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Individual differences in the day-to-day variability of pain, fatigue, and well-being in patients with rheumatic disease: Associations with psychological variables

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ABSTRACT

This report examines day-to-day variability in rheumatology patients' ratings of pain and related quality-of-life variables as well as predictors of that variability. Data from 2 studies were used. The hypothesis was that greater psychological distress (i.e., depression and anxiety) and poorer coping appraisals (i.e., higher pain catastrophizing and lower self-efficacy) are associated with more variability. Electronic daily diary ratings were collected from 106 patients from a community rheumatology practice across 28 days (study 1) and from 194 osteoarthritis patients across 7 days (study 2). In multilevel modeling analyses, substantial day-to-day variability was evident for all variables in both studies, and individual patients differed considerably and somewhat reliably in the magnitude of their variability. Higher levels of depression significantly predicted greater variability in pain, as well as in happiness and frustration (study 1). Lower self-efficacy was associated with more variability in patients' daily satisfaction with accomplishments and in the quality of their day (study 2). Greater pain catastrophizing and higher depression predicted more variability in interference with social relationships (study 2). Anxiety was not significantly associated with day-to-day variability. The results of these studies suggest that individual differences in the magnitude of symptom fluctuation may play a vital role in understanding patients' adjustment to pain. Future research will be needed to examine the clinical utility of measuring variability in patients' pain and well-being, and to understand whether reducing variability may be an important treatment target.

1. Introduction

Pain research and practice have traditionally focused on patients' average or usual symptom levels [10,29]. This is not surprising, given that most clinical and research evaluations have relied on patient recall over days or weeks. However, the focus on average pain does not capture the dynamic ebb and flow in everyday life. Recent methodological advances using diaries have made it possible to characterize and examine the short-term fluctuations of pain symptoms within individual patients with high resolution [1,6,8,22,23,38]. Fluctuations can be a debilitating aspect of the chronic pain experience [2,19,26]. For example, research has found variability to be associated with level of depression [26] and reduced work productivity [19], whereas intensity of pain was not. Clinical researchers suggest that these associations may be due to variability inducing a sense of loss of predictability and control in the patient's life [27].

To date, most research has examined pain fluctuations from a state perspective [1,44]. A typical question is: "What makes a given person experience more pain at one point compared with another point in time?" On the other hand, surprisingly little attention has been paid to variability as an individual difference variable. From this perspective, the question is: "What makes one person characteristically experience more fluctuations in pain than another person?" Measuring how patients differ in variability of pain symptoms may provide insight into biological and psychosocial disease processes and may assist with treatment planning [18].

Psychological factors such as depression, anxiety, and coping skills might explain individual differences in pain variability, but only a few studies have addressed this question [3,12,15,21,26]. Depression [21,26] and anxiety [21] have been shown to be associated with pain variability in some studies, but not in others [12]. Similarly, coping has been inconsistently shown to predict pain

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variability [3,28]. The methodology used in these studies has, with 1 exception [15], involved paper diaries that are vulnerable to reporting problems [39]. Some studies quantified variability retrospectively as the difference between recalled worst and least pain [19,28], which does not capture daily variability. Furthermore, sample sizes have generally been small.

In this report, we examine psychological predictors of individual differences in the day-to-day pain variability of patients using electronic end-of-day diaries. To enhance the generalizability of the findings, we analyzed data from 2 existing studies. Each study included several psychosocial variables of interest, however studies specifically designed to investigate pain variability would undoubtedly have included other variables as well. In addition, we broadened the scope in this investigation to other key variables, for example, fatigue, pain interference, and satisfaction with accomplishments. We hypothesized reliable individual differences in day-to-day variability in these variables. We examine psychological predictors, available in these data sets, important in understanding regulation of the pain experience: depression and anxiety (psychological distress variables), and self-efficacy and catastrophizing (coping appraisals). We hypothesized that patients with greater distress and poorer coping would show greater day-to-day variability in pain, fatigue, and adjustment.

