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Abstract

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Purpose. The current study evaluates whether patients are more adherent to morning versus evening doses of medication and if morning doses show evidence of greater habit strength than evening doses.

Methods. Objective adherence data (exact timing of pill dosing) were collected in an observational study by electronic monitoring pill bottles in a sample of patients on twice-daily pills for Type 2 diabetes (N = 51) over the course of 1 month.

Results. Data supported the hypothesis that patients would miss fewer morning than evening pills. However, counter to the hypothesis, variability in dose timing (an indicator of habit strength) was not significantly different for morning versus evening pills.

Conclusions. Findings suggest that medication adherence may be greater in the morning than in the evening. However, more research is needed to evaluate the role of habitual action in this greater adherence. Furthermore, future research should evaluate the validity of behavioral timing consistency as an indicator of habit strength.

Keywords

Medication adherence, Objective data, Habit strength, Habitual behavior, Medication Event Monitoring Systems

Disciplines

Applied Behavior Analysis | Health Psychology | Psychology

Comments

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Time-of-Day Differences in Treatment-Related Habit Strength and Adherence

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Many of the behaviors that individuals engage in on a daily basis are *habitual*, that is, occurring automatically in response to learned contextual cues [1, 2]. Recent research has focused on the importance of behavioral habit strength for health and other outcomes [3, 4]. This focus is warranted by both the theoretical and empirical importance of habits for behavioral engagement and outcomes: theory states that habits promote health behavior engagement and maintenance because they are nondeliberative, relatively efficient, frequent, and do not tax cognitive and self-regulatory resources to enact [5]. Empirical evidence shows that behavioral habit strength predicts behavior incrementally to (and in some cases more strongly than) conscious, reflective factors, such as behavioral intentions and beliefs or attitudes [6, 7].

Treatment nonadherence is pervasive, with an estimated 50% of patients not adhering to daily medications for chronic illness management, and it contributes substantially to unnecessary health care costs [8, 9]. Recent research has demonstrated the importance of medication-taking routines, or habits, for long-term adherence to treatments in several chronic illness domains (asthma: [10, 11]; Type 2 diabetes: [6]; hypertension: [12, 13]). Therefore, researchers are now testing interventions to promote habit development (e.g., [14]), which could be used to improve treatment adherence. Simple, universal strategies have shown some promise at helping

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individuals form new habits and break bad habits. For example, making action plans (e.g., “When I make coffee in the morning, then I will take my pills”) have helped individuals increase their level of physical activity, change their diets, and quit smoking (see [15] for a review). These interventions may be tailored to each individual’s own goals and contexts (e.g., choosing meaningful, feasible, and personal cues for action). Piggybacking is a similar technique for forming a new habit that entails combining a new behavior with an existing habit or sequence of habitual actions (e.g., pairing flossing with one’s teeth-brushing routine; [16]).

To-date, few researchers have investigated the possible influence of time-of-day (morning vs. evening) on successful habit formation. Differences in habitualness throughout the day could determine when it would be best to implement action plans. For example, piggybacking may be more successful if the timing coincides with an individual’s most highly structured/repetitive time of day. Although no one has tested this in the published literature, contexts (such as activities and location) may be more or less stable in the morning than in the evening. Anecdotally, one might expect individuals to have a stable time they get up in the morning because of work schedules but have a more variable dinner and bed time, depending on how the rest of the day unfolds (e.g., with disruptions in plans that may be more likely to occur as time passes). Unpublished data from Wood et al. [2] indeed demonstrate that individuals showed their greatest number of habitual actions occur in the morning versus in the evening (with an average spike in habitual behavior between 7 and 9 AM; *personal communications with study authors*). Further, Domke et al. [17] found that action-plan enactment was highest in the morning and decreased throughout the day, causing the authors to speculate that behavioral routines are more stable in the morning. Lastly, research by Fournier et al. [18] found that participants were quicker to form a simple habit (doing a stretch) when this was done in the morning compared to evening, potentially due to a facilitative effect of higher cortisol levels in the morning on habit formation.

