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Ecological momentary assessment of pain, fatigue, depressive and cognitive symptoms reveals significant daily variability in multiple sclerosis

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Abstract

Objective—To describe the daily variability and patterns of pain, fatigue, depressed mood, and cognitive function in persons with multiple sclerosis (MS).

Design—Repeated-measures observational study of seven consecutive days of home monitoring, including ecological momentary assessment (EMA) of symptoms. Multilevel mixed models were used to analyze data.

Setting—General community.

Participants—Ambulatory adults (N=107) with MS recruited through [Masked] and surrounding community.

Interventions—Not applicable.

Main Outcome Measure(s)—EMA measures of pain, fatigue, depressed mood, and cognitive function rated on a 0–10 scale, collected five times a day for seven days.

Results—Cognitive function and depressed mood exhibited more stable within-person patterns compared to pain and fatigue, which varied considerably within-person. All symptoms increased in intensity across the day (all $p < 0.02$) with fatigue showing the most substantial increase. Notably, this diurnal increase varied by sex and age; women showed a continuous increase from wake to bedtime, whereas fatigue plateaued after 7PM for men (wake-bed $B = 1.04$, $p = 0.004$). For the oldest subgroup, diurnal increases were concentrated to the middle of the day compared to younger subgroups, which showed an earlier onset of fatigue increase and sustained increases until

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bed time (wake-3pm $B=0.04$, $p=0.01$; wake-7pm $B=0.03$, $p=0.02$). Diurnal patterns of cognitive function varied by education; those with advanced college degrees showed a more stable pattern across the day, with significant differences compared to those with bachelor-level degrees in the evening (wake-7pm $B=-0.47$, $p=0.02$; wake-bed $B=-.45$, $p=0.04$).

Conclusions—Findings suggest that chronic symptoms in MS are not static, even over a short time frame; rather, symptoms –fatigue and pain in particular - vary dynamically across and within days. Incorporation of EMA methods should be considered in the assessment of these chronic MS symptoms to enhance assessment and treatment strategies.

Keywords

multiple sclerosis ecological momentary assessment; diurnal; pain; fatigue; depressed mood; cognitive function

Multiple sclerosis (MS) is a chronic, progressive neurological disease that causes inflammation, myelin damage and axonal destruction of the brain and spinal cord^{1–3}. In addition to physical impairment, people with MS experience a constellation of symptoms, including chronic pain^{4–7}, fatigue^{8–13}, depression^{14–16}, and cognitive dysfunction^{17–22}. Although efforts to manage symptoms and improve functioning are mainstays of MS care, the ability to provide optimal treatment for symptoms is stymied by a poor understanding of the nature of symptoms.

Depressive symptoms²³, pain^{24,25}, and cognitive dysfunction^{26–28} can change over the long term in MS. Symptom variability over time is associated with emotional distress²⁹, which has been attributed to symptom uncertainty^{30,31}. Few studies have examined short-term (e.g. moment-to-moment) symptom variability. Studies that examined daily symptoms in MS have shown significant within-person variability in fatigue and depressed mood, with less variability for pain intensity^{32,33}, significant individual differences in diurnal fluctuations in fatigue³⁴, and significant daily fatigue fluctuations that are more related to physical exertion in those with compared to those without MS³⁵. While these studies provide initial evidence as to daily symptom variability in MS, they are somewhat limited by small sample sizes^{32,33,35} and a focus on fatigue^{33,34}. Greater understanding of the variability of MS symptoms could provide insight into how symptoms are experienced in daily life, inform approaches to measuring symptoms, and optimize behavioral and pharmacological treatments for symptoms in MS.

The objective of this study was to assess temporal patterns of four common symptoms (pain, fatigue, depressed mood, and cognitive function) in persons with MS using *ecological momentary assessment* (EMA)^{36,37} – real-time assessment of symptoms. EMA offers benefits over recall surveys, including improved reliability, and the ability to examine within-person dynamics^{36,37}. In this study, we examined within-person variability and diurnal patterns in pain, fatigue, depressed mood, and cognitive function over 7 days. Based on previous findings^{32,34,35}, we hypothesized that fatigue and depressed mood would demonstrate relatively higher levels of within-person variability compared to other symptoms and that all symptoms would exhibit a diurnal increase in severity throughout the

day. We explored whether age, sex, MS subtype, MS duration, work status, and education level were related to different diurnal symptom patterns.