2. Materials and methods

2.1. Study 1

2.1.1. Participants

Patients were recruited from 2 local community rheumatology practices. Eligibility criteria for study participation were (1) $\geqslant$18 years of age; (2) physician-confirmed diagnosis of a chronic rheumatological illness (see Section 3 for specific diagnoses); (3) self-reported experience of pain or fatigue during the last week; (4) no significant sight, hearing, or writing impairment; (5) English fluency; (6) normal sleep-wake schedule; (7) availability to participate for 30 consecutive days and ability to come to the research office for study visits twice within a month; and (8) no previous study experience with electronic diaries in the last 5 years. Potential participants were screened by telephone for eligibility. A total of 106 patients completed the study.

2.1.2. Procedure

The Stony Brook University Institutional Review Board approved the study protocol. Participants provided informed consent and were compensated with up to $100 for their participation. During their first study visit, participants came to the research office to complete measures about their physical and mental health, including the scales that would be used as predictors of day-to-day variability. In addition, they were instructed in the use of an electronic diary (ED) that was given to participants to collect end-of-day ratings for 28 days. The ED software program was provided by Invivodata, inc. (Pittsburgh, PA). The research staff conducted a 24-hour follow-up telephone call to answer questions and ensure competency using the ED. For the next 3 weeks, weekly telephone calls were made to participants to ensure proper functioning of the ED and to answer any questions. At the end of the month, patients came for their second visit to the research office and returned the ED.

2.1.3. Measures

2.1.3.1. Daily ratings. Patients completed the following ratings on the ED using a 101-point horizontal visual analog scale with anchors "not at all" to "extremely" at the end of each day for 28 successive days:

- Pain intensity: What was the average level of your pain today?
- Fatigue: What was the usual level of your fatigue today?
- Happiness: During the day: How feeling? Happy.
- Frustration: During the day: how feeling? Frustrated.

2.1.3.2. Baseline psychological characteristics.

2.1.3.2.1. Beck Depression Inventory II. The Beck Depression Inventory II (BDI) is a 21-item self-report instrument that measures cognitive, affective, and somatic aspects of depressed mood [5]. The BDI has demonstrated validity in distinguishing levels of depressed mood and has also been found to be sensitive to treatment change [6]. Internal consistency has been found to be Cronbach α = .86 for psychiatric patients and α = .81 for nonpsychiatric samples. In the present study sample, internal consistency was α = .94.

2.1.3.2.2. Spielberger State-Trait Anxiety Scale. The trait version of the Spielberger State-Trait Anxiety Scale (STAI) is a 20-item questionnaire that measures how much anxiety one experiences in general. The instrument correlates well with other measures of anxiety, and has demonstrated responsiveness to change [37]. In the present study sample, internal consistency was α = .95.

2.2. Study 2

2.2.1. Participants

These patients were part of an ongoing randomized controlled clinical trial on the effectiveness of pain coping skills training (CST) for patients with osteoarthritis. Recruitment was conducted at local community clinics in New York, Virginia, and North Carolina. Eligibility criteria included (1) $\geqslant$21 years; (2) physician-confirmed American College of Rheumatology (ACR) diagnosis of osteoarthritis of the hip or knee; (3) usual pain $\geqslant$4 (on a 10-point scale) for at least 6 months; (4) the ability to read, write, and understand English; (5) availability to participate in 10 individual treatment sessions; and (6) access to a telephone to complete daily automated telephone ratings. Data from 194 participants were available from the ongoing trial for the present analyses.

2.2.2. Procedure

The institutional review boards for the multisite trial approved the study protocol. Clinic physicians and staff informed patients of this research opportunity. Interested patients were called by the research staff and received a detailed explanation about the study and CST treatment protocol and were screened for eligibility. Patients completed their baseline assessment at the recruitment clinic. Afterward, patients were instructed in the use of an interactive voice response (IVR) telephone system to complete 7 days of ratings after their baseline study visit. The IVR system called participants on the subsequent 7 evenings to complete ratings about their symptoms and well-being. Participants first completed the ratings on paper questionnaires. Then, they called into the IVR system to enter their ratings, thus providing a time and date stamp. Baseline data included in this study were collected before the patients were randomized to condition in the clinical trial.

