Mobile Assessment and Intervention:

Applicability to the Research and Treatment of Mood Disorders

Alexander Belser, M.Phil.

Columbia University Teachers College

Abstract

Since Emil Kraepelin first classified "manic-depressive insanity" and proposed a spectrum of severity over a century ago, bipolar disorders have continued to pose a host of research, diagnostic, and clinical challenges.  Pharmacotherapeutic interventions for bipolar disorders have proven somewhat effective, but there is significant subsyndromal interepisode morbidity, relapse rates are high, and a "full" recovery is rare.  Further improvement in these areas requires more sophisticated assessment methodologies, improved differential diagnosis techniques, and clinical advances, such as earlier identification and intervention, and better medication adherence. Recent advances in mobile technology have reframed mobile assessment and experience sampling methodologies as viable tools to advance these goals. Digital device adjuncts provide novel means to track the degree and duration of mood lability and other symptoms over time. A rationale for the integration of mobile assessment into current practices is presented.  In the research domain, mobile assessment may help answer outstanding questions regarding the frequency distribution of cycling disorders.  In clinical practice, mobile adjuncts may be incorporated into existing psychosocial interventions to digitally monitor prodromal and subsyndromal symptoms, and to more closely relate these symptoms to proximal causes (e.g., mood triggers, social stressors, and sleep patterns).  Weaknesses of experience sampling methods (ESM) and mobile assessment are also addressed, including its use with elderly individuals, participant burden, sampling issues, reactivity, and privacy concerns.  Finally, future directions in research and clinical application are suggested.

Mobile Assessment:

Applicability to the Research and Treatment of Mood Disorders

In his seminal research in the late nineteenth century, Emil Kraepelin was the first to differentiate *dementia praecox* from what he termed "manic-depressive insanity" (Kraepelin, 1921).  He accomplished this through his devotion to a specific method: the recording of patient symptoms upon index cards (Noll, 2007).  Each index card acted as an independent data point upon which symptoms were recorded over the course of weeks and months.  Kraepelin was nearly obsessed with finding patterns over time, course and prognosis (Noll, 2007).  Writing in 1896, he states: "What convinced me of the superiority of the clinical method of diagnosis (followed here) over the traditional one, was the *certainty with which we could predict (in conjunction with our new concept of disease) the future course of events*" (italics in original) (Kraepelin, 1896, as quoted in Noll, 2007, p. 126).

Kraepelin's method, utilizing frequent data collection and pattern analysis, provided groundbreaking nosologic and diagnostic advantages over contemporary approaches, especially with bipolar disorders.  Also, Kraepelin's finding that close tracking of patient symptoms over time had predictive validity has implications even today for the clinical management of patients.  As Goodwin and Jamison have noted, clinicians today no longer have the time to devote close attention over many months to the diagnosis and observation of their bipolar patients, as Kraepelin once did (2007).  However, advances in mobile technologies may have far-ranging implications for research and clinical practices that echo the original spirit of Kraepelin's pattern seeking in a stack of index cards.

The prevalence of bipolar disorders is reviewed, and the ongoing challenge of differential diagnosis is addressed. A summary of pharmacotherapeutic and psychosocial interventions for

bipolar disorders is provided, with a focus on areas requiring improvement, such as early

identification and intervention, and medication adherence.  Given the recent proliferation of

mobile devices, I propose that mobile assessment and experience sampling methods can augment

existing approaches and will have significant research and clinical applications in the treatment

of bipolar disorders.  Specifically, mobile assessment methodologies may be particularly well

suited to investigate outstanding research questions in the field, such as whether bipolar disorders

occur as a categorical or along a spectrum (Goodwin & Jamison, 2007, p.  131).  Weaknesses of

experience sampling methods (ESM) and mobile assessment methods are summarized.  Finally,

directions for future research and clinical application are proposed.  The emergence of new

mobile assessment methods provides capabilities for more sophisticated research tools and

improved clinical management in the study and treatment of bipolar disorders.

**Bipolar Disorders: Overview, and Differential Diagnosis**

The Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (Text

Revision) (DSM-IV-TR) outlines a number of categorical mood disorders.  The cardinal

symptoms of bipolar disorders are periods of abnormal mood that define depressive, manic, or

hypomanic episodes.  Although the full diagnostic criteria are available elsewhere, these

disorders can be summarized as follows: bipolar I disorder (major depressive episode and a

manic/mixed episode), bipolar II disorder (major depressive episode with a hypomanic episode),

dysthymic disorder (chronic subsyndromal depression), cyclothymic disorder (chronic

fluctuations between subsyndromal depression and hypomania), as well as mixed episode

(criteria for both manic episode and major depressive episode are met) (American Psychiatric

Association, 2000).  Bipolar I or type II can additionally be diagnosed with a rapid-cycling

specifier (at least four episodes of a mood disturbance in the previous 12 months) (American

Psychiatric Association, 2000).  For convenience purposes, throughout the course of this article, the aforementioned DSM-IV-TR disorders will collectively be referred to as "bipolar disorders."

The National Institutes of Mental Health (NIMH) Epidemiologic Catchment Area study (ECA) found a prevalence of 1.2% for combined bipolar I and bipolar II variants (Weissman et al., 1998).  Using data from the National Comorbidity Survey Replication, Kessler and colleagues found that bipolar I and bipolar II disorders have a 3.9% lifetime prevalence rate and pose a projected lifetime risk of 5.1% (Kessler, Berglund, Demler, Jin, & Walters, 2005). Individuals with bipolar I and type II disorders exhibit high prevalence of very low work, marital, social, and recreational function (First & Tasman, 2004, p. 813).  After schizophrenia, bipolar disorder has the highest rate of hospitalization among the major mental disorders (Klerman et al., 1992).  Research demonstrates that rates of suicide attempts and the use of alcohol and substance abuse are dramatically higher amongst individuals with bipolar disorders than individuals with other Axis I disorders (Chen & Dilsaver, 1996).

