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Prediction of Near-Term Increases in Suicidal Ideation in Recently Depressed Patients with Bipolar II Disorder Using Intensive Longitudinal Data

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Abstract

Background—There are substantial gaps in understanding near-term precursors of suicidal ideation in bipolar II disorder. We evaluated whether repeated patient-reported mood and energy ratings predicted subsequent near-term increases in suicide ideation.

Methods—Secondary data were used from 86 depressed adults with bipolar II disorder enrolled in one of 3 clinical trials evaluating Interpersonal and Social Rhythm Therapy and/or pharmacotherapy as treatments for depression. Twenty weeks of daily mood and energy ratings and weekly Hamilton Depression Rating Scale (HDRS) were obtained. Penalized regression was used to model trajectories of daily mood and energy ratings in the 3 week window prior to HDRS-SI ratings.

Results—Participants completed an average of 68.6 (sd=52) days of mood and energy ratings. Aggregated across the sample, 22% of the 1675 HDRS Suicide Item ratings were non-zero, indicating presence of at least some suicidal thoughts. A cross-validated model with longitudinal ratings of energy and depressed mood within the three weeks prior to HDRS ratings resulted in an AUC of .91 for HDRS Suicide item 2, accounting for twice the variation when compared to baseline HDRS ratings. Energy, both at low and high levels, was an earlier predictor than mood.

Limitations—Data derived from a heterogeneous treated sample that may not generalize to naturalistic samples, and identified suicidal behavior was absent from the sample so could not be predicted.

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Conflicts of Interest: None

Contributors

CD: Developed the hypotheses and led development of the manuscript; WT: Developed and implemented the statistical approach; EF and HS: Developed the parent studies, assessment and intervention protocols and all authors contributed to and approved the submitted manuscript

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Conclusions—Prediction models coupled with intensively gathered longitudinal data may shed light on the dynamic course of near-term risk factors for suicidal ideation in bipolar II disorder.

Keywords

Statistical modeling; suicide prevention; ecological momentary assessment; depression; bipolar disorder

Introduction

Bipolar disorder is associated with the highest risk of suicide among psychiatric illnesses (Schaffer et al., 2015b). Rates of suicide are approximately 20 to 30 times that in the general population; 5–10% of people with bipolar disorder die by suicide, and 50–60% of patients attempt suicide in their lifetimes (Pompili et al., 2013; Schaffer et al., 2015b). Bipolar II disorder is associated with similar risk of self-harm as bipolar I disorder (Novick et al., 2010). In addition to their enormous toll on individuals and families, suicidal behaviors produce enormous direct and indirect costs (Stensland et al., 2010). Despite the clear public health need for *indicated* prevention strategies in bipolar disorder (Rihmer, 2007), much of the approach to prediction of suicidal risk in bipolar disorder is based on risk factors that do not change over time (e.g., family history of suicide attempt) and thus have limited prognostic utility in monitoring variation in risk longitudinally or predicting near-term risk (Schaffer et al., 2015a). Indeed, little is known about near term risks for exacerbations in suicidal thoughts despite the potential importance to timely suicide prevention (Glenn and Nock, 2014). Given the heterogeneous, fluctuating course that is characteristic of bipolar disorder, temporally finer-grained assessments obtained during days and weeks of acute illness may enhance near-term risk assessment of suicidal ideation, and may provide greater insight into the warning signs of suicide-related crises in this high-risk group of patients (Claassen et al., 2014).

