

An Open Label, Longitudinal Trial Of An Internet Application Designed To
Stabilize The Daily Rhythms Of People With Bipolar Disorder

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Abstract

Objective: Although mood stabilizing medication is an essential part of the treatment of bipolar disorder, most patients experience residual symptoms, functional impairment, and syndromic relapse. The addition of an appropriate psychotherapy has been shown to improve outcomes, but very few patients have access to clinicians who are trained in evidence-based, bipolar-specific modalities. The current study tested an Internet-based fully automated adaptation of social rhythm stabilization. Methods: Sixty-four participants were recruited over the Internet into a 90 day, single arm, prospective study. Using a version of the NIMH Life Chart Methodology participants performed a daily rating of mood, anxiety and depression. The time of five key daily activities was recorded using the social rhythm metric (SRM), and participants were encouraged to perform these activities within 45 minutes of the habitual time. Results: At study endpoint social rhythm stability increased by 31%. There were statistically significant relationships between time in the study and SRM score ($p < .001$), and between SRM and mood symptom rating ($p < .001$), although the effect size for the latter was small ($r = -.143$). Conclusions: An online adaptation of one of the components of interpersonal and social rhythm therapy successfully increased social rhythm stability, and was associated with a small decrease in mood instability.

Introduction

Bipolar disorder is an illness of chronic and recurrent instability that requires complex treatment. Mood stabilizing medications play an essential role in the treatment of bipolar patients, but they are rarely fully effective by themselves. Residual symptoms often persist despite careful medication management, and even those patients who achieve symptomatic remission may experience continued impairment in occupational, interpersonal, and other domains of functioning (1). Adding a bipolar-specific psychotherapy can improve outcomes compared to the use of medication management alone (2).

Stabilization of daily routines is a component of a number of evidence-based bipolar-specific psychotherapies (3, 4). It plays the most prominent role in interpersonal and social rhythm therapy (IPSRT) (5). Irregular routines are widely targeted by bipolar psychotherapies because they occur frequently, and have the potential to destabilize mood.

A prospective two-year study of IPSRT with a sample of bipolar I patients found that subjects who received IPSRT in the acute treatment phase remained in remission longer than those who received intensive clinical management. IPSRT increased the regularity of social rhythms, and higher regularity was associated with reduced likelihood of recurrence (6).

Despite the demonstrated efficacy of IPSRT and other bipolar-specific psychotherapies, most patients are unable to access this type of treatment. Developing an effective treatment is only the first step. Before patients can benefit, the treatment must be made widely available. This essential second step may be the most challenging. Many mental health programs do not provide evidence-based practices to the great majority of their

patients (7), and encouraging the adoption of new techniques through commonly used dissemination strategies, such as conferences or educational materials, has been shown to result in little or no changes in health outcomes related to treatment practices (8).

A number of computer-aided psychotherapies (CP) have been developed to address this problem. An effective CP can allow a clinician with non-specific therapy skills to deliver an evidence-based treatment with a high degree of fidelity. CP can lower the cost of therapy by allowing most treatment tasks to be delegated to patient-computer interactions. CP can also help overcome barriers of distance and time for patients who do not live near a trained therapist, or who have work or child care responsibilities that conflict with available clinic hours.

Programs have been developed for major depressive disorder (9), panic disorder (10), problem drinking (11) and other psychiatric disorders. Bipolar disorder has not yet received the same level of attention. The goal of this study was to test an automated adaptation of one of the elements of IPSRT for people with bipolar disorder, and evaluate the extent to which the program was associated with increased regularity of daily rhythms, and diminished mood instability.

Methods

Participants

Participants were recruited via the Internet using advertisements that were displayed with bipolar related searches. The inclusion criteria required participants to have a diagnosis of bipolar disorder I, II, or NOS based on participant-reported history. Participants had to be 18-years-old or older and have access to an Internet-connected computer.