2.2.3. Measures

2.2.3.1. Daily IVR ratings. Patients completed the following ratings on a 0 to 10 numeric rating scale (scores were transformed to a 0 to 100 scale for the present analyses) at the end of each day for 7 successive days:

- Pain intensity: What was the average level of your pain today? (no pain–pain as bad as you can imagine).

- Fatigue: What was the usual level of your fatigue (weariness, tiredness) today? (no fatigue–fatigue as bad as you can imagine).
- Interference with walking: How much did your arthritis interfere with your walking ability today? (not at all–extremely).
- Interference with work: How much did your arthritis interfere with your work (job or home) today? (not at all–extremely).
- Interference with social relations: How much did your arthritis interfere with your relations with other people? (not at all–extremely).
- Quality of day: Overall, how would you rate the quality of your day today? (extremely bad–extremely good).
- Satisfaction with accomplishments: Overall, how satisfied are you with what you accomplished today? (not at all satisfied–extremely satisfied).

2.2.3.2. Baseline psychological characteristics.

2.2.3.2.1. BDI. The BDI has been described in Study 1 earlier. Cronbach alpha was .89 in this sample.

2.2.3.2.2. Arthritis Impact Measurement Scale–tension subscale. The Arthritis Impact Measurement Scale (AIMS2) is a 78-item questionnaire that covers 5 health components assessing the health status of patients with arthritis and has been widely used in survey and treatment outcomes research. Reliability and validity of the measure have been demonstrated [32]. This study used scores on the AIMS2 tension subscale, which captures anxious mood. Internal consistency of the AIMS2 tension subscale was adequate at $\alpha = .87$.

2.2.3.2.3. Arthritis Self-Efficacy Scale. Self-efficacy for coping was assessed by the 8-item Arthritis Self-Efficacy Scale (ASES) [14]. Patients rate on a scale from 0 = very uncertain to 10 = very certain their confidence in their abilities to control their arthritis; the total score is the mean of 8 items. The scale has been demonstrated to have high internal consistency, test-retest reliability, and validity [14,30]. In the present sample, internal consistency was high at $\alpha = .91$.

2.2.3.2.4. Coping Strategies Questionnaire–catastrophizing subscale. The 6-item Coping Strategies Questionnaire (CSQ) pain catastrophizing subscale has good internal consistency [24,25], and has been shown to be associated with measures of functioning in patients with a variety of pain conditions [24,25]. Scores can range from 0 to 36, with higher scores indicating greater catastrophizing. In the present sample, internal consistency was adequate at $\alpha = .79$.

2.3. Analytic strategy for both studies

Individual differences in within-person variability have most commonly been examined by using a 2-step approach: first, the within-person variance or standard deviation is computed separately for each individual, and then these computed values are used as observations in subsequent analyses [3,15,26,38]. This analytic strategy is suboptimal, however, in that it disregards the multilevel structure of daily diary data: observations at different time points are nested within individuals. Multilevel models are designed to accommodate nested data, and can be used to assess variability between individuals as well as within individuals. Oftentimes, the goal of these models is to examine individual differences in the average score across multiple observations, in which case the within-person variance is considered measurement error. However, an extension known as multilevel model for heterogeneous variances, or dispersion model, can be used to also predict individual differences in within-person variance [34]. We used this multilevel approach in the analyses. Statistical tutorials are provided by Hoffman [17] and Hedeker and Mermelstein [16].

2.4. Analysis using the multilevel model for heterogeneous variances

Using the multilevel model for heterogeneous variances provided us with several advantages over the traditional 2-step approach. First, it allowed us to examine between- and within-person sources of variance simultaneously in the same model. That is, we could estimate the effect of psychological predictors on within-person variability while simultaneously acknowledging the effect of these predictors on patients' mean levels of pain, fatigue, and wellbeing across all days. Second, multilevel models do not assume that every person contributes the same number of assessments, such that standard errors are appropriately adjusted for unbalanced designs due to missing data. Third, the flexibility of the model made it possible to incorporate time-varying predictors that may influence daily ratings. Following prior recommendations [17,43], we statistically controlled for weekday–weekend differences as time-varying predictor; hence, we examined whether psychological person characteristics predicted individual differences in day-to-day variability that was not systematically explained by weekday–weekend effects.