Bipolar disorders are associated with extremely high rates of drug abuse and suicide attempts.  Using the NIMH ECA dataset, Chen and Dilsaver (1996) compared these phenomena across Axis I disorders.  The study included subjects with bipolar disorder (n = 168), subjects with unipolar disorder (n = 801), and those meeting the criteria for any Axis I disorder other than bipolar disorder or unipolar disorder (n = 5697).  Chen and Dilsaver found that individuals with bipolar disorder had rates of suicide attempts and drug and alcohol abuse that were approximately double that of unipolar depressed individuals and seven times higher than individuals with any other Axis I disorders.  The lifetime rate of suicide attempt was 29.2% for bipolar individuals, higher than that of subjects with any other Axis I disorder, regardless of sex, ethnicity, age, socioeconomic status, comorbidity for panic disorder, and marital status.  There

were also high rates of substance abuse comorbidity: 61% percent of the bipolar subjects in the ECA database have a history of abuse of or dependence on alcohol and drugs, compared to only 27% of subjects with unipolar depression (Chen & Dilsaver, 1996).

**Differential Diagnosis**

Differential diagnosis poses a major challenge in the evaluation of bipolar disorders.  The DSM-IV-TR presents a "rather complicated set of diagnostic rules" (Milkowitz, 2008b, 422).  Clinicians often struggle to distinguish between bipolar I and bipolar II, unipolar depression from bipolar depression, subsyndromal mood disorders from Axis II disorders such as borderline personality disorder (Akiskal, 2003), and rapid and ultra-rapid cycling from cyclothymia (Milkowitz, 2008b; Goldberg & Kocsis, 1999).  Patients may experience subsyndromal or subaffective symptoms, or may not reliably report their history in a clinical setting.  It is particularly difficult to distinguish between cyclothymic disorder and bipolar II.  Patients with cyclothymic disorder experience brief periods of depression that do not meet criteria for a major depressive episode, then alternate to periods of hypomania.  If the cyclothymic patient has a manic or depressive episode, the diagnosis of bipolar I or II is substituted (Milkowitz, 2008b).

The distinction between these DSM-IV diagnoses concerns "the degree and duration of symptoms," which requires a close clinical attention to mood lability over time (Milkowitz, 2008b). There are important distinctions between a diagnosis of cyclothymic disorder and bipolar II disorder, with serious clinical implications.  As differential diagnosis in this context primarily concerns the degree and duration of symptoms over time, and as a patient's historical reporting is subject to bias and recall issues, the current standard diagnostic approach seems insufficiently sensitive to the time-sensitive nature of these disorders.  As Milkowitz remarks:

"Sometimes it is better to observe the mood lability of patient over tim*e* than to attempt to distinguish cyclothymic disorder and bipolar disorder cross-sectionally" (2008b, p. 424) Future study using mobile assessment of mood lability and the degree and duration of symptoms, when shared with clinicians, may improve differential diagnosis in this domain.

**Pharmacotherapies and Psychosocial Interventions**

Although standard pharmacotherapy for bipolar disorders poses significant undesirable side effects, it has been shown to be effective in bipolar I and bipolar II patients (Goldberg, 2004). However, rapid-cycling patients do not respond well "to any medication," including lithium or anti-convulsants (Goodwin & Jamison, 2007, p. 132). With pharmacotherapies, three outstanding areas of concern remain: (1) there is significant subsyndromal interepisode morbidity, (2) relapse rates are high, and (3) a "full" recovery is rare. First, in a longitudinal study of 37 patients with major affective disorders and on a course of continuous lithium treatment, Nilsson and Axelsson (1989) found that despite the continuous administration of lithium, substantive interepisode morbidity was still present. There has only been one longitudinal study of the weekly symptomatic status of individuals with bipolar I. In this study, Judd and colleagues (2002) found that over a mean 12 years of follow-up, patients were symptomatically ill 47% of weeks. They conclude: "the longitudinal weekly symptomatic course of BP-I is chronic" (Judd et al., 2002, p. 530). This research suggests that even with pharmacotherapeutic management, bipolar patients experience chronic subsyndromal effects.

Secondly, relapse is an ongoing concern. Survival analysis is a useful statistical method in the study of relapse; it concerns the time to occurrence of an event, instead of simply analyzing frequency of event occurrences. The survival rate (i.e. the proportion of patients not relapsing) with pharmacotherapies is low, with only a quarter of patients not experiencing a

recurrent episode after five years (Milkowitz, 2008; Gitlin, Swendsen, Heller, & Hammen, 1995). Survival analysis is hampered in bipolar studies because dropout rates often exceed the 20% level needed for statistical confidence (Goodwin & Jamison, 2007, pp. 711-712). Third and finally, even in treated patients who no longer meet the DSM-IV-TR criteria for a bipolar disorder, the degree of recovery is quite low, with lingering symptoms and low levels of functional recovery (Keck et al., 1998).

In the STEP-BD study of bipolar patients (N = 293), Milkowitz and colleagues found that "identifying and intervening early with prodromal symptoms, [and] enhancing patient's compliance with medications" contributed to more rapid recoveries and had stronger effects on mania (2008b, pp. 431; Milkowitz, 2008a). Key factors in the successful treatment of bipolar disorders include (1) early identification, (2) appropriate levels of intervention, and (3) medication adherence (Milkowitz, 2008a). There is room for improvement upon current practices. Each of these three factors may be enhanced with a mobile adjunct for bipolar patients, which could (1) assist the patient in active self-monitoring of prodromal symptoms, (2) dynamically suggest graded interventions hours or days before the patient meets with a clinician, and (3) improve daily medication-taking either through active recording or through the use of digitally instrumented pill bottles (Byerly et al. 2005). Used as a complement to treatment as usual, mobile self-monitoring may improve upon current identification, intervention, and medication adherence strategies. Further research regarding the feasibility, acceptability, and effectiveness of these adjuvant tactics is required.