Inclusion criteria included completion of 90 days of mood rating using the NIMH Life Chart Methodology (12) adapted for online use (13). An initial 90 day charting period was required in order to select a sample that would be most likely to consistently record the times of daily activities over the duration of the study. All participants gave informed consent before any study procedures began. The study was approved by the George Washington University Institutional Review Board.

Data collection

Each day, participants were requested to provide the following information: mood, anxiety, irritability, time of awakening, time of first contact with another person, time of the start of work (which could include paid work, volunteer work, housework, child care, or school), dinner time, and bedtime. In lieu of providing an activity time, participants could indicate that for a given day they did not have contact with another person, engage in any work, or eat dinner.

Mood was rated using the NIMH Life Chart Methodology conventions, with scores ranging from 0 to 4. Participants were given multimedia instructions on how to choose the correct level of severity. Examples of both manic and depressive symptoms consistent with each level of severity were provided. Rating conventions and symptom examples were included on the web page that participants filled out each day. Anxiety and irritability were rated on a scale of scale of 0-3.

For the first seven days of the study, participants were asked to record the times of daily activities without attempting to make any changes. This initial seven day period allowed a baseline SRM to be calculated.

On the eighth day, participants were asked to set target times for each of the activities, and then attempt to perform each activity within 45 minutes of the target time (5). In order to help participants track their success, a “hit rate” was calculated, and displayed on the participant’s mood chart (Figure 1). The hit rate was the percent of time each activity was performed within 45 minutes of the target time over the past seven days. Counters were displayed on the chart page indicating the total number of days rated, and the total number of consecutive days rated. The counters were used to help motivate participants to rate consistently (14).

In order to make it easier to perform daily ratings, each day participants received a daily rating email. The email contained nine links corresponding to each of the nine possible mood ratings (Figure 2). Clicking on a link triggered a web browser to open the rating page (Figure 3). On this page participants could modify their mood rating, and record the other required information. The links embedded within each participant’s email contained three codes: the subject identification code, the date being rated, and the mood rating score. The page that opened in response to the email link was simply a form for information entry. No participant data was displayed, and none could be accessed unless the participant signed in with a user name and password.

In order to minimize the privacy risk to participants, the only piece of identifying information collected was an email address. The email address was stored in encrypted form using triple DES (data encryption standard) (15), and all data was sent between the server and the participants’ computers using secure socket layer (SSL) encryption. Participants were advised to avoid using work computers and email accounts for the study, because some employers monitor their employees’ computer use.

Data analysis

The primary outcome measure was change over time in the social rhythm metric (SRM), which was calculated as a 7 day moving average using the standard scoring methodology (5). Scores range from 0 (the activities are never performed around the habitual time) to 7 (the activities are performed every day around the habitual time). For the group as a whole, Pearson correlation was used to evaluate the relationship between the SRM and the number of days that the program was used. Mixed-model analysis was used to evaluate within-individual change over time.

A secondary analysis addressed the question of whether greater rhythm stability would reduce mood symptoms. Total symptom burden (TSB) was defined as the sum of the depression score and the mania score. SPSS 14.0 software was used for data analysis.

Results

Sample description

Sixty-four participants gave informed consent, and were enrolled in the study. Most participants were women with at least some college education who reported a diagnosis of bipolar II disorder (Tables 1 and 2). The majority of participants were non-Hispanic White. Five participants identified themselves as Hispanic or Latino, 1 as American Indian or Alaskan Native, and 2 as Black or African American. Nine participants declined to give demographic information. Data was collected between 12/28/2007 and 1/6/2010. Overall, adherence to rating was high during the 90 day study. The mean number of days rated was 84.0 (SD 11.0), which provided a total of 5,376 days of data to analyze.