The multiple equation form of the model was as follows:

$$\begin{aligned}
&\text{Level 1:} && y_{ij} = \beta_{0j} + \beta_{1j}\text{Weekend}_{ij} + r_{ij}, \ \text{where } r_{ij} \sim N(0, \sigma_j^2)\\
&\text{Level 1 residual variance:} && \sigma_j^2 = \alpha_0[\exp(\alpha_1 \text{PC}_j)]\\
&\text{Level 2:} && \beta_{0j} = \gamma_{00} + \gamma_{01}\text{PC}_j + u_{0j}\\
& && \beta_{1j} = \gamma_{10} + u_{1j}
\end{aligned} \tag{1}$$

The Weekend variable was coded 0 for weekdays (Monday through Friday) and 1 for weekend days (Saturday and Sunday). Psychological person characteristics serving as predictor variables (indicated by PC in Eq. (1)) were standardized above the grand mean to facilitate interpretation of the results.

In the Level 1 model for within-person variation, the score on a given outcome variable (pain, fatigue, or wellbeing variable) of person j on day i (y_{ij}) is a function of an intercept (β_{0j}), which represents the weekday mean for person j; a weekend effect (β_{1j}) representing the weekday–weekend difference for person j; and a within-person residual deviation term r_{ij}. Whereas the same (homogeneous) variance model assumes that the variance of the within-person residual is equal across all people, the heterogeneous variance model allows it to differ between people. As shown in the Level 1 model for residuals of Eq. (1), the residual within-person variance (σ^2_j) is explicitly expressed for person j and can be modeled as a function of person characteristics (PC). A log-linear representation is used to normalize the variance and to generate a linear prediction model for PC [16,17]. Accordingly, the residual within-person variance σ^2_j is expressed as the residual variance for the average person (α_0) multiplied by the exponent of the effect of PC (α_1). In the MIXED procedure of SAS (version 9.2; SAS Institute, Cary, NC), this is achieved by adding the LOCAL = EXP() option to the REPEATED statement. In the Level 2 model for between-person variation, person j's average score across all weekdays (β_{0j}) is a function of an intercept (γ_{00}) representing the mean weekday score across all people, and a linear effect of PC on the person's average score (γ_{01}). Also at Level 2, the Level 1 effect of Weekend (β_{1j}) is a function of the average Weekend effect for all people (γ_{10}) and a variance component (u_{1j}), which allows for individual differences in this effect.

2.5. Model-building strategy

For the analysis of data from each study, we first estimated unconditional multilevel models (i.e., no predictors entered) with

homogeneous Level 1 residual variances as baseline models. Next, we included the weekday–weekend distinction as both a fixed effect and a random effect in the models. Controlling for weekday–weekend effects, we then tested the presence of significant individual differences in Level 1 variances with a procedure described by Hoffman [17]: for each individual, a residual variance is estimated using ordinary least squares regression, from which a standardized dispersion score is calculated. The sum of squared dispersion scores can be compared against a χ^2 distribution with degrees of freedom equaling the sample size − 1 to establish Level 1 variance heterogeneity.

Finally, we added psychological predictor variables to the multilevel models. In an initial set of models, each psychological predictor was entered individually both as a fixed effect (i.e., as predictor of a person's average level of pain, fatigue, and wellbeing) and as a random effect on the Level 1 residual variance (i.e., as predictor of within-person variability on these variables). Psychological variables that showed significant effects in these models were then entered simultaneously in the final multilevel models to examine their relative contribution to average levels and within-person variability. The analyses were conducted using the MIXED procedure in SAS.

2.6. Supplemental analyses based on the probability of acute change

To facilitate interpretation of the magnitude of the effects of psychological variables, we present supplemental analyses based on the probability of acute change (PAC) [11,20]. The PAC is an illustrative measure of within-person fluctuation: it captures how often a person experiences day-to-day changes above a given threshold, that is, the probability of substantial (acute) shift from any given day to the subsequent day.