Methods

Participants

Adults with a clinical diagnosis of MS were recruited. Inclusion criteria were: 1) 18 years of age; 2) able to speak/read English at 6th grade level; and 3) able to ambulate with minimal assistance (use of cane/walker permitted). Exclusion criteria were: 1) MS exacerbation within the past 30 days; 2) atypical sleep/wake pattern (e.g. shift work); 3) diagnosis of rheumatologic disease or fibromyalgia; and 4) change in disease-modifying therapy during study.

Study Procedures

This study utilized baseline surveys, EMA of symptoms, and end-of-day (EOD) diaries from a study that also measured physical activity and was conducted at [masked] between October 2014 and March 2016. Medical Institutional Review Board approval was granted prior to study initiation. Participants were recruited through physician referrals, flyers placed in [masked] medical clinics and community locations, outreach at community events, electronic medical records queries, existing participant registries, and the [masked] human subjects recruitment website. Screening was conducted via telephone; eligible volunteers were scheduled for a baseline visit where they underwent informed consent, completed surveys online via Qualtrics³⁸, and were trained to use the PRO-Diary wrist-worn monitor and complete EOD diaries through Qualtrics. The 7-day home monitoring period commenced the day following the baseline visit.

During home monitoring, participants wore the PRO-Diary^a (CamNTEch, Cambridge, United Kingdom) on their non-dominant wrist continuously and entered self-reported ratings of pain, fatigue, depressed mood, and cognitive function 5 times a day: upon waking, 11AM, 3PM, 7PM, and bedtime. An audible alarm alerted participants to enter ratings during the day and participant initiated ratings at wake and bed times. As detailed in the companion paper³⁹, participants completed a brief EOD diary of validated surveys each night via a Qualtrics link. After the home monitoring period, participants returned their PRO-Diary to the lab, where data were downloaded. Participants received compensation based on the number of days that they completed.

Measures

Baseline Measures—Surveys of demographic (age, sex, race, education) and clinical (year of diagnosis) variables were administered. Physician diagnosis and MS subtype were confirmed through medical record review. Validated self-report measures were used to characterize the sample. Fatigue severity was assessed with the Fatigue Severity Scale (FSS)⁴⁰, a validated 9-item measure; average scores of 4 are suggestive of fatigue^{40–44}. Depressive symptoms were measured with the Patient Health Questionnaire–9 (PHQ-9)⁴⁵

^aCamNTEch Ltd., Upper Pendrill Court, Ermine Street North, Papworth Everard, Cambridge, CB23 3UY, United Kingdom

which assesses frequency of 9 depressive symptoms in the past 2 weeks. The PHQ-9 has been validated in MS^{46,47} and provides clinical cut-points. On the Brief Pain Inventory (BPI)^{48–51} participants rated their current, worst, and average pain intensity on a scale from 0 (no pain at all) to 10 (pain as bad as it can be). A composite score, “characteristic pain,” was calculated by multiplying the mean of these three items by ten to better captures a reliable hierarchy of pain intensity⁵². Perceived cognitive functioning was assessed with the Perceived Deficits Questionnaire (PDQ)⁵³, which asks respondents to rate how often they experienced different types of cognitive dysfunction in the past 4 weeks, on a scale from 0 (never) to 4 (almost always). Higher scores indicate greater perceived cognitive dysfunction.

Ecological Momentary Assessment—Four EMA symptom items were developed for the study due to a lack of available validated measures. Pain and fatigue items were based on the “right now” items of the BPI^{48–51} and the Brief Fatigue Inventory⁵⁴. Items for depressive and cognitive symptoms were developed with parallel response scales to limit response burden and make for straightforward statistical comparisons.

Pain intensity was assessed with the question: “What is your level of pain right now?” rated on a scale from 0 = “no pain” to 10 = “worst pain imaginable.”

Fatigue intensity, defined as tiredness or weariness⁵⁵, was assessed with the question: “What is your level of fatigue right now?” rated on a scale from 0 = “no fatigue” to 10 = “extremely severe fatigue.”

Depressed mood assessed with the question: “What is your level of depression right now?” rated on a scale from 0 = “not at all depressed” to 10 = “extremely depressed.”

Cognitive function (perceived) was assessed with the question: “What is your level of cognitive functioning right now?” rated on a scale from 0 = “good: my thinking is sharp and quick” to 10= “bad: my thinking is very difficult or slow.”