A number of prospective and retrospective studies have identified increases in time-varying constructs, such as agitation, dysphoric depression, anxiety, and mixed states, that seem associated with higher risk of suicidal ideation in bipolar disorder I or II (Novick et al., 2010; Schaffer et al., 2015a). These mixed affective states appear to be unique prognostic indicators of suicide risk in bipolar disorder compared to unipolar depression, and do not appear to differ between bipolar I and II in terms of frequency or strength of association (Novick et al., 2010; Schaffer et al., 2015a). In contrast, euphoric mania and psychomotor retardation have been associated with comparatively lower risk for suicidal ideation and behavior (Miller et al., 1985). Thus, co-occurring and opposite valence changes in mood and energy that frequently accompany mixed states are potentially prognostic indicators of suicide risk. However, it is unclear 1) when the earliest changes in mood and energy can be detected that predict elevated risk for future suicidal ideation, 2) what kind of change occurs first—i.e., mood or energy, if either, and 3) whether these time-varying changes provide greater predictive accuracy than risk factors that do not change over time. Given that changes in mood and energy occur over days or even hours, intensive longitudinal data (ILD) collection strategies in which high frequency repeated measures are gathered may be of great benefit for delineating the precursors of suicidal exacerbations in bipolar disorder.

Although suicidal ideation is an insensitive and imperfect predictor of suicidal behavior, ideation is a major risk factor for suicide attempts (Valtonen et al., 2006) and is associated with other negative events such as hospitalization.

A handful of prior studies have examined ILD-based collection strategies in the context of predicting suicidal ideation and self-injury (Armey et al., 2011; Ben-Zeev et al., 2012; Muehlenkamp et al., 2009; Thompson et al., 2014). In a recent pilot study of 35 clinically euthymic patients with bipolar I or II disorder followed for 8 weeks, we found that changes in daily mood ratings (particularly increase in negative affect) accurately predicted increases in clinician-rated suicidal ideation and behavior in the period 1–3 weeks prior to direct clinical observation (Thompson et al., 2014). We applied functional linear models for this purpose (Ramsay, 2006), a statistical method well suited to ILD because it reduces the potential for over-fitting, which occurs when models are unduly influenced by error or noise. We found this approach more sensitive and specific in predicting suicidal exacerbations than in-person data collected at routine intervals analyzed with ordinary least squares regression. This study provided preliminary evidence that a frequently captured, time-varying predictor (negative affect) could be modeled to accurately predict *future* risk of suicidal ideation at a time point prior to the clinician's first awareness of an exacerbation. This study was limited by inclusion of euthymic patients, a small sample size, and the brief observation period.

Our objective for this study was to extend our prior work on prediction of suicidal ideation in bipolar disorder using ILD, by applying the statistical method to a comparatively larger sample of patients with bipolar II disorder, selected for the presence of a current depressive episode. We used pooled data from participants meeting criteria for bipolar II disorder, currently depressed, and enrolled in one of three clinical trials of Interpersonal and Social Rhythm Therapy (IPSRT) and/or pharmacotherapy. As part of their participation, participants completed the Social Rhythm Metric (SRM) (Monk et al., 1991), a self-report diary that included daily questions about mood and energy for 20 weeks. Since a central aspect of IPSRT is the collection of this daily diary, participants generate a large amount of intra-individual longitudinal data that can be used in prediction models. Moreover, bipolar II disorder is a subtype of the illness that is understudied but associated with high rates of suicide attempts, comparable to those with bipolar I disorder (Novick et al., 2010). We hypothesized that changes (worsening) in daily self-rated mood and energy over a 3-week window would precede a subsequent change (exacerbation) in suicidal ideation as indicated by weekly suicide item ratings on the Hamilton Depression Rating Scale (HDRS-SI). We hypothesized that the combined predictive accuracy of daily self-reported mood and energy ratings would be greater than either item alone and account for a greater variation in suicide ratings than would baseline HDRS Total score or baseline HDRS-SI score. We varied estimation across the 3-week window prior to clinician-reported suicide rating to explore the temporal sequence and direction of change in mood and/or energy.

