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Electronic Ecological Momentary Assessment (EMA) in youth with bipolar disorder: Demographic and clinical predictors of electronic EMA adherence

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ABSTRACT

Background: Ecological momentary assessment (EMA) is increasingly used to characterize patients' daily lives, monitor mood, and test efficacy of treatment interventions. However, few studies have examined patient characteristics impacting adherence with EMA protocols, and to our knowledge, no such study has been conducted in youth with bipolar disorder (BD).

Methods: As part of a larger observational study, 14- to 21-year-olds diagnosed with BD, and who were between episodes of illness ($n = 39$, 19.0 ± 2.05 Mean ± Standard Deviation years old, 74.4% female) and psychiatrically healthy controls ($n = 47$, 18.3 ± 2.40 years old, 66.0% female) completed baseline diagnostic and symptom severity interviews, and were instructed to complete diary assessments of mood, sleep, and behavior electronically three times per day for 21 consecutive days (i.e., in total 5418 (or 63 per person) diary entries). Multiple regression was used to examine effects of BD participants' demographic and clinical characteristics on diary completion rates.

Results: 53.8 ± 9.3 diary entries per person were actually completed. Adherence rates were high (87.5% of healthy controls and 80.4% of adolescents with BD), but were still significantly poorer in youth with BD. Adequate adherence (≥80%) rates were also significantly poorer in youth with BD relative to healthy controls (56.4% versus 83.0%). Among youth with BD, more lifetime suicide attempts and higher current mood elevation symptom severity predicted significantly poorer adherence.

Limitations: Limited sample size/generalizability.

Conclusions: Findings highlight the importance of considering the impact of patient characteristics on adherence with EMA protocols among youth with severe mental illness.

1. Introduction

Bipolar disorder (BD) is a chronic and disabling psychiatric disorder that affects 1–4% of the U.S. population (Merikangas et al., 2007), with the majority of onsets occurring by adolescence (Perlis et al., 2004). The impact of BD is particularly devastating when onset is early in life (Leverich et al., 2007; Lewinsohn et al., 2002; Perlis et al., 2004). There is a need for improved detection and treatment of BD in youth.

In recent years, BD detection and treatment strategies have been significantly enhanced by methodological advances in data collection. Ecological Momentary Assessment (EMA) is a data collection methodology that uses repeated sampling to capture real-time activities, cognitions, and/or emotions from participants in their natural environments (Shiffman et al., 2008). Compared to traditional (longer-term, in person) retrospective assessments, EMA minimizes recall bias (Ebner-Priemer and Trull, 2009) and maximizes the ecological validity of data (aan het Rot et al., 2012). Initially applied using paper diaries and/or telephone interviews, EMA has been advanced considerably by the availability of mobile electronic technology. The ubiquity of smartphones has made it possible to employ electronic EMA on a large scale with relatively low costs and high reliability. Over the last decade, EMA has also been increasingly used with clinical populations for tracking illness course and evaluating treatment response. Furthermore, EMA has shown promise as a prognostic tool for detecting real-time shifts in illness thus allowing for "just-in-time" interventions (Depp et al., 2017; Thompson et al., 2014).

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The feasibility of EMA in patients with mood disorders has been demonstrated in adult samples (aan het Rot et al., 2012). Studies have shown that daily assessments were generally well-received by patients (Scharer et al., 2002) and helped patients gain more insight into their symptoms as a result of the daily tracking (Schwartz et al., 2016). Daily patient monitoring using EMA has been successfully applied as a component of traditional treatment interventions for mood disorders (Parrish et al., 2009; Wichers et al., 2011). Psychiatric interventions delivered exclusively through electronic means have also incorporated EMA (Depp et al., 2010; Faurholt-Jepsen et al., 2015; Myin-Germeys et al., 2016).