End-of-Day Diaries—Four short-forms from the Patient Reported Outcomes Measurement Information System (PROMIS)^{56–58} or the Quality of Life in Neurological Disorders (Neuro-QoL) measurement system^{59,60}, were adapted for daily use by changing the recall format from the past 7-days to “Today”.⁶¹ *Daily Pain* was assessed with the PROMIS pain intensity 3-item short-form^{61,62} which has demonstrated validity across conditions^{63,64}. Respondents rated their daily worst, average, and current pain on a 1 (no pain) to 5 (very severe) scale.

Daily Fatigue was assessed with the PROMIS fatigue 6-item short-form, which has demonstrated validity across conditions^{63,65,66} and ecological validity when administered in diary format⁶⁷, and has been linked to legacy fatigue measures in MS⁶⁶. Respondents rated general, mental, and physical fatigue, and fatigue impact on a 1 (not at all) to 5 (very much) scale.

Daily Depressed Mood was assessed with the PROMIS 8-item short-form, which has been validated in MS⁴⁶. Respondents rated eight depressed feelings on a scale from 1 (never) to 5 (always).

Daily Cognitive Function was assessed with the Neuro-QoL 6-item applied cognition-general concerns short-form. Respondents rated perceived cognitive difficulty on a scale of 1 (never) to 5 (always).

Data Analyses

Preliminary Data Analyses—Descriptive statistics for all variables and missing data rates were calculated. To examine convergent validity of EMA items, we used multilevel modeling (MLM), regressing the EOD diary score on the corresponding EMA symptom variable (daily aggregate) and calculating the amount of shared variance (pseudo- R^2) between the measures for each symptom⁶⁸. Shared variance 49% (roughly corresponding to $r=0.70$) was considered evidence of convergent validity of the EMA items.

Primary Data Analyses—To calculate within- and between-person variability, we ran “null” MLMs (i.e., SAS PROC MIXED) for each of the four symptoms, with no covariates and the symptom variable under consideration as criterion. We calculated the proportion of variance accounted for by the intercept, indicating between-person variance (i.e., intraclass correlation), and residual variance, indicating within-person variance. We created a ratio of these variance estimates. In MLMs that examined diurnal symptom changes across the day; we tested the effects of time point, treated as a categorical variable with wake as the reference, to determine whether symptoms changed between wake and bed times. To test whether diurnal symptom patterns varied based on age, sex, MS subtype (relapsing-remitting MS (RRMS) versus progressive subtypes), MS duration, work status, or education level, interaction terms were created and entered as predictor variables into MLMs where the criterion was one of the EMA symptoms. Significant interactions were graphed to aid interpretation. Analyses were completed using SAS^b version 9.4 (SAS Institute, Cary, NC, USA). Critical alpha level was 0.05.

Results

One hundred and eight participants enrolled and completed the baseline surveys. One participant withdrew before starting home monitoring; data from the remaining 107 were analyzed. Descriptive statistics (Table 1) indicate that the sample, on average, was middle-aged and most were female, white, and had RRMS. Data were adequately normally-distributed for parametric statistical analyses. For EMA measures, 83.4% (3,145/3,745[35*107]) of the data were complete; 17 participants had no missing data and 55 had 3 missing data points. Mean number of missing EMA data points was 5.79 ± 6.35 .

All EMA measures showed high levels of shared variance with EOD diary measures of the same constructs, supporting convergent validity of the EMA items (Table 2.).

Examination of between- and within-person variance components of symptoms

As shown in Table 3, the proportion of within-person and between-person variance in fatigue was equal (50%/50%). In contrast, the between-person variance for pain accounted for a

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relatively larger proportion of the variance (59%), as compared to within-person variance (41%). For cognitive function, within-person variance accounted for only 36% (64% between-person variance) of the total variance. Depressed mood had the smallest proportion of within-person variance (31%), with 69% of the variance being between-person. While all symptoms demonstrated notable levels of within-person variability, fatigue demonstrated the largest proportion and depressed mood the smallest proportion of within-person variability.

Diurnal symptom patterns

As expected, all symptoms increased steadily and significantly from wake to bed time (See Figure 1 and Table 4). In Figure 2, a single illustrative case demonstrates both the differences in proportion of between-and within-person variance components as well as the diurnal effects of symptoms.