A variety of psychosocial interventions have been used to treat bipolar disorders, with mixed success. As somatotherapy for bipolar disorder has produced only "modest improvements" in clinical outcomes, psychosocial interventions are often used as adjuvant

therapies (Bauer, 2001, p. 109). Reviews of randomized controlled trials (RCTs) demonstrate that a broad field of psychotherapeutic interventions may be effective in the treatment of bipolar disorders, including couples/partners, cognitive-behavioral therapy (CBT), group interpersonal psychotherapy, family therapies, Interpersonal and Social Rhythm Therapy (IPSRT), and psychoeducational interventions (Bauer, 2001; First & Tasman, 2004, pp. 832-834; Frank et al., 2005). In a more recent meta-analysis of randomized or quasi-randomized controlled trials, Beynon and colleagues found that CBT, group psychoeducation and possibly family therapy may be beneficial as adjuncts to pharmacological maintenance treatments (Beynon, Soares-Weiser, Woolacott, Duffy, & Geddes, 2008). Many of the aforementioned therapies have common elements, such as psychoeducational components and mood monitoring. Mobile devices may strengthen these components. For example, mobile adjuncts may be incorporated into existing mood monitoring strategies already used in psychotherapies such as CBT. Also, mobile applications could buttress primary psychoeducation with daily tips and hints regarding the self-management of bipolar illness.

**Mobile Assessment Methodologies**

Mobile assessment methodologies, including the use of audio, visual, and screen-based interactive methods, are enabled by the continuous technological development and proliferation of mobile devices (Kjeldskov & Stage, 2004). The integration of these technologies into psychological methodologies promises a variety of novel research and clinical applications. Technological advances in mobile applications and distributed networks provide new research capabilities that will change the traditional modes of self-report data collection, field research, and study design. How can researchers take advantage of these innovative methods, and what is to be gained as the site of application migrates from the laboratory to our pockets?

Since Wilhelm Wundt first established a laboratory in Leipzig in 1879, research in psychology has been driven by large, centralized and well-financed university laboratories. This mode of research has vastly added to our knowledge of mental processes and human behaviors, but it has also been critiqued for a number of theoretical concerns. In summary: (1) the laboratory setting is an artificial environment to study human behavior and is susceptible to demand characteristics and experimenter expectancy effects; (2) the time periods of such research irregularly punctuate human behavioral continuums; and (3) the results of such research may have low ecological validity.

Proliferating mobile platforms (e.g., Palm Pilots, PDAs and smartphones) can be put to use in novel ways. Already, patient populations have adopted mobile psychological instruments. For instance, the MoodTracker application for the iPhone is a one dollar application that has been downloaded by thousands of users; it provides day-by-day mood tracking and data export capabilities. This sort of application may provide a feasible digital self-monitoring adjunct for bipolar individuals. Other telehealth applications now enable participants to transmit data such as sleep logs, depression and anxiety self-report measures and clinician-administered diagnostic tests. Also, the National Institutes of Health has provided a grant to Kaiser Permanente to develop mobile data collection devices as part of their initiative into electronic medical records and biobank data (Bernay, 2009). The emergence of mobile assessment and remote monitoring tools is facilitating new approaches to clinical research. Studies using Palm Pilots are currently underway at the psychology departments at Berkeley, Stanford, Yale and the University of Pennsylvania (S. Johnson, personal communication November 11, 2009; I. H. Gotlib personal communication, November 12, 2009; J. Gruber, personal communication, November 11, 2009; A. M. Ruscio, personal communication, November 12, 2009).

These technological advances have major implications for the future of clinical study and treatment. Mobile assessment methods provide novel ways to investigate dynamic transformations and to experimentally evaluate therapeutic interventions over time. Data can be collected at multiple assessment points (even intra-day) *in situ*. Potential application areas include emotion regulation, anxiety monitoring, mood disorders, substance-related disorders, eating disorders, pain management, sexual dysfunction, circadian processes, sleep disorders and developmental disorders. Here we will focus on the use of mobile devices for mood monitoring and in the research, diagnosis, and treatment of mood disorders.

As a complement to traditional laboratory research modalities, mobile assessment methods provide certain capabilities: (1) they can be used by subjects in the field instead of the laboratory; (2) they are temporally flexible, in that the devices can be used multiple times per day over long stretches of time; (3) they are relatively inexpensive when compared to staffed laboratory visits and the expense of data transcription; (4) they allow for rapid scalability to a large sampling population; and (5) they provide researchers with a means to design a highly interactive subject-instrument interface beyond the capabilities of paper-and-pencil instruments. While mobile assessment provides many advantages, it also involves significant challenges to its adoption, such as its use amongst elderly populations, participant burden, sampling issues, reactivity, and privacy concerns, discussed in greater detail below.

As costs come down, mobile assessment technologies will be commonly incorporated into the design of randomized controlled trials and will augment our methodological toolkit (Kjeldskov & Stage, 2004). They may also be combined with other assessment and methodological approaches, such as interpersonal interaction diaries (Reis & Wheeler 1991), ambulatory physiological monitoring (Kop et al. 2001), and collection of medication compliance

data by instrumented pill bottles (Byerly et al. 2005).  Mobile assessment projects pose significant methodological, theoretical and clinical challenges.  These developments require prudent guidance for the implementation of distributed methods in research studies, in therapeutic evaluations and in the development of innovative self-monitoring practices by patient populations.

**Experience Sampling Method**

ESM was developed by Mihalyi Csikszentmihalyi and Reed Larson at the University of Chicago in the 1970s to study the subjective experiences of individuals in their natural environments (Csikszentmihalyi, M.  & Larson, R., 1987).  Dissatisfied with the inaccuracies of retrospective self-report data, Csikszentmihalyi and Larson drew upon antecedent methods, such as time budgets and psychological studies of everyday experience to design an ecologically-valid sampling method (Hektner, J.  M., Schmidt, J.  A., & Csikszentmihalyi, M., 2007).  In ESM, study participants frequently record their subjective experiences in standard journals (or later, using digital devices) over the course of the day, often for many days or weeks.  Data collection times may be pre-determined or randomized through the use of beepers.  Various self-report psychometric data can be collected.  Participants report their findings in their own natural environments, "in the moment," thereby approximating "real life" conditions for the report of subjective data with high internal validity (Cherubini, M.  & Oliver, N., 2009).  ESM minimizes many of the experimental biases stemming from the presence of the experimenter (e.g., observer-expectancy effect) found in laboratory studies.