METHODS

Study Overview

We aggregated data from three trials of IPSRT/quetiapine in bipolar II disorder in which each study included the SRM daily rating. All study procedures were reviewed and approved

by the Biomedical Institutional Review Board of the University of Pittsburgh. Potential participants provided informed written consent after receiving a complete description of the study, including a full description of risks associated with study participation. Participants were eligible for inclusion in the current analyses if they were treated in the Depression and Manic Depression Prevention Program at the University of Pittsburgh, were participants in one of the clinical trials for bipolar II disorder described below, and met the following inclusion criteria: Age 18–65 years; lifetime diagnosis of bipolar II disorder and current major depressive episode according to DSM-IV criteria as determined by the SCID-IV (First et al., 1997), currently experiencing at least a moderate level of depressive symptoms as indicated by a 25-item version of the Hamilton Rating Scale for Depression score ≥ 15 . Potential participants were excluded from analyses if they met any of the following criteria: currently receiving treatment with psychoactive medications other than the study medications; diagnosis of substance abuse or dependence within the prior six months; currently pregnant or lactating; diagnosis of borderline or antisocial personality disorder as determined by the SCID for DSM-IV Personality Disorders (SCID-II); or unstable medical condition (such as untreated hypothyroidism) that could produce symptoms that would confound accurate assessment of mood. Suicidal ideation was not an exclusion criteria, although those required a higher level of care (i.e., hospitalization) were excluded.

All participants received twenty weeks of treatment according to the protocol to which they were assigned. 1) STUDY 1 (previously described) (Swartz et al., 2009) consisted of open treatment with Interpersonal and Social Rhythm Therapy (IPSRT), an evidence based psychotherapy for bipolar disorder (Frank et al., 2005), followed by the addition of lamotrigine at week 12 for IPSRT non-responders ($n=11$), 2) STUDY 2 (previously described) (Swartz et al., 2012a) was a randomized trial comparing weekly IPSRT to quetiapine ($n=21$) or 3) STUDY 3 was a randomized trial of IPSRT plus quetiapine or IPSRT plus placebo ($n=54$). In all studies, IPSRT was administered weekly. In Study 1 and 2, pharmacotherapy was administered openly and flexibly dosed according to participants' symptoms. In Study 3, quetiapine/pill placebo was administered in a double-blind fashion and flexibly dosed according to participants' symptoms. Participants were assessed weekly by a rater blind to their treatment condition (see Assessments below). We assessed whether there were potentially important differences among the three studies via ANOVA, and we found that there was study-wide variation in age $F(2, 83)=3.7, p=0.029$ and age was included subsequent models. However, there were no significant omnibus differences in regard to sex (Chi-square 0.14, $p=0.928$), baseline depressive symptom severity ($F(2,83)=0.9, p=0.415$), or baseline suicidal ideation severity (Chi-square 4.7, $p=0.317$).

Baseline Clinical Assessments

Demographic data and psychiatric history were recorded on standardized research forms. Lifetime and current psychiatric diagnoses were assigned using the Structured Clinical Interview for DSM-IV, Clinician Version (SCID). Depressive symptoms were assessed weekly using the expanded 25-item version of the Hamilton Depression Rating Scale (HDRS) (Miller et al., 1985) that includes reverse neurovegetative symptoms. Research assessments were conducted by raters who were blind to participants' treatment assignment.

Interrater reliability as measured by intraclass correlations (ICC) were excellent: ICC=0.99 and 0.98 for YMRS and HDRS, respectively.

From these assessments, potential baseline predictors included: Age at study onset, Gender, Marital Status, Diagnosis of Anxiety Disorder, Years Since First Hypomanic Episode, Number of Hypomanic Episodes, Years Since First Depressive Episode, and Number of Depressive Episodes. We did not systematically collect data on prior history of suicide attempts or hospitalizations.

Intensive Longitudinal Assessments

Participants also completed the self-report 5-item SRM (Monk et al., 1991), starting the third week of the studies. The SRM is a measure of lifestyle regularity that quantifies the extent to which an individual initiates five pre-specified activities at the same time every day. It also asks patients to record daily mood ratings on a paper and pencil scale of -5 (very depressed) to +5 (very manic) with 0=euthymic, thereby providing a continuous measure of mood over time. For studies of BP II, we adapted the SRM (Swartz et al., 2012b), to also ask participants to rate their energy level daily on a scale of -5 (low energy, anergic) to +5 (high energy, very activated). The mood and energy level variables were the predictors used in the analyses. Participants are asked to complete the form prospectively—that is, fill in daily ratings each day of the week, preferably just before bedtime. The SRM is reviewed by the IPSRT therapist at each weekly visit. If participants have difficulty completing the form, therapists provide coaching to overcome barriers to SRM completion during sessions.