Individual differences in diurnal symptom patterns

Diurnal symptom patterns did not differ by MS subtype/duration or work status (all $p>0.13$). There was a significant difference by age in change in fatigue ratings from wake to 3PM (ageXtime $B=0.04$, $SE=0.01$, $t=2.44$, $p=0.01$) and from wake to 7PM (ageXtime $B=0.03$, $SE=0.01$, $t=2.29$, $p=0.02$). A graph of fatigue ratings across the day (Figure 3) shows that among the youngest (23–38 years; 33% of sample) and middle-aged (39–52yrs; 33%) groups, fatigue largely plateaus from wake to 11AM, followed by a modest, steady increase toward bed time. In contrast, among the oldest group (53–67 years; 33%), fatigue ratings were relatively stable from wake to 3PM, but then steeply increased from 3PM to 7PM before stabilizing. There was one significant finding for sex; there was a significant difference between men and women in terms of the change from waking to bedtime fatigue (sexXtime $B=1.04$, $SE=0.36$, $t=2.92$, $p=0.004$). A graph of fatigue ratings across the day (Figure 4) shows that while fatigue rises steadily across the day and peaks at bedtime for women, fatigue ratings plateau at 7PM and decline toward bedtime for men. There was a significant difference in the diurnal pattern of cognitive function by education level; those with an advanced degree were significantly different from those with a college education in terms of changes from wake to 7PM (educationXtime $B=-0.47$, $SE=0.22$, $p=0.02$) and from wake to bedtime (educationXtime $B=-0.45$, $SE=0.22$, $p=0.04$). A graph of cognitive function ratings (Figure 5) shows that in the context of overall very modest diurnal effects for all levels of education, those with advanced degrees showed the most stable and those with a college education the most variable diurnal pattern.

Discussion

This study is the first to use EMA to examine daily variability and temporal patterns of pain, fatigue, depressed mood, and perceived cognitive function in MS. Consistent with previous research^{32,34,35}, these data show that in ambulatory people with MS, symptoms are not static, but are experienced dynamically. Fatigue emerged as the most variable symptom, with a high ratio of within- to between-person variability, and the greatest change from wake to bed time. Unexpectedly, depressed mood was the most static symptom; it is plausible that this lack of variability may be due to low levels of depressed mood in the sample. However, levels of other symptoms were also modest and yet demonstrated higher within-person

variability. People with MS often experience considerable disease course-variability and illness uncertainty, which are associated with emotional distress^{29–31,69}. Whether daily symptom variability and uncertainty could add to distress associated with illness uncertainty across longer time spans has yet to be explored. Our findings highlight a potential role for assessment and integration of thoughts, behaviors, and emotions related to symptom variability and unpredictability, which may need to be incorporated into self-management interventions for MS symptoms.

As anticipated, all symptoms showed a significant worsening across the day, although, on average, diurnal increases were modest. Diurnal fatigue patterns varied by age and sex/Older individuals showed a delay in the onset of fatigue worsening, and women showed a continuous worsening of fatigue that peaked at the end of the day. In contrast, men's fatigue plateaued at 7PM. Different fatigue patterns by age may be due to increased use of planning and activity pacing⁷⁰ in older individuals, to account for greater fatigability⁷¹. These findings are consistent with a previous study suggesting significant individual differences in diurnal fatigue patterns³⁴ and suggest a need to further explore individual differences in the experiences of symptoms, and identification of prototypical symptom profiles, which could offer the ability to tailor treatments based on a person's "symptom phenotype". These data have implications for energy conservation, a common behavioral strategy based on the premise that people need to "budget" energy, suggesting that that clinicians should consider individual differences by age and sex in daily fatigue and the potential that pacing may be naturally occurring, especially in older persons with MS⁷². Diurnal cognitive functioning patterns differed by education with those with advanced degrees showing almost no change in perceived cognition across the day; in contrast, those with lower education showed worsening of cognitive function across the day, although these increases are modest and significantly different only in the evening for those with college degrees vs. advanced degrees. Notably, those with at least a college degree reported lower levels of cognitive problems across the day compared with those with less than a college education. This finding is somewhat consistent with previous findings supporting the cognitive reserve hypothesis, that higher education mitigates cognitive problems associated with MS^{73–75}.

Average EMA ratings were low, particularly when compared to scores on standardized symptom measures that suggest a higher symptom burden. This incongruity between EMA and baseline survey scores could be due to a number of factors. Methodological studies of EMA of symptoms demonstrate surveys that rely on respondent recall, such as the baseline measures in this study, are biased toward peak (worst) and recent symptoms^{76–78}; EMA ratings may provide a more valid estimate of true symptom intensity compared to standardized surveys. Additionally, people may respond differently to an in-the-moment compared to a recall question about symptoms, such that responding in real-time shifts or constricts the range of responses or reflects a different construct altogether. These possibilities warrant further examination to improve the psychometric characteristics and clinical usefulness (e.g. comparability to screening measures) of EMA measures.