Stabilization of daily rhythms

At baseline, the mean SRM was 3.63 (SD 0.93), and increased to 4.76 (SD 1.19) on day 90. Nearly all of the increase in the SRM occurred during the first 30 days of the study (on day 30, the mean SRM was 4.62, SD 1.11). There was a statistically significant relationship between SRM and days in the study ($r=.128$, $p<.001$). A graphical representation of this relationship is displayed in Figure 4. When examined in 30 day segments, there was a statistically significant relationship in the first 30 days ($r=.164$, $p<.001$), a slight, non-significant relationship in the 31-60 day segment ($r=-.042$, $p=.087$), and no relationship in the 61-90 day segment ($r=-.006$, $p=.835$).

The longitudinal mixed model analysis also showed a significant interaction between days in the study and SRM (estimate .00626, SE .00268, df 157.607, t 2.331, $p=.021$) indicating that use of the program was associated with increased stability of the times of daily activities.

Stabilization of mood

Participants were more likely to report depressed days than manic days, and the severity of depression was greater. On average, participants rated 36.4 (SD 25.1) days depressed, and 15.8 (SD 18.0) days manic. The large standard deviations indicate a large amount of variability among participants. The mean severity of depression was 1.51 (SD 0.47) and the mean severity of mania was 1.11 (SD 0.47).

There was a significant negative correlation between SRM and the Total Symptom Burden (TSB, $r=-.143$, $p<.001$). The same was seen when manic symptoms ($r=-.048$, $p=.002$) and depressed symptoms ($r=-.133$, $p<.001$) were evaluated separately. Both anxiety ($r=-.226$, $p<.001$) and irritability ($r=-.182$, $p<.001$) were also negatively correlated with SRM.

Mixed model analysis also showed a significant negative interaction between SRM and TSB (estimate -.0877, SE .0262, df 183.443, $t = -3.346$, $p = .001$), anxiety (estimate -.0653, SE .0226, df 188.882, $t = -2.892$, $p = .004$), and irritability (estimate -.0544, SE .0214, df 175.249, $t = -2.545$, $p = .012$).

Construct validity

Expected relationships between variables were explored in order to support the construct validity of the Internet-based self-report methodology. At baseline the mean SRM of married participants (3.82, SD 0.76) was greater than the SRM of those who were not married (3.41, SD 1.06). The SRM was greater for those who were employed full time (3.65, SD 0.94) compared to those who were unemployed (3.44, SD 1.01). Mood symptoms as measured by the TSB were well-correlated with both anxiety ($r = .549$) and irritability ($r = .533$).

Discussion

Participants using an automated, online adaptation of social rhythm therapy increased their mean SRM from 3.6 at baseline to 4.7 by the end of the study. The SRM has a maximum score of 7, which is achieved by performing all activities within 45 minutes of their usual time every day of the week. A score of 5 could indicate that, on average, activities are performed around their usual times on weekdays, but not on weekends.

A score of 5 might appear to represent a typical score for a healthy person, however a study of 96 subjects recruited at random from a university alumni list reported a mean score of 3.43 (16). This figure is similar to what was seen in this study at baseline. Although the two samples are not directly comparable, the mean SRM of 4.7 achieved at day 90 in this study may represent greater than “normal” daily rhythm stability.

Swartz has compared rhythm stabilization in bipolar patients with dietary control in diabetics (17). Just as diabetics must maintain extremely tight control of their intake of potentially unhealthy foods, bipolar patients may benefit from “supra-normal rhythm stability,” because of fragile circadian systems that are easily dysregulated.

Essentially all of the improvement in the SRM score occurred during the first 30 days of the study. It is likely that interest in daily rhythm stabilization was highest in the beginning of the study, and led to an initial rapid increase in the SRM. After day 30, no further net gain was achieved, although the improvement was maintained.

A secondary aim of the study was to evaluate the effect of daily rhythm stabilization on mood. Mood symptoms were collected using an online adaptation of the NIMH Life Chart Methodology. One of the weaknesses of this instrument is that it relies on self report, and therefore participants may rate moods inconsistently. This weakness was minimized by providing online training to the participants so that they would understand the conventions for choosing the correct rating. The conventions were reinforced at every rating.