In contrast, information on the utility and feasibility of electronic EMA in samples of youth with mood disorders is lacking. A recent review of EMA studies in youth with mood disorders identified only 13 published studies (Baltasar-Tello et al., 2018), with all 13 studies using paper diaries or phone interviews for the delivery of EMA. Given the ubiquity of smartphones (especially among youth), and the recent growth in using electronic-based EMA for investigating BD (Matthews et al., 2016), it is rather surprising that there has been no published report on electronic EMA in youth with mood disorders. Nevertheless, the available evidence for EMA studies suggests that this methodology could be successfully used in youth with mood disorders (Axelson et al., 2003).

The use and feasibility of EMA methodology in research and treatment hinges on participant adherence with the EMA protocol. However, the available data on adherence with EMA protocols in youth suggest adherence rates are sub-optimal. Two reviews of studies that used EMA in mostly non-clinical samples of youth (age $\leq$18 years old) reported an average adherence rate of 76% and 78%, respectively (Heron et al., 2017; Wen et al., 2017). Although reasons for non-adherence are rarely assessed, both reviews noted the importance of scheduling momentary assessments at times that were convenient for participants, limiting number of questions, using prompts/alarms, providing incentives for completion of diaries, and incorporating training in how to complete diaries (Heron et al., 2017).

Daily tracking of mood and behavior has potential to help patients with BD manage illness course, and would be particularly useful to implement early in the course of BD. However, in order to do so, we first have to assess young patients' ability to track mood and behavior daily, and understand the factors impacting adherence. Accordingly, the aim of our study was to assess adherence with a smartphone-based EMA protocol, and participant characteristics associated with adherence, in a sample of youth who were diagnosed with BD, relative to healthy controls.

2. Method

2.1. Participants and procedure

Participants were 14–21 years old, fluent in English, and were recruited from the San Francisco Bay Area community. The Stanford University Administrative Panel on Human Subjects in Research approved all study procedures, and all subjects provided written consent/assent prior to participations.

Participants were initially screened for likelihood of meeting the study's eligibility criteria (described below) with a phone interview. Potential participants who appeared likely to meet the study's eligibility criteria were invited for a lab visit to complete in-person interviews. Those aged 18 and older provided written informed consent. If less than age 18 years, youth provided written assent and parents provided written informed consent.

Eligible participants were requested to complete 63 ($=3 \times 21$ days) brief electronic diaries delivered to their personal smartphones via text messages containing links to online surveys assessing mood, sleep, and behavior, three times per day (morning, afternoon, evening) over 21 consecutive days. Text messaging schedules were constructed collaboratively with participants to accommodate participants' schedules. Participants were instructed to respond within a 2-h window of the receipt of each text message. Participants were familiarized with the diary during the in-person visit. Participants were paid $65 for the in-person visit and $20 per week for completing at least 80% of diary assessments, for a total of $60 over the three-week study period. As a disincentive for non-adherence, $5 was deducted for each 5% reduction in diary completion (e.g., participants who completed 75% of diaries were paid only $55).

Participants were included in the BD group if they met diagnostic criteria for bipolar I disorder or bipolar II disorder based on the Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (APA, 2000) and were inter-episode at study entry (i.e., no current (past-month) depressive, manic, hypomanic, or mixed episode). Control group individuals were eligible if they did not meet diagnostic criteria for any DSM-IV Axis I disorder and had no first-degree relative with a lifetime history of mood disorder or psychosis, as assessed in one parent.

Exclusion criteria included a history of neurological or developmental disorders, head injury with loss of consciousness for over 5 min, or seizures. Exposure to psychotropic medications was an exclusion criterion for control group participants. Participants in the BD group were not excluded for current use of psychotropic medication(s) nor on the basis of current comorbid psychiatric diagnoses, with the exception of alcohol or substance abuse/dependence in the previous six months.

2.2. Measures

Psychiatric diagnosis and current mood symptoms. Current and lifetime psychiatric disorders were assessed using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Kaufman et al., 1997), administered separately to participants and their parents for youth under age 18 years, and the Structured Clinical Interview for DSM-IV (SCID-IV) (First et al., 2007), administered for youth over age 18 years.

The Family History-Research Diagnostic Criteria (FH-RDC) (Andreasen et al., 1977) was administered to assess history of mood disorder or psychosis in first-degree relatives of control group participants.