These novel findings warrant replication in larger and more diverse MS samples and call for a number of future directions, some of which we are examining in these data, including moment-to-moment and day-to-day covariation of symptoms⁷⁹, daily association of

symptoms to functional and affective outcomes³⁹, and the association between symptoms and physical activity.

Study Limitations

Because this study focused on symptoms that are common targets of behavioral self-management interventions, evaluation of other MS symptoms, such as weakness and sensory disturbances were not included. Only ambulatory individuals were included due to the use of an accelerometer; exclusion of the most disabled individuals could limit our ability to generalize findings to the broader MS population. Use of single item measures that have not been validated to assess momentary symptoms is a limitation of this study. Although there are examples of 0–10 numerical rating scale use in EMA studies of pain^{80–82} and fatigue^{33,35,82}, to our knowledge there are no standard, validated EMA measures of the symptoms examined in this study. Convergent validity of the EMA items, relative to more robust daily measures of each construct, was supported in this study. Further work to psychometrically evaluate EMA symptom measures is needed, with the goal of developing standard validated EMA items and brief scales that could be used across studies. Examination of individual differences in symptom experience (versus group-level analyses) as well as how total symptom burden (versus individual symptoms) in future research could better reflect the true experience of symptoms in MS; unfortunately, our relatively small sample precludes the type of data modeling that would be required to examine these question. Comparing daily symptom experience and impact in MS to other clinical conditions or to healthy individuals could provide additional insights as to how the symptoms experience is unique in MS, similar to a recent study showing that physical exertion is related to fatigue in MS whereas sleep quality is related to fatigue in healthy controls³⁵.

Conclusions

Findings add to the growing body of evidence that chronic symptoms in MS are not static, but change daily within a person. Improved knowledge of symptom patterns in MS could help refine interventions to target the most severe or impactful symptoms, minimize treatments when they are not needed, develop new interventions and prevention strategies, and guide timing of medications and selection of self-management strategies⁸³. Results highlight the potential of EMA to provide a reliable real-time assay of MS symptoms, which could increase our understanding of MS symptoms, and gauge effectiveness of symptomatic therapies for some of the most common and consequential MS symptoms.

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Abbreviations

EMA	ecological momentary assessment
EOD	end-of-day
MS	multiple sclerosis
RRMS	Relapsing-Remitting MS

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Figure 1.
Diurnal patterns of symptom ratings across the day represented by sample averages for symptoms at each time point, showing a steady increase in all symptoms from wake to bedtime across the sample.
Note. error bars = standard error of the mean

Figure 2.

Single case example (25 year old female with relapsing-remitting MS) of variability in momentary symptoms across 7 days

Note. Fatigue (red line) shows the most obvious within-person fluctuations, with peak values around bed time (corresponding to every fifth tick mark, marked with “B” on horizontal axis). In comparison, pain (blue line) shows slightly less variation across the days, but more variation than cognitive function (purple line) and depressed mood (green line), which shows almost no variability across the entire study period. This single-case example demonstrates both the differences between the symptoms in degree of within-person variability as well as the diurnal effects (evidenced by symptom peaks at bedtime (“B”) and symptom valleys at wake (“W”).

Figure 3.

Difference by age categories (youngest = 23–38 years; middle = 39–52 years; oldest = 53–67 years) in the diurnal pattern (change across the day) of fatigue ratings. Lines depict average fatigue ratings at each time point for the different age groups.

Note. error bars = standard error of the mean; * = time point at which change in fatigue from wake time point is significantly different by sex.

Figure 4.

Differences between men and women in the diurnal pattern (change across the day) of fatigue ratings. Lines depict average fatigue ratings at each time point for men and women. *Note.* error bars = standard error of the mean; * = time points at which change in fatigue from wake time point is significantly different by age.

Figure 5.

Differences by education categories (<college degree = 38.9%, college degree = 28.9%, advanced degree = 22.2%) in the diurnal pattern (change across the day) of cognitive function ratings. Lines depict average cognitive functioning ratings (higher scores indicate worse function) at each time point for each education level category.

Note. error bars = standard error of the mean; * = time points at which change in cognitive function from wake time point is significantly different by education.

