later stages (action, maintenance). Further research is needed using readiness to change to predict adherence in BP-SUD. In addition, few studies have addressed the issue of behavioral non adherence in BP-SUD [14,27]; its causes can differ markedly from medication adherence. Behavioral forms of adherence (e.g., appointment attendance, lifestyle changes) are critical

in maintaining treatment gains, preventing relapse, and improving medication adherence in bipolar disorder and SUDs [28,29].

Conventional, therapist-delivered cognitive behavioral therapies (CBT) show promise for improving adherence in bipolar disorder [30-33], but they are typically time and resource intensive and their effects have been mixed [27,34]. Further, there is a paucity of research on behavioral interventions specifically designed to address SUD-BP [35-37], with minimal success improving adherence in this group to date. For example, a small pilot randomized controlled trial [38] in BP-SUD patients (n=46) indicated that medication adherence was only somewhat better in those receiving intensive CBT compared with those receiving low intensity medication monitoring alone for 12 weeks; although these differences were not statistically significant (50% vs 29%, respectively).

Clearly, adherence is influenced by a number of factors that relate to bipolar disorder and SUDs independently. Developing better adherence interventions hinges on an improved understanding of the environmental barriers operating in patients' daily lives. This can be achieved with real-time assessments using newer mobile technologies (e.g., smartphones) [39], which permit the study of changes in health behaviors within and between days. By better elucidating these changes, it will be possible to advance the field's understanding of the most impactful adherence mechanisms to target in future psychosocial interventions.

Mobile technology offers a unique tool to study substance use and non-adherence. The measurement of adherence barriers, including stressors, mood symptoms, substance use, and related factors like cravings, is best suited to an approach that is sensitive to dynamic changes in behaviors in context. This can be provided through real-time assessment using ecological momentary assessment (EMA) [39]. Mobile devices (e.g. smartphones, PDAs) have become the ideal platform for collecting *in vivo* data. EMA is emerging as a feasible strategy for assessing ecologically-valid predictors of drug and/or alcohol use in SUD populations [40-47]. For example, Epstein et al. [48] studied 114 cocaine/heroin-abusing outpatients and found that 12 triggers (e.g., mood, cravings, seeing the drug) assessed via EMA during the preceding 5 hours predicted later drug use. Additional studies have further demonstrated that EMA is acceptable and feasible in SUD populations and predictive of use [42-48]. Other researchers have begun

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to use data collected via EMA to inform and refine treatments [49,50]. For example, Obermayer et al. [51] used mobile devices to deliver an innovative intervention for smoking cessation informed by previously collected data regarding typical daily smoking times. By programming the device to intervene during a typical smoking time, patients received intervention when they were most at risk to smoke.

However, there are very few studies to date using EMA in bipolar samples in general, and none that we are aware of in those with SUD-BP specifically. A recent pilot study [52] (n = 14) examined the use of EMA in bipolar patients *without* SUDs. All patients found EMA feasible/acceptable and adherence to EMA prompts was 92% in the study. Other preliminary research supports the feasibility and acceptability of EMA in those with bipolar disorder using mobile devices [52-55]. EMA adherence rates in these studies frequently are comparable to those in nonclinical samples. EMA may be able to provide new insights into bipolar illness. For example, Depp et al. [55] reported greater variability in mood self-ratings in a sample with bipolar disorder (n = 40) assessed via EMA compared with traditional paper-and-pencil measures. Also, EMA ratings were significantly correlated with clinician-rated symptoms of depression and mania, whereas paper-and-pencil ratings were not.

Leveraging mobile technology to study the bidirectional relationship between substance use and non-adherence is a necessary next research step. After using EMA to identify the relative importance of substance use and other adherence predictors, as well as the degree to which these variables interact and change over time, brief interventions delivered via a smartphone can be matched to these predictors to improve clinical outcomes, including adherence. For instance, if substance use is particularly impactful on daily adherence, EMA can be used to probe for risk factors for subsequent substance use, and when they occur, the mobile device can automatically respond with a brief intervention to prompt appropriate coping strategies (e.g., cognitive, behavioral, motivational). Thus, EMA offers the hope for more personalized, ecologically-valid interventions for bipolar patients, with substance abuse as a key target.

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