Outcome of Interest

The primary outcome was the weekly Hamilton Depression Rating Scale (HDRS) Suicide Ideation Item (item #3) with a frame of reference of the past week. This is a four point rating from 0 (Absent), 1 (Feels like life is not worth living), 2 (Wishes he/she were dead or any thoughts of possible death to self), 3 (Suicidal ideas or gestures), to 4 (Attempts at suicide). Prior work has indicated that this single item rating from the HDRS has concurrent validity with longer assessments of suicidal ideation (Desseilles et al., 2012) and single item measures of suicide risk are predictive of future attempts (Simon et al., 2013).

Statistical Analyses

In our *Baseline Model*, we first analyzed baseline predictors of Suicidal ideation. Since each subject was evaluated multiple times for each subject, we used linear mixed effects models (LMEs) with time-invariant baseline predictors and a random subject-level intercept to account for within-subject correlation of outcomes. We selected the variables in the model using the Least Absolute Shrinkage and Selection Operator LASSO approach (Hastie and Efron, 2013), including as potential covariates all main effects and pairwise interactions. LASSO is a form of penalized regression that is useful for datasets with highly correlated predictors where the goal is to evaluate the relative strength of association among predictors, making more stringent the selection of regression coefficients than in stepwise variable selection. In the final model we kept variables selected by the LASSO that also had p-values < 0.05. We also performed using the LMEs a model with baseline HDRS total score and baseline HDRS suicide item scores as predictors, examining the variation accounted for by

these static risk factors. We calculated a pseudo- R^2 by correlating fixed predicted values from this model with HDRS suicide item scores.

We next added in longitudinal assessments of mood and energy from the daily SRM diaries to determine whether these data could improve prediction over the baseline model. All available data was used in these mixed models and no imputation was employed. First, we summarized longitudinal mood and energy ratings by weekly averages: for a given instance of an HDRS suicide item rating, we obtained that subject's average mood and energy scores, from week 2 (MW2 and EW2; 8–14 days prior to suicide-item assessment), week 3 (MW3 and EW3; 15–21 days prior), and week 4 (MW4 and EW4; 22–28 days prior). To examine whether non-linear transformations of the variable would better predict HDRS suicide item scores, we placed each of the weekly mood and energy measures into a regression tree algorithm (with one node and two branches) to determine potential cut-points. The resulting transformed variables were again placed into a LASSO algorithm, along with all pairwise interactions to determine the final model.

Accuracy of the resulting baseline and longitudinal models was assessed via leave-one-subject out cross validation (CV) prediction accuracy. Specifically, we deleted the data from a given subject, fit the parameters of the two LMEs, and then used these models to predict the scores of the deleted subject. This was done cycling through all subjects. The resulting prediction accuracy was summarized by CV R-squared and by Area Under the Curve (AUC) for HDRS suicide item responses dichotomized at 1 and at 2. Out-of-sample AUC confidence intervals were calculated using the Wald statistic (Kottas et al., 2014). To interpret interactions terms, we compared the cells by way of ANOVA.

RESULTS

Baseline Sample Description

A summary of the baseline variables for participants is given in Table 1. On average, the sample was mostly female (63.5%) and experiencing a moderate level of severity of depression at baseline (mean HDRS=24.5, sd=4.6). Participants in the study experienced onset of depressive episodes in their late teens and hypomania in their early twenties on average, with a wide range in the number of subsequent depressive and hypomanic episodes. The majority (60%) had a comorbid anxiety disorder. At baseline, half of participants were experiencing at least some passive thoughts of death as indicated by a score greater than zero on the HDRS-SI item. As such, the sample was largely consistent with the population of patients with bipolar II disorder in the midst of a major depressive episode (Judd et al., 2003; Vieta et al., 1997).