The NIMH Life Chart Methodology has some advantages over alternative measures of mood symptomatology. Because ratings occur every day, short term mood instability is captured. By contrast, rating scales such as the Hamilton Depression Rating Scale or the Young Mania Rating Scale summarize data over the course of seven days. As a result, information on day-to-day instability is lost.

Some longitudinal studies of bipolar disorder use relapse or recurrence as an outcome measure, based on whether a participant meets the criteria for a DSM-IV-defined mood episode. Because the threshold for a DSM-IV episode is high, this strategy ignores less

severe manifestations of abnormal mood, and may fail to identify the more subtle effects of an intervention.

The NIMH-LCM measures mood daily, and is able to measure subsyndromal states of abnormal mood. These characteristics allow small effects to be identified, which is important when evaluating a low intensity intervention, such as an automated computerized therapy. One of the drawbacks, however, is that statistically significant effects may be found that are not clinically significant. Many of the p values in this study were $<.001$, but the effect sizes of the relationships were small.

One interpretation of this result is that the program did not help participants in clinically meaningful ways. Alternatively, one might view the successful treatment of bipolar disorder as involving multiple components that can act in synergistic ways. For example, increased daily rhythm stability may create an environment in which medication adherence is more likely to occur, or a reduction in irritability, as was seen in this study, could increase the quality of social relationships, and enhance the level of environmental support. Just as multiple destabilizing factors can combine to trigger a mood episode, multiple therapeutic factors may potentiate one another to reduce mood instability.

It is also possible that some portion of the mood stabilizing effects of daily rhythm stabilization are delayed. In a study that compared IPSRT to intensive clinical management, no differences were seen during the acute phase, but participants randomized to IPSRT survived longer without a new affective episode during a 2 year follow-up period {Frank, 2005 #20}. The current study measured only changes that occurred contemporaneously with the 90 day intervention.

This was a single arm, open label study, therefore causality cannot be inferred from the results. It is possible that improved rhythm stability led to improved mood stability,

however the opposite could also have occurred. Acute mood symptoms interfere with daily rhythm stability, and improvement in mood would be expected to result in more regular rhythms.

It is also possible that the increased SRM scores that occurred during the study were independent of the effects of the Internet program. Individuals often enter studies during periods of symptom exacerbation, and then improve as a result of spontaneous regression to the mean.

Although this mechanism cannot be ruled out, the study design made it less likely. All subjects began by using the online program to rate their mood for 90 days. They were not given any information about the existence of an IPSRT study until they were eligible for enrollment. Therefore the initial 90 period was not a “wait list” condition, which can be associated with an implicit message to participants that they should not change. All the change in SRM occurred during the first 30 days following enrollment. Therefore, out of a total of 6 months, it is unlikely that regression to the mean or spontaneous improvement occurred only during month 4, but not during months 1, 2, 3, 5, or 6.

Participation in this study was exclusively via the Internet, and all data was self report. Communication efficiencies associated with this medium can make subject recruitment easier, achieve greater geographic diversity, and allow access to populations who would not participate in traditional research studies. At the same time, the actual composition of the sample being studied, particularly in the case of anonymous participants, is difficult to know. Subjects working in a non-clinic or laboratory environment might invest less time and energy in accurately completing questionnaires (18).

In spite of these potential problems, a high degree of reliability and validity has been seen when using the Internet as a source of subject recruitment (19), and it may even facilitate

gathering of sensitive information due to a sense of anonymity (20). When participants report on behaviors they are expected to perform, there is a risk that they will report inaccurately as a result of wanting to please the investigator, or feeling embarrassed about failing to accomplish the prescribed task. With an anonymous reporting system, this problem is minimized, and it may be possible to collect more accurate data.

The measures of construct validity support the probability that participants provided accurate information about themselves, and completed the online questionnaires with care. As would be expected in bipolar samples, depression was more common than mania, and there was significant correlation between mood ratings and ratings of anxiety and irritability. Married and employed participants had greater levels of daily rhythm stability compared to their counterparts.