The Children's Depression Rating Scale-Revised (CDRS-R) (Poznanski and Mokros, 1995) and the Young Mania Rating Scale (YMRS) (Young et al., 1978) were used to assess current depression and mania symptom severity.

EMA. Momentary assessments of self-reported mood, sleep, and behavior (e.g., "What is the main activity you are engaged in right now?") were administered using electronic diaries. The results of sleep and mood data are described elsewhere (Gershon et al., in preparation). Adherence rate was calculated for each participant as the proportion of diary entries completed within the 2-h window, relative to the total number of diaries delivered.

2.3. Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Science (SPSS v23.0, IBM Corporation, *Armonk, New York*) software on an Apple MacBook Pro computer (Apple Corporation, Cupertino, CA). Log transformations were used to normalize variables as needed. Group differences (BD versus healthy controls) on demographic variables and clinician-rated symptoms (CDRS-R and YMRS) were tested using t-tests for continuous variables and chi-square tests for categorical variables. Bivariate correlations were used to examine whether demographic or clinical variables were related to adherence. Youth with BD versus healthy controls were compared on adherence rates using t-tests and on adequate adherence ($\geq$80%) rates using chi-square analyses. A regression model was used to test the effects of demographic and clinical variables on adherence.

Table 1
Sample Demographic and Selected Clinical Characteristics.

	Bipolar Disorder (n = 39)	Healthy Control (n = 47)	χ^2 or t value	p value
Age in years, Mean (SD)	19.0 (2.1)	18.3 (2.4)	1.4	0.2
Female gender, n (%)	29 (74.4)	31 (66.0)	0.7	0.5
White ethnicity, n (%)	26 (66.7)	24 (51.0)	2.1	0.2
Annual household income < $140,000, n (%)	19 (48.7)	11 (23.4)	7.6	0.006
Bipolar disorder type I/II, n (%)	28 (71.8)/11 (28.2)	–	–	–
Illness duration, in years, Mean (SD)	6.3 (3.8)	–	–	–
No. of past suicide attempts, Mean (SD)	**0.5 (0.9)**	**–**	**–**	**–**
CDRS-R score, Mean (SD)	25.8 (7.0)	17.8 (1.1)	7.8	< 0.001
YMRS score, Mean (SD)	**3.8 (3.9)**	**0.46 (0.8)**	**5.8**	**< 0.001**

Note. SD = standard deviation. CDRS-R = Children's Depression Rating Scale – Revised; YMRS = Young Mania Rating Scale.
Three bipolar group participants had missing data for annual household income. **Bold font** indicates statistically significant relationships with electronic EMA adherence. Underlined font indicates t- (rather than χ^2) values.

3. Results

Demographic and selected clinical characteristics are presented in Table 1. Our sample included 39 youth with inter-episode bipolar I disorder or bipolar II disorder (Mean ± Standard Deviation age = 19.0 ± 2.1 years, 74.4% female) and 47 healthy youth with no history of psychiatric disorders, and with no first-degree relative with a history of mood disorders or psychosis (age = 18.3 ± 2.4 years, 66.0% female). The BD and control groups did not differ with respect to demographic characteristics except for household income, which was significantly lower among BD versus healthy controls (Chi-Square = 7.62, df = 1, p = 0.006).

As expected, BD group participants scored significantly higher on the CDRS-R and YMRS than did healthy controls. Thirty-three of 39 BD group participants (84.6%) and none of 47 control participants (0.0%) were taking psychotropic medications (Chi-Square = 68.7, df = 1, p < 0.001). Seventeen of 39 BD group participants (43.6%) and none of the control group (0.0%) had at least one comorbid lifetime psychiatric diagnosis (Chi-Square = 38.5, df = 1, p < 0.001).