Experience sampling has been employed in the study of a wide range of psychopathologies and across domains.  In addition to studies of happiness (e.g., Csikszentmihalyi, M.  & Hunter, J., 2003), ESM has been used in trials investigating eating

disorders, anxiety disorders, mood disorders (Myin-Germeys, et al., 2003), sexual dysfunction, ADHD (Schiffman, Stone, & Hufford, 2008), schizophrenia (Kimhy, D. et al., 2006); contingency management for substance abuse treatment (Husky, M., Mazure, C., Carroll, K., Barry, D., & Petry, N., 2008); chronic aphasia (Fitzgerald-DeJean, D., Rubin, S., Carson, R., & Fisher, J., 2008); and exhaustion and clinical burnout (Sonnenschein, M., et al., 2007). Researchers have also utilized ESM to examine issues that require a close fidelity to the participant's inner experiences, as in studies of risk perception (Hogarth, R. M., Portell, M. & Cuxart, A., 2007) and idiographic phenomenology (Hurlburt, R. T. & Akhter, S. A., 2006).

Bipolar disorders have not been studied extensively using ESM approaches. One exception is a study of emotional reactivity to small disturbances in daily life, in which Myin-Germeys and colleagues (2003) utilized a combination of booklets and wristwatch beepers to investigate bipolar disorder and major depressive disorder. However, the study duration was only 6 consecutive days, and a small number of bipolar subjects were included(n=38).

In addition to the broad spectrum of clinical applications mentioned above, ESM may have implications for the traditional researcher-participant power dynamic. Koro-Ljungberg and colleagues (2008) found that study participants who are provided with a mobile device reported greater levels of agency. They argue that the participant's control over the device shifts the balance from the authority of the experimenter toward participant empowerment (Koro-Ljungberg, M., Bussing, R., Williamson, P. & M'Cormack-Hale, F., 2008).

Over the past few decades, advances in technology have been followed swiftly by advances in methodology. This parallel development track is substantiated by the various technological adaptations of ESM. Consider the advent of the telephone, beeper, home internet access, cell phone, PDAs (e.g., Palm Pilots), text messaging (SMS) and mobile devices (e.g.,

iPhone and Android "smartphones").  Each of these technological advances was followed by a parallel advance in method-driven research.  For example, ESM was originally conducted on paper-and-pencil booklets (paper-based ESM; ESMp), and then via telephone (ESMt), beeper-based ESM, digital wristwatch-based ESM, PDA-based ESM, text messaging ESM, and now iPhone-based ESM.

As advances in camera design from daguerreotypes to ten megapixel digital cameras have brought greater clarity and imagery resolution, advances in ESM provide greater clarity and temporal precision in self-report data.  For example, in a comparative study, Kimhy and colleagues (2006) evaluated paper-based ESM with PDA-based ESM as an adjunct to treatment in schizophrenic participants.  They found that schizophrenic subjects reported significantly higher ratings of schizophrenic symptoms (auditory and visual hallucinations, suspiciousness, sense of unreality, lack of thought control, fear of losing control, difficulty expressing thoughts) in the PDA-based group than in the traditional paper-based ESM.  These finding suggest that in addition to the greater frequency of data collection, digital devices may affect levels of self-reporting of socially undesirable behaviors.  The computerized ESM may also affect self-report rates for mood monitoring.  Subjects in the PDA-based group reported significantly higher rates of depression/sadness, loneliness, and less cheerfulness than their paper-and-pencil counterparts (Kimhy et al., 2006).

Further comparative study is required to specify the causes of these reporting disparities between paper-and-pencil assessment and mobile assessment.  There have been some fledgling efforts in this regard.  For example, the National Sciences Foundation has funded a methodological comparison of a survey method, a laboratory method, and a hybrid Palm-pilot/paper-and-pencil based ESM to investigate moral identity, behavior and emotions (Osborn,

S. N., and Stets J. E., 2007). Study participants preferred to use the palm pilot to enter data to the use of paper-and-pencil recordings, although a larger sample will be required to make significant differentiations.

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**Cycling Lengths Between Mood Episodes:**

**Assessing the "Beat Phenomenon"**

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**Circadian Rhythms**

Mood disorders are primary candidates for mobile assessment as they are complexly intertwined with the temporally sensitive phenomena of circadian rhythms and sleep cycles. Circadian rhythms are synchronized with endogenous (internal) and exogenous (external) rhythms. The relationship between exogenous zeitgebers ("time-givers") and mood is well established, as seen in studies of jet lag, sleep wake cycles, sleep deprivation, and light exposure (Wehr et al., 1993; Wehr, 1996; Goodwin & Jamison, 2007). However, the relationships between internal components of the circadian processes are not as well understood and have proven difficult to study.

As far back as 1947, Georgi proposed that patients with mood disorders may experience desynchronized circadian phases, sometimes referred to as "internal phase disorder." This was a critical step in understanding the how severe mood disorders arise in bipolar patients. In internal phase disorder, components of endogenous circadian rhythms may not synchronize to the sleep-wake cycle. This may cause a "beat phenomenon" of multi-week cycles (Wehr et al., 1998; Halberg, 1968). For example, Seasonal Affective Disorder (SAD) may be explained by phase delays or phase advances in melatonin onset, a process driven by exposure to sunlight (Goodwin & Jamison, 2007). Lewy and Sack (1987) have suggested that patients with winter depression

experience a phase delay in dim-light melatonin onset (DLMO) (Shafii, 1992, p. 95; Lewy et al., 1990). This phase-shift hypothesis is the leading explanation for SAD (Lewy et al., 2006).

**Phase Cycling**

This "beat phenomenon" may explain the cycling nature of bipolar disorders. If circadian rhythms comprise multiple components, and if one of these free-running components of the circadian rhythm is longer or shorter than 24 hours, the component will progressively cycle out of phase with the dominant day-night cycle. For example, if a component of a circadian rhythm completes a complete daily cycle in 26 hours, and the day-night cycle is 24 hours, one phase will gain two hours every day. The resultant pattern of desynchrony will recur as the desynchronous component comes in and out of phase with the dominant day-night cycle (Goodwin & Jamison, 2007, pp. 667-669). Therefore, the component phase is aligned with the dominant phase at time $T_1$; it will be two hours ahead on day $T_2$; four hours ahead on day $T_3$, and will come full circle at time $T_{12}$, converging with the dominant phase every twelve days. In this example, the patient may experience a hypomanic episode every twelve days as one component of the circadian rhythms cycles out of phase with the dominant cycle. This sort of phase shift cycling may explain aspects of many mood cycling disorders, such as diurnal variation (e.g., a gradual improvement in the patient's depressed mood as the day wears on), and may prove to be a useful model to investigate shorter duration disorders, such as cyclothymia and rapid cycling and ultra-rapid cycling disorders (Leibenluft, 1996).