Estimation of the PAC requires choice of a threshold for acute daily change that can be made based on the distribution of day-to-day change scores for all participants in the study [11,20]. We dichotomized the daily change scores into categories of acute change versus no acute change using a cutoff of ±1 SD around the sample average change score. A 1-SD change is generally considered a large effect size. Our empirical cutoffs for acute change ranged from 16 points (for happiness, Study 1) to 22 points (for interference with work, Study 2) on a 100-point scale, which corresponds with prior research documenting that a change of 17 points (1.7 points on a 0 to 10 numerical rating scale) in pain should be considered clinically important [13]. As such, the PAC measure may be interpreted as the frequency of potentially clinically meaningful day-to-day shifts in each outcome variable. Multilevel logistic regression analyses (observed acute changes nested within people) were used to analyze the PAC. Weekday–weekend effects were again controlled at Level 1, and psychological characteristics were entered as predictors at Level 2. M*plus* Version 6.1 [33] was used for the multilevel logistic regression analyses.

3. Results

3.1. Study 1

3.1.1. Participants and missing data

Participants were 106 patients with rheumatic diseases. The most prevalent physician-made diagnoses in the sample were osteoarthritis (49%), rheumatoid arthritis (29%), lupus (16%), and fibromyalgia (10%). Participants had a mean age of 56 years (range 28 to 88, SD = 11.0), and were predominantly female (86%), white (92%), and married (65%). Most were high school graduates (95%), with 72% having completed some college. One fourth (25%) of the sample was receiving disability compensation. Daily pain intensity, fatigue, and mood variables (happiness and frustration) were collected across 28 consecutive days. Across all 106 participants and 28 days, a total of 49 (1.7%) of 2968 days' ratings were missing.

Depression and anxiety scores at baseline were used as predictor variables. The mean BDI depression score in the sample was 12.97 (SD = 10.84), with 64.2% of the participants showing minimal (scores 0 to 13), 14.2% mild (scores 14 to 19), 10.4% moderate (scores 20 to 28), and 11.3% severe (scores 29+) depression. The mean STAI trait anxiety score was 39.70 (SD = 12.08), which is the 59th percentile of the normal adult population in this age group [37].

3.1.2. Individual differences in within-person variability

We first estimated multilevel models assuming homogeneous Level 1 residual variances (i.e., equal within-person variance for all people) as baseline models to examine the composition of variances between and within people for the daily ratings of pain, fatigue, happiness, and frustration. Table 1 shows the means and variance components for each variable, displayed as standard deviations. Each of the outcome variables showed pronounced variation both between and within people. The percent of the total variance (between plus within persons) attributable to within-person day-to-day fluctuations was 34% for pain, 41% for fatigue, 39% for happiness, and 34% for frustration. The within-person SDs can be roughly interpreted as the magnitude of day-to-day fluctuation in scale points on the 101-point scale: the amount of fluctuation for the average person ranged between 12.8 points for happiness to 17.3 points for fatigue ($P < .001$ in all cases; Table 1).

We next examined systematic weekday versus weekend differences in the daily ratings to determine whether these would need to be considered in our final models. We expanded the baseline multilevel models by entering a weekday–weekend predictor as a fixed effect (to capture weekend effects on average across all people), and as a random effect (to capture individual differences in weekend effects). Significant fixed effects were found for happiness and frustration: on average across all people, happiness was 3.2 points higher on weekends (SE = .67, $P < .001$), and frustration was 2.3 points lower on weekends (SE = .75, $P < .01$) than on weekdays. In addition, the random effects estimates indicated that weekend effects varied significantly across people for pain, fatigue, happiness, and frustration ($P < .05$). Thus, we entered the weekday–weekend variable as a covariate in all subsequent models to control for these systematic effects on day-to-day ratings.