Longitudinal HDRS Suicide Item and Social Rhythm Metric data

There were 86 participants with longitudinal SRM diary measurements available. There were 1,575 total in-person HDRS suicide item assessments, or roughly 18 per subject (min =3 and max=37). Of these 1,575 suicide item assessments, 1,233 (78%) were rated a 0 (no suicidal ideation), 300 (19%) were rated a 1 (thoughts of being better off dead), 40 (2.5%)

were rated a 2 (thoughts of self-harm), and 1 (0.06%) was rated a 3 (suicidal ideas or gestures). There were no instances where the item was rated a 4 (suicide attempts).

There were 5900 ratings of mood (15% missing data) and 4380 (37.5% missing data) ratings of energy across the subjects. These ratings were normally distributed with a mean value between 0 and -1 (indicating slightly depressed and slightly diminished energy on average). Participants contributed an average of 68.6 days of mood ratings ($sd=52.5$) and 50.9 days of energy ratings ($sd=39.0$). Mood and energy ratings were highly correlated ($r=0.813$, $p<0.001$). Neither the individual-level mean value of mood or energy ($r=-0.077$, $p=0.486$ and $r=-0.079$, $p=0.496$, respectively), nor the number of energy or mood ratings per person ($r=0.011$, $p=0.916$ or $r=0.136$, $p=0.212$) correlated with baseline HDRS Total scores. Similarly, baseline HDRS Scores were not associated with either average mood or energy across the study period ($F(2,82)=0.642$, $p=0.529$, $F(2,73)=0.317$, $p=0.729$).

Baseline and Longitudinal Prediction Models

Performing variable selection via the LASSO followed by linear mixed effects models resulted in the baseline model given in Table 2. Only one baseline variable was predictive of HDRS suicide item: the interaction between Age and Years Since First Depressive Episode ($t=3.517$, $p<0.001$). Inspection of this interaction revealed that older age and a longer duration of lifetime illness were more strongly related to the suicide HDRS Suicide item. This variable alone was predictive of HDRS Suicide item, having a cross-validated R-squared $R^2_{cv}=0.12$. Moreover, the cross-validated AUC from this baseline model was $AUC_{cv}=0.70$ when dichotomizing HDRS Suicide item scores at 1 and $AUC=0.79$ when dichotomizing HDRS Suicide item scores at 2. Similarly with the baseline HDRS suicide-item and HDRS total score (without the suicide item) included in a separate model, the R-squared value was $R^2=0.12$.

The longitudinal model selected additional variables: Mean level of mood in second week and third week prior to HDRS Suicide Item ratings and level of energy in third week prior to HDRS Suicide Item ratings, as well as their interactions (see Table 2). The cross-validated R-squared was $R^2_{cv}=0.20$. The cross-validated AUC from the longitudinal model was $AUC_{cv}=0.78 (\pm 0.02)$ when dichotomizing HDRS suicide item scores at 1 and $AUC=0.91 (\pm 0.07)$ when dichotomizing HDRS suicide item scores at 2. As seen in Table 2, the interaction of energy at Week 3 and mood at Week 2 was significant, as well as the interaction between mood and energy at Week 3. To further assess the meaning of the interaction, we compared groups based on assigned cut points derived from the regression tree algorithm. We found that decreased energy (score below mean of -0.55) in Week 3 followed by decreased (more depressed) mood (score below mean of -1.26) in Week 2 were associated with the highest predicted HDRS-SI score (estimated score = 0.56), and that high energy in Week 3 followed by decreased (more depressed) mood in Week 2 was associated with the next highest predicted HDRS (estimated score = 0.42). Rating above the cut-off for both mood and energy predicted the lowest HDRS item scores (estimated score = 0.08).