**Investigating the Beat Phenomenon**

Conventional means of investigating the beat phenomenon have not yet yielded a breakthrough treatment for cycling mood disorders. Studies using constant routine and forced synchrony procedures are laborious and onerous to conduct. They are "precluded by ongoing

obstacles, including the inherent difficulties and risks of these procedures, ethical considerations, and costs and funding priorities" (Goodwin & Jamison, 2007, p. 669). Additionally, the expense and difficulty of tracking neurotransmitter dysregulation, such as that of serotonin, dopamine, norepinephrine, and hormone levels, such as that of melatonin, can be prohibitive. Given these ethical and cost-considerations, study methods using mobile assessment measures may provide an alternative means of investigating internal phase disorder phenomena generated in cyclothymia and other mood conditions in a large community sample (Shin, Schaffer, Levitt & Boyle, 2005).

In addition to ethical and cost considerations, cycling epiphenomena assessed via standard methods (e.g. at the same time each day) may be susceptible to misinterpretation (Goodwin & Jamison, 2007, p. 669). For example, if a biological variable is sampled at a fixed time of the day (as with many mood studies), its level appears to change day-to-day as it passes in then out of phase with the sampling time. Nevertheless, the cycle's course may be regular over a 25-hour period. While there are strengths to regular, fixed-time assessment, the flexibility afforded by randomized time assessment may provide critical insight in these temporally sensitive phase-shifting cycling patterns.

**The Distribution of Cycle Durations**

The DSM-IV-TR delineates rapid cycling as four or more episodes in a twelve-month period, although recent research suggests there is no firm basis for this "magic line" of four episodes (Grunze & Walden, 2005). Many authors have suggested that the number of annual episodes should be modeled upon a spectrum rather than in distinct categories (Phelps, 2010; Goodwin & Jamison, 2007, p. 131). Further research may reveal the distribution of cycle length along a theoretical rapid cycling spectrum and a cyclothymic spectrum. As Goodwin & Jamison

(2007) note, "Data are insufficient to determine whether cycle length is distributed normally" (p. 131).

A regular frequency distribution has already been demonstrated in bipolar patients with biannual peaks in the spring and early fall (Zis & Goodwin, 1979; Goodwin & Jamison, 2007, p. 681). See, for example, the clear peaks and troughs in Figure 1 below. Along this spectrum, it is possible that the mean length between cycling episodes may coalesce around known durations, such as the seasonal duration and the monthly hormonal cycle. Researchers may begin by asking if rapid cycling and cyclothymia are associated with common cycle lengths. That is, do duration periods coalesce at certain common cycling durations?

In their excellent and comprehensive review of bipolar disorders, Goodwin & Jamison address this question. They assert that "[a] study of the frequency distribution of cycle lengths could answer the question of whether rapid cycling represents a distinct subgroup or is simply one end of a continuum" (2007, p. 131). Research questions include: do the rapid cycling and cyclothymic disorders also coalesce around a repeating time pattern? That is, if cycling disorders are multi-phasal, perhaps they are also multimodal. What are the mean frequency distributions of peaks and troughs of mood for rapid-cycling individuals? Are there regularly coalescing patterns at one month, in conjunction with hormonal cycles, or at some time interval shorter than a month, perhaps even intra-day?

**Figure 16–8.** Frequency distribution of cycle lengths among bipolar patients, showing 12-month peaks. BP-I = bipolar-I; BP-II = bipolar-II. (*Source:* Zis and Goodwin, 1979.)
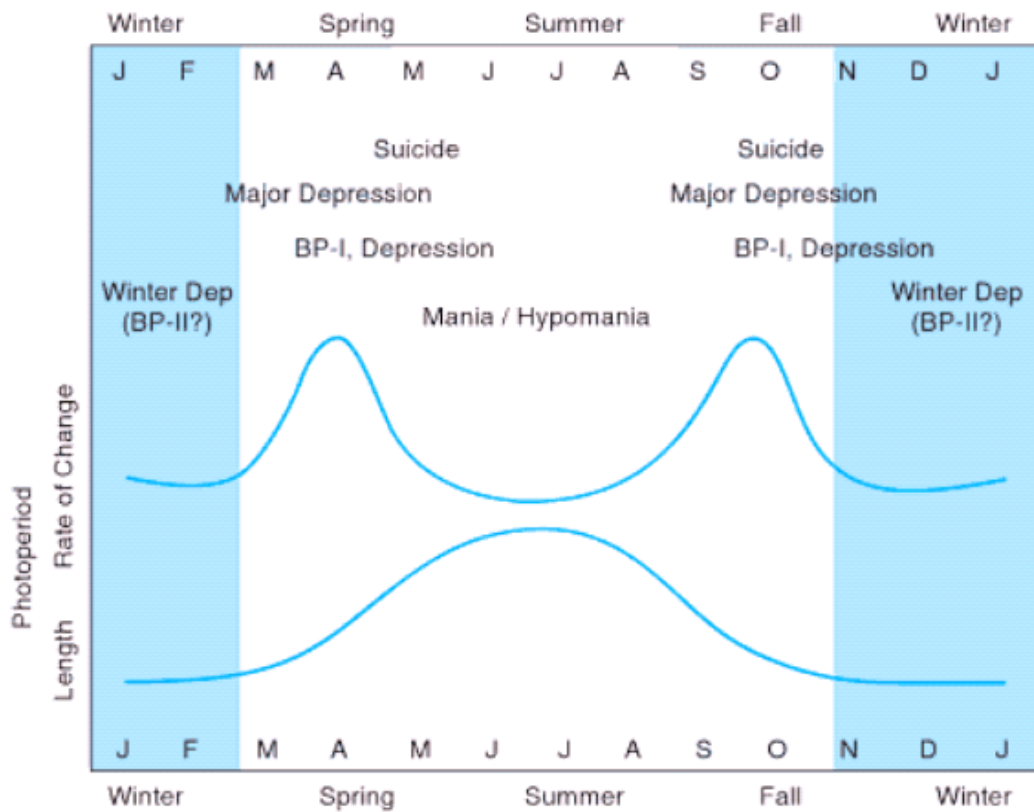


Figure 1.  Frequency distribution of cycle lengths among bipolar patients, showing 12-month peaks (Goodwin & Jamison, p.  681, 2007).