Table 2 presents EMA adherence and adequate EMA adherence rate (≥80% EMA adherence) for youth with BD and healthy controls. The BD and control groups both had relatively high EMA adherence rates (87.5% and 80.4%, respectively). However, the BD versus healthy control group had significantly poorer EMA adherence (t (84) = 2.63, p = 0.011, Cohen's d = 0.58, actual power = 0.76). The BD versus healthy control group also had significantly fewer participants who achieved adequate EMA adherence rates (≥80% EMA adherence) (56.4% versus 83.0%, Chi-Square = 7.30, df = 1 p = 0.007).

Table 3 presents results of the linear regression analysis with electronic EMA adherence rate as the outcome index and with demographic and clinical variables entered as predictors. The overall model was statistically significant and accounted for 45.8% of the variance in adherence (F (9,26) = 2.45, p = 0.03). As shown, only a greater number of past suicide attempts and higher current (hypo)mania scores significantly predicted poorer EMA adherence in the BD group. No other variable yielded statistical significance.

4. Discussion

To our knowledge, our study is among the first to demonstrate mostly adequate electronic EMA adherence among youth with BD completing smartphone-based thrice-daily electronic diaries administered over three weeks. Our findings also demonstrate that the presence of more severe (hypo)manic symptoms, even while participants were inter-episode, and a lifetime history of more suicide attempts significantly predicted poorer electronic EMA adherence among BD youth. Taken together, these findings suggest that although using electronic EMA-based methods over multiple weeks was feasible in youth with BD, investigators should consider illness severity as a potential predictor of participants' ability to adhere with electronic EMA protocols.

In our study, the BD and control groups achieved electronic EMA adherence percentiles (80.4% and 87.5%, respectively) which were relatively high compared to similar pen and paper EMA-based protocols with youth (Heron et al., 2017; Wen et al., 2017). Previous reviews of pen and paper EMA studies in youth have noted that accommodating participants' schedules, limiting the number of questions per entry, using prompts, and providing incentives for timely diary completion, can enhance EMA adherence (Heron et al., 2017). Our study applied each of these strategies, which may have contributed to our relatively high adherence percentiles for both groups.

Nevertheless, youth with BD showed significantly poorer adherence with electronic EMA completion than did age- and gender-matched healthy controls. To our knowledge, our study is among the first to test the participant characteristics that affected EMA adherence rates in BD youth, and points to current mood elevation severity and lifetime suicide history as important predictors of electronic EMA non-adherence. Reporting adherence rates and identifying factors that impact adherence will be necessary if we hope to improve design of future electronic EMA studies in clinical samples (Fleming et al., 2018), and develop retention strategies that improve data quality.

In addition, it will be important to consider the type of missingness that occurs in electronic EMA studies. Data that are missing completely at random may result in less biased averaged estimates when compared to missingness that is conditional on other variables (Wen et al., 2017). Our findings suggest that among youth with BD, there are systematic differences in missingness of electronic EMA data based upon participants' illness severity suggesting that this variable needs to be considered in studies. Future studies must develop methods to prevent missing data. These may include additional reminders to complete assessments, engagement of family members in the EMA protocol, shorter

Table 2
Group Differences in Electronic Ecological Momentary Assessment Adherence.

	Bipolar Disorder (n = 39)	Healthy Control (n = 47)	t or χ^2	p value
EMA adherence percentile, Mean (SD)	80.4 (15.1)	87.5 (8.2)	2.6	0.01
Adequate EMA adherence rate, n (%)	22 (56.4)	39 (83.0)	7.3	0.007

Note. Adequate EMA adherence was defined as having completed ≥80% of entries. Underlined font indicates t- (rather than χ^2) value.

Table 3
Linear Regression Using Demographic and Selected Clinical Characteristics to Predict Rate of Adherence Among 39 Bipolar Youth Across 21 days *of Electronic Ecological Momentary Assessment.*