Regarding time-of-day effects on treatment adherence, there are only two small studies, to our knowledge, that evaluated whether morning or evening routines were associated with greater adherence. Both studies were conducted with patients on glaucoma medications. Kahook and Noecker [19] determined that nonrandomly assigned patients with morning routines had fewer missed days of treatment than patients with evening routines, although overall adherence was not significantly different between groups. Ford et al. [20] randomly assigned patients to a morning or evening routine and found that, although patients reported preferring the morning routine, there was no statistically significant difference in adherence by time

of day. Lastly, although Ford et al. [20] had every participant try a morning and an evening routine (1 month each; counter-balanced and randomly assigned order), their study design did not allow for a direct comparison within subject of morning versus evening routines; that is, trying one routine before another necessarily introduces problems associated with forming a routine and then having to change that routine in order to try the alternative timing of the routine.

Existing research is limited in evaluating time-of-day factors because of the way habits and behaviors are typically measured, which is not specific to a particular time of day. For example, habit strength is measured with self-reports of the perceived automaticity or context stability of a particular action without reference to specific timing or context (e.g., “Taking my pill is something I do automatically: strongly disagree to strongly agree”; [21]). Furthermore, measures that ask whether individuals engage in the behavior at the same time and in the same location each day (e.g., [22]) assume that there is only one relevant time point (behavior is done only once per day) and/or do not evaluate time-of-day effects. Most adherence data similarly do not allow evaluations of intraindividual differences, particularly on a daily measurement level, since they utilize patient-reported adherence measures as outcome variables (e.g., “In the past week, how many pills did you miss?”). Objective data from electronic monitors allow a fine-tuned and specific time-of-day look at adherence to medications and habitualness (consistency) in pill timing. First, morning activity can be separated from evening activity objectively. Second, exact timing and consistency of timing across days can be measured for each individual. The latter use of the monitors offers a proxy for habit strength. This use of time consistency (i.e., lower levels of variance in timing) as a measure of habit strength is supported by theory and evidence in the literature (e.g., [2, 22, 23]). Hoo et al. [23] recently utilized electronic data capture (EDC) from nebulizers to create a habit index created from the product of the timing stability of nebulizer use over a week’s time period with adherence (% of days nebulizer used). Although this index utilized time stability as part of its calculation, a limitation of the index is that it also uses frequency of behavior in its calculation, which will be related to subsequent behavioral frequency for reasons other than habit strength (e.g., deliberative adherence mechanisms).

The purpose of the current study was to utilize an existing, rich data set that can evaluate the relationship between the time of day and behavioral frequency and habit strength—namely, whether medication adherence depends on dosing timing and whether there is evidence of greater habit strength in pill-taking behavior, operationalized as lower variation in the time a pill is taken from day-to-day (greater consistency of

pill timing indicating stronger routine/habit formation). Data from Medication Event Monitoring System bottles (MEMS bottles) in a sample of patients on twice-daily pills for Type 2 Diabetes were used to test the following hypotheses: For patients taking two pills per day [1], the number of missed doses (i.e., medication nonadherence) will be significantly greater for the evening dose than the morning dose, and [2] the variability (variance) in time the pill is taken will be significantly greater for the evening dose than the morning dose (i.e., habit strength will be weaker in the evening vs. morning).

Method

Participants and Procedure

Data are from an archived data set that utilized MEMS bottles for measuring patients' adherence to medication. The data set has MEMS data for patients on Type 2 diabetes medication (pill form; e.g., Metformin). Twenty-five patients in this data set were on a once-daily regimen and are excluded from analyses, which are within-person comparisons. Fifty-one patients were on a twice-daily regimen and were used to test the hypotheses. More details on the sample and procedure can be found in [6]. The analyses conducted in this paper are post hoc analyses of only the MEMS data and do not repeat any of the published relationships.

In the study, patients were recruited via patient records and were on existing treatments for their Type 2 diabetes. Participants ranged in age from 30 to 70 years of age, approximately 50% completed a bachelor's degree or higher education level, and a majority self-identified as Black/African heritage (70%) and female (59%).