To investigate these questions, frequent and irregularly timed assessments will be required in a large community sample of many thousands of participants.  Actigraphs, instruments that measure body movement, are conventionally used to record sleep times in circadian studies of this nature (Lewy et al., 2006).  However, future studies should combine sleep/wake time recording with comprehensive mood recording over the course of weeks and months.  Large sample sizes are achievable through the distribution of scalable mobile

applications, such as the existent Mood Tracker application for the iPhone and HealthCentral's

Mood 24/7 Project (www.mood247.com).  Additionally, in regards to the prevalence of

cyclothymia, a study of this nature that tracks daily fluctuations in mood may also shed light on

this neglected area of research, as "little is known regarding the prevalence of cyclothymic

disorder" (First & Tasman, 2004).

There are important clinical consequences to unidentified subsyndromal cycling and

unpredictable cycling (Goodwin & Jamison, 2007). In a large epidemiological study of mood

cycling, a series of complex analyses (e.g. curvilinear best fit models and moving average

analysis) could be conducted to determine the mean cycle duration and amplitude within each

individual participant.  In a study with a sufficient sample size, when these data are aggregated,

these cycle lengths might demonstrate a multimodal frequency distribution, with biannual,

monthly, biweekly, daily, and possibly shorter cycle lengths (e.g., Egloff et al., 1995; Larsen and

Kasimatis, 1990; Lucas, 2000).  Conversely, it may be found that beneath the biannual peak

pattern found in bipolar patients due to seasonal light changes, there is simply a diffuse field of

average cycle lengths, with no frequency concentrations.

To this author's knowledge, no analysis of this type has yet been conducted.  Considering

the barriers to conducting appropriate neurotransmitter studies and forced synchrony studies,

mobile assessment may prove to be a feasible alternative.   As mobile assessment is easily

scalable, it may more readily scale to a large sample necessary to examine cycle lengths,

frequencies, and distribution patterns (Scollon, Kim-Prieto, & Diener, 2003).

**Idiographic Data Analysis and Aggregation**

Following data collection, the researcher is often confronted with troves of ecological

data points.  Proper data analysis requires combinations of idiographic analysis with multiple

levels of aggregation. As Larson and Delespaul (1992) note, "ESM data have a complexity which defies textbook analysis" (p. 58). For example, Larsen and Kasimatis (1990) have found that mood variations repeat during the course of the week, with a 7-day cycle sine curve. The highest level of affect occurs during the weekend on Saturday, and the low point occurs on Monday. In a large data sample, an analysis of a weekly sine curve hypothesis would require best fit data modeling on an idiographic level followed by subsequent aggregation across participants. One could begin with the entire data set and determine mean mood levels on each day of the week and compare these in aggregate, this sort of premature aggregation would overlook cycling variabilities that could be discovered through a within-individual analysis.

At the idiographic level of analysis, straight line and curvilinear best-fit models would have to be applied over the course of multiple hypothetical time scales (e.g., daily, weekly, monthly, seasonally, annually, etc.). However, instead of imposing a set timeframe upon the data, in a rapid cycling population, a more sophisticated data analysis is required. For example, curvilinear (sine) variations for each individual case could be determined through a moving average graph of daily average mood level. See Figure 2 for an example of a rapid-cycling patient's mood cycle. The patient used an iPhone application called MoodTracker to record his daily mood over the course of many months. The data, once exported for analysis, did not reveal a recurring pattern using spectral analysis. When a five day moving average was applied over the data though, a clear biweekly cycling pattern was indicated, with peaks every two weeks. More sophisticated spectral analysis of the time data may reveal a best fit model for this individual's recurring mood cycle (Scollon, Kim-Prieto, & Diener, 2003).

Unanswered questions regarding the frequency and severity of episodes remain. In a large population of individuals with mood disorders, multiple subsets of ideographic analysis,

classed according to average days between episodes, may reveal common durations (e.g.,

biweekly, as with the patient in Figure 2).  As with this data collection methodology, there are so

many data it is often difficult to tell the forest from the trees.  In their comprehensive review and

critique of ESM, Scollon, Kim-Prieto, and Diener (2003) summarize the data analysis issues

inherent to studies utilizing ESM.  They may involve aggregation issues, frequency counts, time

dependencies within data (e.g., to account for diurnal variation) challenges in analyzing data,

spectral analysis instead of within-person standard deviations, and best fit for curvilinear (sine