Predictors	Bivariate Models			Multivariate Model		
	β (SE)	t value	p value	β (SE)	t value	p value
Age in years	0.008 (0.006)	1.4	0.2	−0.001 (0.01)	−0.08	0.9
Female gender	0.05 (0.03)	1.8	0.08	0.09 (0.05)	1.6	0.1
Non-White ethnicity	−0.04 (0.03)	1.3	0.2	−0.08 (0.05)	−1.6	0.1
Income < $140,000	−0.3 (0.03)	−0.9	0.4	−0.04 (0.04)	−0.8	0.4
BD-I	−0.04 (0.05)	−0.7	0.5	0.05 (0.05)	1.0	0.3
Illness duration in years	0.007 (0.006)	1.1	0.3	0.01 (0.006)	1.7	0.1
No. past suicide attempts	**−0.06 (0.03)**	**2.1**	**0.04**	**−0.14 (0.05)**	**−2.7**	**0.01**
CDRS-R score	−0.09 (0.05)	1.7	0.09	−0.05 (0.09)	−0.6	0.6
YMRS score	**−0.05 (0.02)**	**3.2**	**0.002**	**−0.06 (0.03)**	**−2.2**	**0.04**

Note. BD-I = bipolar I disorder; CDRS-R = Children's Depression Rating Scale – Revised; YMRS = Young Mania Rating Scale. β is the unstandardized parameter estimate. Multivariate model adjusts for all covariates in table. **Bold font** indicates relationships with electronic EMA adherence rates that remained statistically significant with linear regression.

assessments to reduce participant burden, and the use statistical techniques that deal with this limitation beyond imputation for data that are missing at random.

Several limitations of the current study should be noted. First, this study is based on a small sample of youth followed for a brief time period. Evaluation of factors impacting adherence with electronic EMA, especially in chronic disorders, likely requires longer assessment periods allowing for more variability in symptom profiles including syndromal episodes. Second, the BD group had significantly lower household income than healthy controls. Given that participants were paid for their participation, the BD group may have been more incentivized than were controls, contributing to the relatively high adherence rates observed in the BD group. Third, daily measures were not standardized for EMA use, per se. This limitation is not unusual in EMA research (aan het Rot et al., 2012). Fourth, youth with BD (but not healthy controls) were taking various psychotropic medications, and our study lacked a pen and paper EMA comparator. Finally, this study did not include data passively collected from smartphones and sensors (e.g., physical movement, use of social media). Passive data have been shown useful in assessing key dimensions of BD (Faurholt-Jepsen et al., 2016), and may ultimately reduce the need for extensive EMA collected via self-report or diary.

Despite these limitations, the current findings provide evidence that electronic thrice-daily monitoring can be successfully implemented with BD youth over a three-week period and highlight the importance of considering clinical characteristics of participants with regard to electronic EMA adherence. Empirically supported psychotherapeutic interventions for BD commonly integrate the use of daily monitoring (Miklowitz, 2006), yet the utility of this monitoring depends upon adherence. Research is urgently needed to assess strategies for improving adherence—possible examples being the types of data collection software, diary lengths, and number of diary entries per day. Previous reports of EMA-based protocols have noted that daily monitoring could assist in fostering insight and engagement for patients (Scharer et al., 2002). Thus, ensuring that electronic EMA-based protocols are optimal for patient adherence could have far-reaching benefits in research and treatment.

Conflicts of interest

Drs. Gershon, Kaufmann, Torous, and Depp report no financial relationships with commercial interests. Dr. Ketter has received grant/research support from the Agency for Healthcare Research and Quality, AstraZeneca Pharmaceuticals LP, Cephalon Inc., Eli Lilly and Company, National Institute of Mental Health, Pfizer Inc., and Sunovion Pharmaceuticals; Consultant Fees from Allergan, Inc., Avanir Pharmaceuticals, Bristol-Myers Squibb Company, Cephalon Inc., Forest Pharmaceuticals, Janssen Pharmaceutical Products, LP, Merck & Co., Inc., Neurocrine Biosciences, Sunovion Pharmaceuticals, and Teva Pharmaceuticals; Lecture Honoraria from Abbott Laboratories, Inc., AstraZeneca Pharmaceuticals LP, GlaxoSmithKline, and Otsuka Pharmaceuticals; and Publication Royalties from American Psychiatric Publishing, Inc. In addition, Dr. Ketter's spouse is a former employee of and still holds stock in Janssen Pharmaceuticals.

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