Discussion

In a longitudinal study in treated patients with bipolar II experiencing a depressive episode at baseline, we found that frequent ratings of daily mood and subjective energy prospectively predicted subsequent changes in clinician-rated suicidal ideation. The precision of the final model that incorporated these longitudinal data was AUC=0.91 when predicting an increase to a score equal to 2 on the HDRS Suicide item. Accuracy was lower in predicting the more common HDRS suicidal ideation item rating of 1 which is inclusive of passive thoughts that life is not worth living (for which AUC = 0.78). Longitudinal trajectories of energy and mood reported accounted for twice the variation produced by our baseline model, which included baseline HDRS Suicidal Ideation and HDRS Total Score ratings as predictors of subsequent levels of HDRS suicidal ideation. Notably low energy level was an earlier predictor (emerging 3 weeks prior to when suicide risk ratings were obtained) than depressed mood (emerging 2 weeks prior). These preliminary findings indicate that intensive longitudinal data, such as those that are increasingly gathered with mobile technology, wearable devices, or daily diary ratings recorded in interventions such as IPSRT, integrated with statistical predictive models, could shed light on the dynamic sequence and interaction among precursors of suicidal exacerbations in bipolar II disorder.

Our study was somewhat inconsistent with prevailing assumptions about the specific increased risk of suicide associated with mixed symptoms (Balázs et al., 2006; Swann et al., 2013). There was not a clear indication that the specific combination of increased subjective energy with depressed mood, which would be consistent with a mixed state, was associated with elevations in suicidal ideation; rather we found that depressed mood (vs. euthymic or hypomanic) was associated with increased risk of later increases in suicidal ideation. However, this risk was modified by level of subjective energy, with both decreased and increased energy associated with elevated risk. It is likely that population heterogeneity is present in which some individuals may experience increased suicidal thoughts in the context of high energy and low mood whereas others experience increased ideation in the context of anergic depression (low energy; low mood). These are both recognized as clinically important, difficult to treat, mood states (Joseph F. Goldberg et al., 2009; Rastelli et al., 2013), and, based on these findings, may also represent prodromal risk periods for suicide. It would be important to understand whether these patterns are consistent within-patients over time (e.g., “signature” warning signs (Lobban et al., 2011)) which could be studied with longer term follow up capturing repeated events within patients.

Further, main effects revealed that daily ratings of energy appeared to be earlier markers of elevations in the suicide rating. The final model included energy changes occurring *3 weeks* prior to observed increased suicide risk, whereas mood changes were predictive only at *2 weeks prior*. Few studies have examined the interaction among symptom clusters and their sequence, even though the period prior to suicidal crises is described as a cascade of dynamic and interacting risks (Claassen et al., 2014). Moreover, it is unclear at this point if subjective energy level is associated with objectively measured movement or activity patterns, but given that most mobile devices are capable of passive collection of movement and activity, longitudinal passive monitoring (with consent) of at risk persons with bipolar disorder through mobile devices (Mohr et al., 2013) could inform suicide prediction models.

Limitations

Our study had several strengths. It is the first, to our knowledge, to use intensive longitudinal data to predict suicidal ideation in a well characterized sample of treated depressed patients with bipolar II disorder. The study is further strengthened by drawing from participants in three different clinical trials, increasing the generalizability of findings. However, there are a number of important limitations. The sample was modest in size and all participants were enrolled in clinical trials that included both a psychosocial intervention and pharmacotherapy interventions, and our analyses did not tease out impact of treatment assignment on suicidal ideation. Although half of participants registered non-zero responses on the HDRS Suicide Item at baseline, the frequency of subsequent non-zero HDRS Suicide Item ratings was much lower concurrent with treatment. As such, these findings do not apply to untreated samples or to samples not recruited in a depressive episode. Participants received different treatments, depending on the research protocol in which they enrolled, and these analyses did not control for variability in treatment received or cohort effects. We were limited, as with all long-term monitoring studies, to participants who were adherent to daily monitoring (65 to 85% data completion rate) and so these findings may not apply to participants who are unwilling or unable to participate in long-term self-monitoring. The HDRS measure of suicidal ideation was collected weekly, and we therefore we cannot pinpoint more precisely than the one-week time frame when suicidal ideation emerged as we were limited by when it was assessed. There were no documented instances of suicidal behavior and so we could not use this model to predict conversion of ideation to behaviors, and we lacked a measure of the number of prior suicide attempts. Future studies assessing suicidal ideation and behavior separately in real-time with intensive longitudinal paradigms would better enable finer-grained understanding of the temporal precursors of suicidal exacerbations. Of course, such studies would need to be of substantially greater size to detect precursors of rarer events such as attempts or completed suicide. Moreover, other predictors that are indicators of mixed symptoms, such as irritability/agitation, or elements in theoretical models of the near term precursors of suicide (Claassen et al., 2014), such as interpersonal stressors as or hopelessness, might account for more variation in suicidal ideation.