wave) data patterns (Scollon, Kim-Prieto, and Diener, 2003).
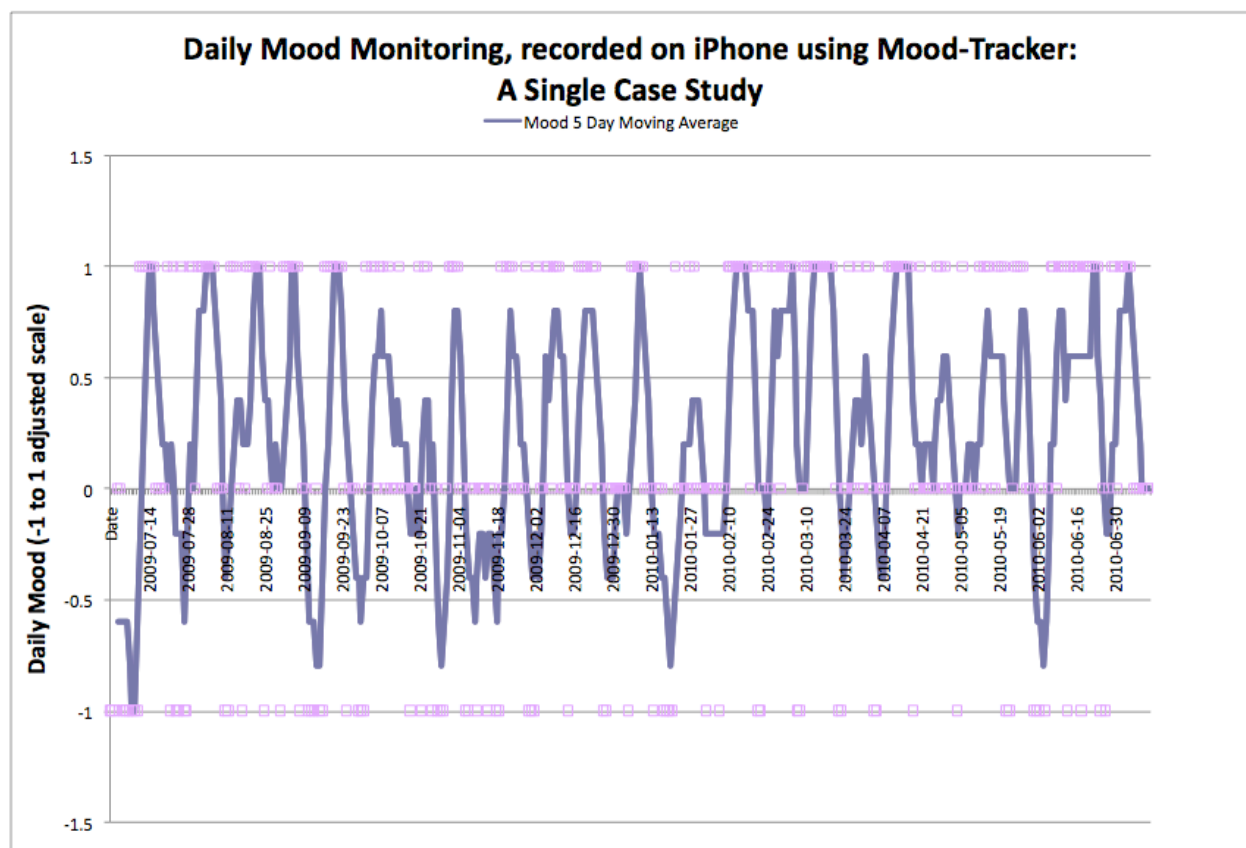


Figure 2.  Daily Mood Monitoring, recorded on iPhone using the Mood-Tracker Application: A

single case study.  Source: David Brody, MD, with authorized permission of patient.

**Weaknesses of Experience Sampling and Mobile Assessment Methodologies**

ESM poses a number of specific drawbacks.  These include the onerous nature of participation in ESM studies, sampling issues, and subsequent over- and underrepresentation issues, especially amongst older individuals or the chronically ill.  Additionally there are issues of participant drop-out, reactivity, differential disclosure of sensitive or socially undesirable behaviors, and privacy concerns.

Participation in an ESM study with a mobile device places a variety of burdens upon the study participant.  The participant must constantly carry an electronic device, must be willing to be interrupted from social or work obligations, and must make a considerable commitment of time to respond to multiple, perhaps hundreds or thousands of assessments over the course of the study.  Many ESM studies are designed with relatively short durations, such as a week, as a means of ameliorating the cumulative investment required from the participant.  However, to properly study mood disorders, study designs would last months or even years.  If there are benefits to the participating individual (e.g., patient data could be made available to patients and their clinicians to enhance self-monitoring; HealthCentral's Mood 24/7 Project provides the participant with a graph of his or her mood as a benefit of study participation), these benefits may ameliorate the burden of study participation.

Nevertheless, ESM poses a variety of sampling and representational issues.  Less strongly motivated individuals would be prone to drop-out of the study or would respond to prompted assessment points at insufficient rates to be included in the final sample.  On this point, Scollon, Kim-Prieto, and Diener (2003) observe that the remaining participants are non-representational-- they may demonstrate greater motivation or conscientiousness, for example.  The authors remark: "After all, participants who forget the palmtop at home half of the time are likely to

differ from participants who remember to take the palmtop with them everywhere and everyday; unfortunately, there will be a preponderance of data on the latter" (2003, p. 14).

While well designed and funded ESM studies issue mobile devices to study participants, studies may also sample from the general population with existing mobile device users. As with online surveys, which require study participants to own a home pc and an Internet service provider, the sampling issue is compounded when study participants are required to own an iPhone or Android device with a mobile carrier contract. The advantage of this approach is that it is significantly cheaper, as mobile devices do not have to be purchased, study participants tend to be highly motivated, and a large sample size can be quickly achieved. However, these issues may skew the composition of the sample, undermining generalizability of clinical recommendations.

The use of ESM and mobile assessment may not be feasible or ecologically acceptable with elderly participants. In a study using ESM to evaluate mood in a depressed sample of elderly individuals, Wilson and colleagues (1992) found that difficulties with concentration and poor volition reduced the level of completion of ESM assessments. Chronic illness and the small size of display screen fonts also disaffected the level of compliance. If the sample is limited to young and middle-aged individuals, findings will not be generalizable to mood disorders in the elderly. Future ESM work should evaluate the acceptability and feasibility of ESM in specific patient populations, and explore alternative methods of data acquisition if ESM if found to be an inappropriate method.

Reactivity in ESM studies of mood disorders poses both methodological and ethical concerns. The timeframe of assessment may influence the participant's own concept of his or her mood cycle phase. If participants are expecting a depressive or hypomanic episode, that may

affect self-reporting (e.g., "I should be having nearing the peak of my cycle, so today's negative affect must be a fluke").  For example, in a study of premenstrual symptoms, women who were led to believe they were premenstrual reported greater pain, water retention, change in eating habits, and sexual arousal than women who were led to believe they were midcycle (Ruble, 1977).  Belief about cycling status may affect self-reporting of mood levels.  Repeated assessments may also prime participants to pay attention to certain affective states.  Thus far, data on this topic is scant; further research on reactivity in ESM studies may illuminate these methodological and ethical issues.