Measures

Four variables were created [1]: the number of missed doses in the morning was calculated to represent adherence to morning doses [2], the number of missed doses in the evening was calculated to represent adherence to evening doses [3], the patients' variance in morning pill timing was calculated to represent [lack of] habit strength in taking the morning dose, and [4] the patients' variance in evening pill timing was calculated to represent [lack of] habit strength in taking the evening dose. Although MEMS software (Powerview) allows export of exact times, the pill bottles were open, two coders went through these data to ensure that times were appropriately allocated to morning versus evening doses. The coders were in agreement on 98% of cases. One patient had such highly variable data (times on which he/she took the "morning" and "evening" pills) that it was

difficult to assign "morning" versus "evening" status to pills that were taken or missed. This patient is one of the two univariate outliers on pill-timing variance, and so results were determined with and without his/her inclusion in the data as described below.

Baseline data from the Self-Reported Behavioral Automaticity Index (SRBAI; 21) were used to evaluate whether the variance measures of pill timing had convergent validity with a widely used measure of habit strength. This self-reported measure was not specific to time of day ("Taking my medication is something I do automatically: strongly disagree (=1) to strongly agree (=5)" rather than "Taking my *morning/evening* dose is something I do automatically") and so could not be used to test the hypotheses, which are regarding morning- and evening-specific pill-taking habit (within-person).

Statistical Analyses

The data are first evaluated for univariate and multivariate outliers. In the case of outliers, the data are analyzed with and without the outliers included as recommended in recent literature on data transparency and reproducibility [24]. The hypotheses are tested with paired samples *t*-tests for the difference between patients' morning and evening missed pills and between patients' morning-dose timing variance and evening-dose timing variance, respectively.

Results

There were $N = 51$ patients on twice daily regimens with MEMS data. The modal number of days observed was 28 days, mean of 27.8 days, ranging from 17 to 31 days. There were two univariate outliers (determined as having variances greater than 3 standard deviations [*SDs*] from the mean) in pill-timing variance. Skewness and Kurtosis values were high only for the pill-timing variance variables. When the outliers are removed, the skewness and kurtosis are acceptable. Variance in pill timing (both morning and evening) significantly correlated with self-reported behavioral automaticity, with correlations ranging between -0.24 and -0.40 (correlations were stronger when outliers were removed). Results are presented with and without outliers, when exclusion of outliers meaningfully influenced the results.

Hypothesis 1

As hypothesized, the number of missed doses in the evening (average = 5.27 pills, $SD = 6.01$) was significantly greater than the number of missed doses in the morning (average = 3.96 pills, $SD = 4.62$): paired samples $t(50) = -2.41, p = .02$, (two-tailed), Cohen's $d = 0.34$.

Hypothesis 2

The variability in dose timing did not significantly differ between patients' morning and evening doses. With outliers excluded, the average variance for the morning dose = 6.26 min ($SD = 4.12$ min) and for the evening dose = 6.54 min (6.07 min) had a nonsignificant paired t -test: $t(48) = 0.36$, $p = .72$ (two tailed) and a Cohen's $d = 0.05$. With outliers included in the data, the average variance for the morning dose = 6.70 min ($SD = 4.70$ min) and for the evening dose = 7.26 min ($SD = 7.46$ min) had a nonsignificant paired t -test: $t(50) = 0.59$, $p = .56$ (two tailed), Cohen's $d = 0.08$.

Discussion

Behavior is determined through automatic and conscious processes [3, 5]. Individuals may take medications out of habit and/or because of purposeful intentions to do so. Although researchers talk about habits versus nonhabits, habit strength is theoretically a continuum, and so behavioral action is likely multidetermined, particularly in real life, for which contexts are not always perfectly stable [2].

In the current study, it was proposed that individuals on twice-daily, oral diabetes medication would be more adherent and more behaviorally consistent (have greater habit strength) in the morning than the evening. Regarding medication adherence, results indeed showed that there were fewer missed pills in the morning than in the evening within person. Participants did not report issues in using the MEMS bottles that might offer an alternative explanation for these findings, but this is nonetheless possible. In the future, researchers should explicitly ask whether patients used this or other strategy that could have interfered with the validity of the MEMS data.