The next analyses examined evidence for sufficient individual differences in the amount of day-to-day variability. If ratings of pain, fatigue, and mood fluctuated equally strongly in all people, there would be no basis for examining predictor variables. Significant individual differences in variability were evident for all variables, with weekend effects controlled: pain intensity, $\chi^2(105) = 1109.93$, $P < .001$; fatigue, $\chi^2(105) = 1082.13$, $P < .001$; happiness, $\chi^2(105) = 2055.46$, $P < .001$; and frustration, $\chi^2(105) = 2153.07$, $P < .001$. Fig. 1 illustrates the magnitude of individual differences of within-person variability for pain intensity ratings. The histogram shows the distribution of variances (in SDs) in pain intensity across individuals; within-person variability estimates ranged from SD = 3.8 to SD = 32.5. The figure also includes the 28 daily ratings of 3 selected participants at the lower end (within-subject SD = 6.2), the middle (SD = 15.7), and at the higher end (SD = 24.8) of the distribution to illustrate the range of individual differences in the amount of day-to-day fluctuation in pain.

3.1.3. Psychological factors as predictors of within-person variability

Next, we entered BDI depression and STAI anxiety scores as predictors of a person's mean level and day-to-day variability in pain,

Table 1
Study 1 (28 days)—means and variance components for daily variables.

	Mean	SD		Within-person variance (%)
		Between-person	Within-person	
Pain	47.13	21.85	15.51	34
Fatigue	50.91	20.50	17.25	41
Happiness	58.74	16.11	12.76	39
Frustration	29.90	21.43	15.40	34

n = 106; between-person and within-person variances are statistically significant ($P < .0001$) for all variables.

fatigue, happiness, and frustration. Initial models tested depression and anxiety separately, and predictors were only retained in the final models if they showed significant effects. Table 2 shows the results for the final multilevel models, in which depression and anxiety were entered simultaneously. The distinction between osteoarthritis and other diagnoses was included as a covariate to control for differences in rheumatic conditions. As is the case in any regression model, the effect of each predictor represents its unique effect after adjusting for all other variables in the model.

3.1.3.1. Prediction of a person's mean level

As shown in the fixed-effects section of Table 2, higher BDI depression scores predicted higher levels of pain (estimate = 4.4, SE = 2.1, $P < .05$) and frustration (estimate = 7.4, SE = 3.5, $P < .05$). Higher STAI anxiety predicted significantly lower levels of happiness (estimate = −7.2, SE = 2.8, $P < .05$).

3.1.3.2. Prediction of within-person variability

As shown in the within-person random effects part of Table 2, osteoarthritis patients showed significantly less variability in frustration than patients with other diagnoses (estimate = −.15, SE = .06, $P < .01$). Controlling for diagnosis, higher BDI depression predicted significantly greater variability in pain (estimate = .13, SE = .03, $P < .001$), happiness (estimate = .07, SE = .03, $P < .01$), and frustration (estimate = .20, SE = .05, $P < .001$). This yields the following estimated within-person standard deviations for low (1 SD below average) versus high (1 SD above average) BDI depression: for pain intensity, within-person SD = 14.35 at low and SD = 16.28 at high depression levels; for happiness, SD = 12.03 at low and SD = 12.94 at high depression levels; and for frustration, SD = 13.52 at low and SD = 16.49 at high depression levels (values estimated as follows: given that the predictors were standardized to a mean of 0 and SD of 1, within-person SD = sqrt[Level 1 intercept $*$ exp(−1 $*$ estimate)] for low depression, and within-person SD = sqrt[Level 1 intercept $*$ exp(+1 $*$ estimate)] for high depression). STAI anxiety scores did not uniquely predict individual differences in variability.

3.1.4. Supplemental results based on the PAC

To facilitate interpretation of the effects, we repeated the analyses using the PAC as an indicator of day-to-day fluctuation. The results paralleled those described earlier, with depression significantly predicting the PAC in pain intensity ($P < .001$), happiness ($P < .05$), and frustration ($P < .001$). The PAC in pain intensity as a function of BDI depression scores is illustrated in Fig. 2. The x axis denotes BDI as both z-scores and raw depression scores, with marks showing standard clinical descriptions of depression level [5]. The y axis indicates a person's probability of an acute day-to-day shift in pain exceeding a threshold of ±17 points on the 101-point scale, that is, the likelihood of experiencing daily changes in pain that might be considered clinically meaningful [13]. Individuals with low levels of depression are estimated to have a 19% to 22% chance of acute shifts in pain, whereas those with severe depression have a 30% to 32% chance of acute shifts in pain intensity. The odds of acute day-to-day shifts in pain intensity increase by 25%per SD higher depression. In addition, the estimated odds of acute shifts in happiness increase by 11%per SD higher