<div align="center">**Future Directions in Research and Clinical Application**</div>

**Mobile Audio Computer-Assisted Self Interviewing (MA-CASI)**

The audio capabilities of mobile devices enable the use of complementary data assessment methods, such as Audio Computer-Assisted Self Interviewing (A-CASI). The A-CASI technique is one of the most promising advances in self-reporting methodologies (van Griensven, 2006).  In this approach, the participant listens to pre-recorded questions through earphones, and responds to questions on a computer screen, or in the case of mobile assessment, on the device screen.  In this way, the responses are not colored by the intonations and inflections of the interviewer (Perlis et al.  2003: 895).  This technique has been shown to be especially adept at broaching sensitive or threatening topics.  Considering the issues of hypersexuality (Goodwin & Jamison, 2007, pp.  191) and comorbid substance use (Chen & Dilsaver, 1996) with bipolar disorders, a methodology that facilitates a more accurate self-report rate of these stigmatized behaviors would be quite valuable.

In an assessment of A-CASI and face-to-face interviews at drug treatment programs, researchers found that "A-CASI was associated with greater reporting of potentially stigmatized

drug, sex and HIV risk behavior," and that a majority of participants preferred answering

sensitive questions on the computer than in person (Perlis et al.  2003: 885).  In a related study,

researchers interviewed injecting drug users at syringe exchange programs in the United States.

The participants were interviewed on a weekly basis, alternating between A-CASI and face-to-

face methods.  The study found that respondents under-reported HIV risk behaviors such as

needle sharing in the face-to-face structured interviews (Des Jarlais 1999: 1657).  The

combination of computer and pre-recorded audio questions creates a safe, anonymized interface

which seems to encourage higher self-reporting of stigmatized behaviors.

When A-CASI is conducted on a mobile device, it will be referred to as Mobile Audio

Computer-Assisted Self Interviewing (MA-CASI).  MA-CASI may prove to be more efficacious

than standard on-screen assessment for socially undesirable behaviors of concern in a mood

study, such as medication non-adherence, behavioral activation non-compliance, sexually risky

behaviors, and the use of alcohol and substances.  However, Newman and colleagues have found

that in certain categories (e.g.,  psychological distress), interviewees were more likely to report

sensitive data to a human than to a machine (Newman, Jarlais & Turner et al., 2002).  Factors

such as "maintaining social respect, obtaining social support, and altruism" may explain this

exception to the general superiority of A-CASI interviews in regards to sensitive data (Newman,

Jarlais & Turner et al., 2002).

**Cycle-Responsive Interventions**

There is evidence that episode frequency is a familial trait.  Fisfalen and colleagues

(2005), conducted a study of families in which at least three members had a major affective

disorder.  They found that episode frequency was correlated among relatives ($r = 0.56$, $p < 0.004$).

Also, when comparing the highest quartile of episode frequency to the lowest quartile, Fisfalen

and colleagues found that the highest quartile had higher prevalence rates of bipolar II disorder, hallucinations or delusions, alcoholism, earlier age at onset, and suicidal behavior (2005). This suggests that the frequency of episodes is central to a proper understanding of bipolar disorders, and that a more sophisticated differential diagnosis system may be necessary to specify treatment interventions that are appropriately scaled and timed.

Research suggests that circadian rhythms can be actively influenced; for example, behavioral arousal may influence circadian onsets (Mrovksy, 1988). The clinical implication is that a cycle-dependent behavioral intervention may be appropriate. We will term these hypothetical forms of intervention "cycle-responsive therapies." The defining characteristic of cycle-responsive therapies is that they assess the patient's position along an oscillating affect cycle and vary treatment accordingly to prevent depressive, hypomanic or manic episodes.

A cycle-responsive therapeutic intervention might actively detect prodromal symptoms (of depression or hypomania/mania) and then prescribe appropriate up-regulating or down-regulating interventions to counter the prodromal trend. For example, during the prodromal phase of depressive episode, a cycle-responsive therapy might call for behavioral activation and morning light therapy (Benedetti, Colombo, Barbini, Campori, & Smeraldi, 2001) as prophylactic measures. Alternatively, during a period of prodromal hypomania, a cycle-responsive therapy may call for extended rest, darkness therapy (Wehr et al., 1998), and limited exposure to stressful situations. In short, to the extent that labile affect can be monitored and predicted, psychosocial interventions might be designed to counteract the onset of severe episodes of mania, hypomania and depression. Close monitoring and individual trend patterning through mobile devices in future research may help identify these windows of opportunity, before prodromal symptoms become fully manifest.

Current psychosocial interventions such as interpersonal and social rhythm therapy (Frank et al., 2005) attempt to regulate cycles by structuring and routinizing sleep/wake cycles, light exposure, and other controllable behavioral and social activities . However, with cyclothymic and rapid cycling patients, a cycle-responsive approach may prove more effective. To accurately gauge prodromal symptoms requires more accurate assessment than the current life events assessments generally employed in memory recall studies of bipolar disorders. Mobile assessment devices, when used by the patient as a treatment adjunct in conjunction with his or her clinician, may provide sufficient assessment accuracy and predictive validity. In future clinical research cycle-responsive interventions may serve as adjuvant therapies to standard pharmacological and psychotherapeutic interventions.

**Conclusion**

Since Kraepelin's time, there has been mixed progress in the research and treatment of bipolar disorders. However, the arrival of mobile adjuncts and the development of more sophisticated assessment methodologies may provide new research capabilities and treatment approaches. Unlike the vagaries of retrospective self-report, immediate ecological assessment is better suited to link mood episodes to their proximal causes. There are promising clinical applications to this form of close monitoring, such as earlier identification and intervention of prodromal symptoms during signs of an impending manic or depressive episode. Mobile device adjuncts enable close attention to individual cycle length and syndromal patterns, which may help a patient to manage his or her own mood in a proactive manner.

Further research of the "beat phenomenon" of circadian processes and the distribution of cycle lengths in an epidemiological sample are warranted. The integration of mobile assessment and ESM approaches into mood disorder research may also have implications for the current

categorical demarcation of rapid cycling disorder at four episodes per year.  Finally, there are

promising future applications, such as the use of mobile audio assessment through MA-CASI

and the development of cycle-responsive interventions to treat cycling mood states.  Recent

advances in mobile technology have reframed mobile assessment and ESM as viable tools to

advance both research methodology and clinical practice.  As proliferating technology moves

from the laboratory to our pockets, it may provide researchers, clinicians, and patients with

expanded capabilities to improve our classification, assessment, and treatment of bipolar

disorders.

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