Conclusions

The use of a fully automated Internet adaptation of social rhythm stabilization for 90 days was associated with a 30% increase in the social rhythm metric, and a small, though significant decrease in symptoms of abnormal mood, anxiety, and irritability. The modest benefit should be considered in the context of a risk benefit analysis. Although adverse effects were not measured in this study, it is generally believed that the adverse effects of psychotherapy are minimal. Because evidence-based bipolar-specific psychotherapy is difficult for most patients to access, an option that can be provided at almost no cost, regardless of geographic location, and at any time of day is potentially important.

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★ daniel.lieberman@moodchart.org to me show details 7:00 AM (7 hours ago) [Reply](#)

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December 2010

Sun	Mon	Tue	Wed	Thu	Fri	Sat
28	29	30	1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	1
2	3	4	5	6	7	8



Current Conditions:
Cloudy, 19 F

Forecast:
Wed - Mostly Sunny/Wind. High: 30
Low: 21
Thu - PM Snow Showers. High: 30
Low: 24

One-Click Mood Chart

Record yesterday's mood - **Tuesday, December 14, 2010** - by clicking on one of the mood levels listed below.

Mood levels are described in more detail a little further down.

- [Severe mania - incapacitated or hospitalized](#)
- [High moderate mania - great difficulty with activities](#)
- [Low moderate mania - some difficulty with activities](#)
- [Mild mania \(hypomania\) - energized, little or no difficulties](#)
- Normal mood**
- [Mild depression - little or no problems functioning](#)
- [Low moderate depression - functioning with some effort](#)
- [High moderate depression - functioning with great effort](#)
- [Severe depression - incapacitated or hospitalized](#)

Figure 2. Daily rating email.

December						
November	2010					January
Sun	Mon	Tue	Wed	Thu	Fri	Sat
28	29	30	1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	1
2	3	4	5	6	7	8

Done. Optional Information - Tuesday, December 14, 2010

Since you already indicated your mood by clicking in the email you received, you are all set for the day. Your mood has been recorded, and you can shut down this browser. It can be really helpful, though, to add some important information by making just a few clicks on this page.

You can check your mood rating here. If your mood was pretty much the same all day, just leave the single rating. If there were important differences, choose the highest and the lowest.

Some of the symptoms of mania
High mood, irritability, less need for sleep, high energy, disrupting others, racing thoughts, easily distracted, impulsive spending, risky behavior, talkative, overly enthusiastic, etc.

Some of the symptoms of depression
Sadness, hopelessness, feelings of helplessness, difficulty thinking or remembering, low self esteem, guilt, decreased interest in things, lack of motivation, low energy, anxiety, etc.

- Severe mania
- High moderate mania
- Low moderate mania
- Mild mania (hypomania)
- Normal mood
- Mild depression
- Low moderate depression
- High moderate depression
- Severe depression

Severe: Completely unable to do usual activities or hospitalized because of mood symptoms.

High moderate: Very difficult to do usual activities because of mood symptoms.

Low moderate: Some difficulty doing usual activities because of mood symptoms.

Mild: Noticeable symptoms, but able to do all usual activities.

Monthly Weight Measurement

Hours of sleep (last night)

Anxiety

- 0-None
- 1-Mild
- 2-Moderate
- 3-Severe

Irritability

- 0-None
- 1-Mild
- 2-Moderate
- 3-Severe

Important Events

If something important happened today that you think might affect your mood, you can describe it here.