Conclusions

Statistical prediction models coupled with frequent data collected over time could be useful in modeling near-term risk factors for suicidal exacerbations in patients with bipolar II disorder. Mixed states (high energy and low mood) were evident but not specific in predicting subsequent suicidal ideation, yet alterations in subjective energy level appeared to be a stronger and earlier prognostic indicator of near term suicide risk than depressed mood in bipolar II disorder. The methodologic approach described here to combining frequent longitudinal data capture with prediction models referenced to subsequent suicide risk assessments (either gathered in typical panel-type trials or observational studies or, better yet, through intensive data capture methods) could provide a useful tool in the goal of modeling and then targeting near-term risks of suicide such as with real-time technologies that gather intensive longitudinal data (Depp et al., 2016).

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Highlights

- Suicidal risk monitoring in bipolar II disorder is hampered by the limited understanding of near-term precursors to increases in suicidal thoughts
- Intensive longitudinal data, such as gathered by daily diary measures, could be used to model trajectories of potential precursors to exacerbations in suicidal thoughts
- Results from this study indicated that changes in daily-rated mood and energy levels accurately predicted subsequent increases in clinician-rated suicidal thoughts
- Changes in energy, both positive and negative, predated increases in depressed mood, in predicting subsequent increases in suicidal ideation.

Table 1

Sample Characteristics (n=86)

Variable	Mean or %	Range
Age	35.3 (12.8)	19–64
Sex (Female)	63.5%	---
Ethnicity		
Caucasian	83.7%	---
Asian	9.3%	
Other	6.0%	
Education (with at least 1 year college)	88.8%	---
Marital Status (Married)	24.4%	---
Age of First Depressive Episode	17.7 (7.0)	5–47
Number of Lifetime Depressive Episodes	10.8 (19.6)	1–100
Age of First Hypomanic Episode	21.7 (9.8)	1–100
Number of Lifetime Hypomanic Episodes	16.3 (22.1)	1–100
Comorbid Anxiety Disorder (Present)	60%	---
Baseline Hamilton Depression Rating Scale Score	24.5 (4.6)	13–40
Baseline Suicide Risk Rating (Hamilton Item 3 Score)	50%	---
	43%	
	7%	
Score= 0	0%	
Score= 1		
Score= 2		
Score= 3 or 4		

Table 2

Baseline and Longitudinal Models Predicting Hamilton Depression Rating Scale Suicide Item Scores

Baseline Model:				
	Estimate	Std. Error	t-value	p-value
(Intercept)	0.0848417	0.0412480	2.057	0.0401 *
Age x Duration of Depression	0.0008851	0.0001898	4.665	<0.001 ***
Longitudinal Model:				
	Estimate	Std. Error	t-value	p-value
(Intercept)	0.0200765	0.0585546	0.343	0.731807
Age x Duration of Depression	0.0008017	0.0001755	4.569	<0.001 ***
Energy (days T-21 to T-14)	0.3322141	0.0692890	4.795	<0.001 ***
Mood (days T-14 to T-7)	0.2362210	0.0801239	2.948	0.003 **
Energy T21-T14 x Mood T-14-T-7	-0.3712541	0.0997091	-3.723	<0.001 ***
Energy T21-T14 x Mood T-21-T-14	-0.1978566	0.0668002	-2.962	0.003 **

Note: Baseline model $R^2=0.12$ and Longitudinal model = $R^2=0.20$; All other variables were not significant at $p<0.05$ and are not shown.