Table 1

Descriptive statistics for demographic and baseline study variables (N = 107)

Variable (possible range)	N (%)	Mean (SD)	Min-Max
Age in years		45.16 (11.73)	23–67
MS Duration in years		9.49 (8.36)	<1 –44
FSS (1–7)		4.94 (1.53)	1–7
Significant fatigue; scores 4–7	85 (79.4%)		
BPI worst pain (0–10)		4.09 (2.92)	0–10
BPI average pain (0–10)		3.09 (2.17)	0–7
BPI current pain (0–10)		2.67 (2.48)	0–8
Characteristic Pain (0–100)		32.99 (23.56)	0–80
Significant pain; scores 40–100	46 (42.9%)		
PDQ (0–80)		28.92 (17.53)	0–74
PHQ-9 Total Score (0–27)		7.61 (5.91)	0–22
PHQ-9 categories			
Minimal depression	42 (39.3%)		
Mild depression	29 (27.1%)		
Moderate depression	21 (19.6%)		
Moderately severe depression	10 (9.3%)		
Severe depression	5 (4.7%)		
Sex (Female)	74 (69.2%)		
MS Subtype			
Relapsing Remitting	78 (72.9%)		
Primary Progressive	14 (13.1%)		
Progressive Relapsing	2 (1.9%)		
Secondary Progressing	13 (12.1%)		
Race			
White	88 (82.2%)		
Black	10 (10.7%)		
Asian	6 (5.6%)		
Native	2 (1.9%)		
Biracial (Black/White)	1 (0.9%)		
Hispanic	1 (0.9%)		
Employment			
Employed Full-time	41 (38.3%)		
Employed Part-Time	19 (17.8%)		
Unemployed	47 (43.9%)		
Education			
Some high school	1 (0.9%)		
HS grad/GED	13 (12.1%)		
Vocational or Tech school	2 (1.9%)		
Some College	26 (24.3%)		

Variable (possible range)	N (%)	Mean (SD)	Min-Max
College Grad	41 (38.3%)		
Graduate school/Prof school	24 (22.4%)		

Note. GED = General educational development; FSS = Fatigue Severity Scale; BPI = Brief Pain Inventory; PHQ-9 = Patient Health Questionnaire – 9; Perceived Deficits Questionnaire.

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Table 2

Results of multilevel models examining the association and shared between-person variance for daily EMA symptom ratings (daily aggregates) and EOD diary survey scores of the same symptom construct

	beta	SE	p	Shared variance [*]
Pain (<i>df</i> = 101, 516)				
EMA pain (daily aggregate)	0.91	0.05	<0.0001	79.8%
EOD diary PROMIS pain intensity (criterion)				
Fatigue (<i>df</i> = 101, 516)				
EMA fatigue (daily aggregate)	1.35	0.09	<0.0001	63.3%
EOD diary PROMIS fatigue (criterion)				
Depressed mood (<i>df</i> = 101, 515)				
EMA depressed mood (daily aggregate)	2.05	0.30	<0.0001	59.2%
EOD diary PROMIS depressive symptoms (criterion)				
Cognitive function (<i>df</i> = 101, 511)				
EMA cognitive function (daily aggregate)	1.27	0.17	<0.0001	54.2%
EOD diary Neuro-QoL applied cognition-concerns				

Note. EMA = ecological momentary assessment; EOD = end-of-day; PROMIS = Patient Reported Outcomes Measurement Information System; Neuro-QoL = Quality of Life in Neurological Disorders measurement system; *df* = degrees of freedom between and within-person; beta = unstandardized beta; SE=standard error; p = significance level;

^{*} pseudo- R^2 calculated according to the recommendations of Singer & Willett⁶⁵;

Table 3

Within- and between-person variance in momentary ratings of fatigue, pain, depressed mood, and cognitive functioning

	Pain	Fatigue	Depressed mood	Cognitive Functioning
Between-person	2.89	3.54	2.54	2.99
Within-person	1.99	3.60	1.15	1.68
Percent Between-person	59%	50%	69%	64%
Percent Within-person	41%	50%	31%	36%

Table 4

Results of multilevel model tests of diurnal effects of time in symptom ratings, showing significant increases at each time point relative to the wake time point (reference)

Time point	Pain	Fatigue	Depressed mood	Cognitive function
(unstandardized beta, <i>p</i>)				
Wake (reference)	-	-	-	-
11AM	0.16, 0.13	-.11, 0.47	0.22, 0.0002	0.05, 0.56
3PM	0.26, 0.02	0.48, 0.006	0.33, <0.0001	0.30, 0.008
7PM	0.51, < 0.0001	0.85, <0.0001	0.42, <0.0001	0.39, 0.0009
Bed time	0.29, 0.03	1.75, <0.0001	0.29, 0.0002	0.43, 0.005