Psychiatry Research 270 (2018) 253–256

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Time-lagged predictors of daily medication nonadherence beliefs during the month post-hospital discharge in patients with psychotic–spectrum disorders

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ARTICLE INFO

Keywords:
Psychosis
Medication adherence
Ecological momentary assessment

ABSTRACT

We used ecological momentary assessment (EMA) to examine the period following hospitalization when risk for medication nonadherence is highest among patients with psychotic–spectrum disorders. EMA data were collected daily via smartphones from 23 patients with psychotic–spectrum disorders (totaling 1149 surveys) in the month immediately following discharge. Nonadherence beliefs significantly correlated with percentage of medication doses. Time-lagged increases in irritability, sadness, life dissatisfaction, functional impairment, and previous day missed medication dose predicted subsequent increases in nonadherence beliefs over time. Future research should study mobile interventions that target the factors found to predict nonadherence beliefs to improve post-hospital recovery.

1. Introduction

Upwards of 50% of patients with psychotic-spectrum disorders (PSD) are nonadherent to medications and also exhibit high levels of treatment drop out (Staring et al., 2010). Furthermore, risks for medication nonadherence and treatment discontinuation are elevated in individuals with PSD in the period immediately following a psychiatric hospitalization (Bergen et al., 1998). Ecological momentary assessment (EMA) allows for convenient in vivo assessment obtained daily via mobile devices (e.g., smartphones). Previous research documents that EMA is feasible and acceptable for patients with PSD, either when completed in inpatient settings with more acutely ill individuals or on an outpatient basis in more stable community samples (Kimhy et al., 2014).

The current investigation is an analysis of data from a larger study testing the feasibility and acceptability of EMA in patients with psychosis leaving the hospital (Moitra et al., 2017). In this previous study, we found EMA completion rates similar to those reported in other studies using acutely ill samples. The vast majority of participants reported being mobile phone users already (97%), and most had their own smartphones (65%). A total of 76% of the sample completed EMA surveys at 1 month follow-up. Those completing EMA responded to an average of 30% of daily surveys over a one month period, which represented an average of 1 EMA survey per day. Usability and likability of EMA also was high in the study. Mean positive attitude score was 4.0 (SD = 0.79) and mean negative attitude score was only 2.0 (SD = 0.78) on a scale from 1 to 5. Feedback from qualitative exit interviews was mainly positive. EMA was seen as having the potential to help participants increase their awareness of symptoms and their management. Negative comments primarily related to technical problems stemming from the earlier version of the mobile device used in the study.

The current study examined completed daily EMA surveys assessing medication nonadherence beliefs, symptoms, affect and other relevant variables (life dissatisfaction, impairment, medication side effects) via mobile devices over the first month post-discharge. Specifically, we examined time-lagged predictors of daily medication nonadherence beliefs in the subset of the sample with consecutive daily EMA surveys available for testing. We examined nonadherence beliefs as a proxy for actual medication nonadherence. We reasoned that nonadherence beliefs would be related to future missed medication doses, but would represent a more dynamic and fluctuating variable to assess via frequent EMA surveys compared with actual medication adherence (which may be less likely to occur on a daily basis). Nonadherence beliefs were rated on a Likert scale at every EMA survey, which gave us more variability in our analyses and thus, greater statistical power to find

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https://doi.org/10.1016/j.psychres.2018.09.048
Received 22 January 2018; Received in revised form 24 August 2018; Accepted 20 September 2018
Available online 21 September 2018

effects. In contrast, missed medication dose represented a categorical outcome that would not be expected to be endorsed as frequently. Furthermore, we reasoned that nonadherence beliefs would be a useful construct to assess clinically because these beliefs may be amenable to psychosocial interventions that target negative cognitions. We further compared EMA-rated nonadherence beliefs with actual medication nonadherence at 1 month follow-up. In the current investigation, we hypothesized that earlier increases in positive psychotic symptoms, negative affect, functional impairment, life dissatisfaction, and medication side effects would predict later increases in nonadherence beliefs, and that nonadherence beliefs would be related to actual missed medication doses over the past month.

2. Method

2.1. Participants

Details of study methods have been previously reported (Moitra et al., 2017). Eligibility criteria were: (a) currently hospitalized (inpatient/partial psychiatric hospital); (b) DSM-5 criteria for a schizophrenia-spectrum disorder or a mood disorder with psychotic features based on Structured Clinical Interview for DSM-IV (SCID); (c) 18 years or older; (d) prescribed oral antipsychotic medication; and (e) ability to speak/read English sufficiently to complete the assessments. Exclusion criteria were: (a) discharge to supervised setting or use of medication packaging; (b) pregnancy or a cognitive disorder (e.g., dementia) contraindicating antipsychotic use; or (c) homelessness.