Regarding habit strength, data did not strongly support the hypothesis that habit strength for taking the morning pill would be greater than habit strength for taking the evening pill. There are several possible explanations for why the variability in pill timing for the morning pill was statistically equivalent to variability in pill timing for the evening pill. First, it is possible that the effect of time-of-day on habit is too small to detect statistically with a small sample. Second, the greater number of missed doses in the evening could plausibly have been due to a weaker habit in the evening as hypothesized, but any doses that were taken could have been taken in line with that weaker habit. That is, instead of variance in timing indicating weaker habit, the missed pills could themselves be indications of weaker habit (existence of disrupted, weaker routines). Third, the greater adherence in the morning may not have been due to stronger habits of pill taking but rather greater cognitive resources in

the morning, such as self-regulation [25] or the presence of other habits [2], which would free cognitive resources for deliberative behaviors (such as remembering to take a pill).

Lastly, operationalizing habit strength as time consistency may not be appropriate. Individuals may have tied taking a pill to a consistent routine, such as making coffee in the morning, or hygiene-related routines, but these routines themselves may have occurred at different times of the day across days. Taking pills could, therefore, still be habitual and even more habitual in the morning and, when evening habits were disrupted, the pill was forgotten entirely rather than remembered and taken at a later time (and so habit strength would be reflected in the number of missed pills but not variation in timing of the pills actually taken). This has potential implications for the habit field in general for habit strength assessment. Specifically, if the contexts that cue habitual actions are not tied to specific and stable times of day, then objective behavioral monitors may not provide valid measures of habit strength since they currently focus on behavioral timing (i.e., consistency of timing across days as in the current study). More complex objective assessment of behavioral patterns may potentially be developed that include action location or allow assessment of preceding actions in combination with behavioral timing. These more complex behavioral patterns located within repeating contexts (that are not necessarily tied to a specific time of day) could potentially be used to assess habit strength and habit development over time. For example, objective monitors could detect higher intensity physical activity and identify locational patterns of that activity across days to identify exercise habits. Electronic monitoring pill bottles could trigger a short survey to be texted to participants when they open the bottles to take their pills, asking where they were when they took the pills and what behaviors they had engaged in directly before taking their pills.

An interesting, separate question is whether *specific times* themselves or the *passage of a specific amount of time* can function as cues-to-action. However, it seems unlikely that a specific time itself (without an associated activity or environmental factor) can be salient enough to automatically trigger an impulse to act.

Although the month-long, objective adherence data and within-person analyses were strengths of the current study, the sample size was relatively small, and future research should use these methods in larger samples, across illness domains to further evaluate the hypotheses. Also, complexity of regimen and comorbidity were not assessed in this study; these factors could have influenced adherence differentially in the morning versus evening, such as if complex regimens are more likely to become disrupted as the day goes on compared to simpler regimens. Furthermore, it is possible that individuals' weekdays differ from weekends (or workdays differ

from days off and so forth) and that this could have influenced pill-timing variance. A post hoc analysis that used participants' weekday data only did not alter the results for either hypothesis. Future research could look at more complex patterns of timing (consistency across some days but not others; of consistency from week to week rather than day to day). Furthermore, future research could evaluate whether work status or other life characteristics might influence pill timing differentially for morning versus evening doses.

Future research could measure separately individuals' intentions and habits for morning versus evening pills using methods such as ecological momentary assessment. Future research could also evaluate interindividual differences that would influence optimal behavioral timing (during the day) for habit formation. For example, individuals' diurnal preference (morningness–eveningness), conscientiousness, or preference for routine/structure in general may influence their relative ability to form a morning versus evening habit [26, 27].

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Compliance With Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards The authors declare that they have no conflict of interest.

Authors' Contributions L.A.P. designed the study, obtained funding for the study, collected the data, analyzed the data, and wrote the manuscript. E.B. and H.L. provided conceptual feedback prior to and after data collection and gave formative feedback and made edits to the manuscript.

Ethical Approval The relevant Institutional Review Board approved all study protocols and materials.

Informed Consent All participants gave informed consent prior to completing any research activities.

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