Figure 3. Rating web page

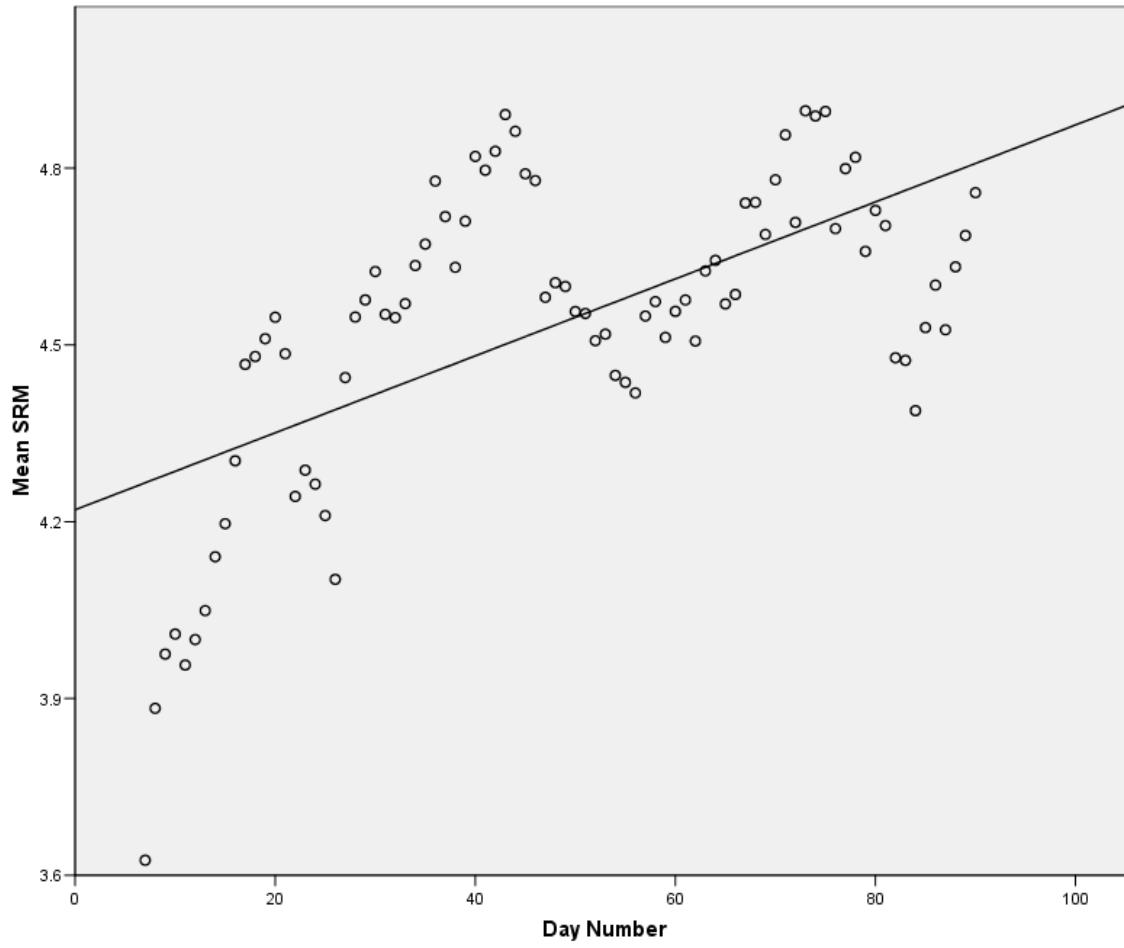


Figure 4. Mean Social Rhythm Metric Score (SRM) by study day.

	N	Percent
Diagnosis		
Bipolar I	11	20.0
Bipolar II	33	60.0
Bipolar NOS	11	20.0
Gender		
Female	48	87.3
Male	7	12.7
Marital status		
Never married	16	29.1
Currently married	22	40.0
Separated	3	5.5
Divorced	13	23.6
Widowed	1	1.8
Employment		
Full time	28	50.9
Part time	7	12.7
Homemaker	3	5.5
Student	6	10.9
Unemployed	11	20.0

Table 1. Sample description

	Mean	SD
Age	43.0	12.5
Age of first mood episode	15.7	8.9
Years of education	15.6	2.68

Table 2. Sample description, continued. SD=Standard Deviation.