2.2. Measures

We used an open-source software package to design and administer our EMA protocol on Windows mobile devices provided to patients as part of the study. EMA consisted of up to 4 surveys daily, each taking 5–10 min to complete. Consistent with typical EMA methodology, we only administered key items of interest from more comprehensive measures to keep the surveys as brief as possible. EMA items included: (1) positive psychotic symptom severity total (0 = “not at all” to 4 = “very much”) that assessed paranoia, mind reading, thought insertion, special messages, and special powers (Granholm et al., 2012); (2) positive (happiness) and negative (irritability, sadness, nervousness) affect (0 = “very slightly or not at all” to 4 = “extremely”), using items from the Positive and Negative Affect Schedule (Watson and Clark, 1994); (3) medication side effects (0 = “not at all” to 1 = “extremely bothered”) (Dibonaventura et al., 2012); (4) life dissatisfaction (0 = “very dissatisfied” to 4 = “very satisfied”) using an item from the World Health Organization Quality of Life-BREF (Skevington et al., 2004); (5) and functional impairment (0 = “not at all” to 4 = “very severely”), using an item from the WHO Disability Assessment Scale-II (Federici et al., 2009). (6) We also measured medication beliefs via EMA by summing items (0 = “not at all” to 4 = “very much”) from the Drug Attitude Inventory (DAI) (Nielsen et al., 2012) assessing nonadherence reasons: ran out, could not afford, do not need to take, forgot to take, makes me feel strange, not helpful, do not trust doctor, and embarrassed to take (Cronbach's $\alpha = 0.77$). (7) Finally, we asked patients via EMA to report whether or not they missed any medication doses since the last assessment.

In addition to EMA surveys, at 1-month post-discharge, we administered the Brief Adherence Rating Scale (BARS) interview (Byerly et al., 2008) to determine percentage of antipsychotic medication doses taken/prescribed over that period of time. Additional assessments were administered as part of the study that are not analyzed here.

2.3. Procedures

The study was approved by the Butler Hospital IRB. Recruitment occurred during patients' psychiatric inpatient or partial hospitalization. Potentially eligible patients were approached after obtaining permission from the attending physician, and written informed consent was obtained. Assessors were trained to initial reliability ($\kappa > 0.80$) on the SCID, and then reviewed weekly by the study investigators. Patients were given the mobile device and were trained to use it prior to hospital discharge, and began using it as soon as they left the hospital.

Table 1
Prior-day (t-1) EMA predictors of nonadherence beliefs for fixed-effects multilevel modeling at time t, controlling for prior-day nonadherence beliefs.

Fixed effects	Coefficient	SE	T-value	P-value
Missed Medication Dose	−2.192	0.736	−2.977	0.004*
Impairment	0.640	0.251	2.550	0.012*
Sadness	3.135	1.297	2.416	0.017*
Irritability	2.859	1.312	2.179	0.031*
Life Satisfaction	−0.511	0.243	−2.097	0.039*
Psychotic Symptoms	−1.257	0.770	−1.633	0.106
Nervousness	0.608	0.395	1.536	0.127
Happiness	−0.573	0.363	−1.580	0.117
Medication Side Effects	0.218	0.446	0.490	0.625

* $p < 0.05$

2.4. Analyses

Skewed continuous variables were corrected using log10 transformations prior to analysis. Multilevel modeling (MML) was used to evaluate lagged behavioral and affective predictors of nonadherence beliefs over the month immediately after hospitalization. To create time-lagged variables, variables from one day prior were shifted to one subsequent time point in order to model for prior-day predictors. The dependent variable used in all models was the total of nonadherence belief items assessed during EMA. The model included a fixed effects regression of individual intercepts modeling adherence beliefs while controlling for prior-day predictor variables and prior-day nonadherence beliefs. Time-lagged analyses only included responses one day apart from one another. These time-lagged prior-day (t-1) predictors were modeled separately (due to smaller sample size) in a hierarchical linear model using a restricted estimated maximum likelihood estimator approach and autoregressive covariance structure. Random effects modeling individual variation in slope were removed from the analysis, as only within-person fixed effects were examined in this study. We chose not to center our variables because they were ordinal (not continuous), they did not have true zero point, and we were not examining interactions among the variables. We were most interested in individual variability (not variation around the individual's mean), and centering would have obscured these effects. All models assumed a linear trajectory with alpha set at $P < 0.05$ (two-tailed).

3. Results

In the “parent study” (Moitra et al., 2017), 49 patients returned the device at 1 month follow-up and 37 completed EMA surveys. In the current analysis, of the 37 who completed surveys, 12 participants were excluded due to completing too few surveys for use in time-lagged analysis (≤10 surveys). The remaining 23 participants were examined and completed 1,149 surveys (M = 50; SD = 27). Multiple survey responses completed over one day were averaged to create one survey per person per day, resulting in 434 surveys for analysis. The sample ($N = 23$) used for analysis was 78% (N = 18) female, with a mean age of 40 years (SD = 10.3). The sample was 78% ($N = 18$) white and 9% ($N = 2$) Latino/Hispanic. Educational attainment was 65% ($N = 15$) high school graduate or above; 26% ($N = 6$) were married; and 69% ($N = 16$) received psychiatric/physical disability income.