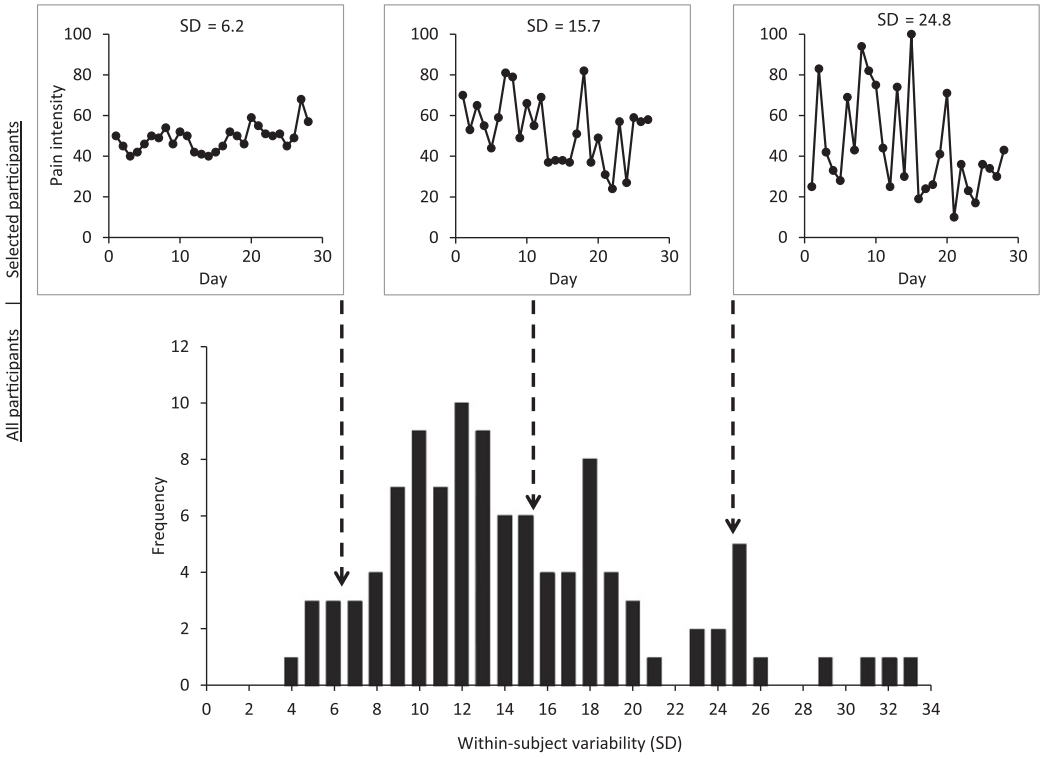

Fig. 1. Study 1: distribution of within-subject variability in pain intensity across participants, with daily ratings of 3 selected participants.

Table 2
Study 1 (28 days)—multilevel models for depression and anxiety as predictors of mean levels and within-person variability.

	Pain intensity		Fatigue		Happiness		Frustration	
	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Fixed effects								
Intercept	47.25	2.10***	50.81	1.93***	58.02	1.50***	30.28	1.88***
Weekend	−.69	.76	−.23	.92	3.20	.67***	−2.15	.75**
Osteoarthritis[a]	−5.75	4.26	−3.12	4.05	−.96	3.15	4.37	3.95
BDI–depression	4.35	2.08*	3.08	3.59	−1.59	2.79	7.44	3.50*
STAI–anxiety	–		4.35	3.54	−7.20	2.75*	3.21	3.45
Random effects								
Level 2 (between-person)								
Intercept variance	455.07	64.77***	379.71	54.88***	229.97	33.13***	362.82	52.20***
Weekend	19.01	8.55*	37.72	12.29**	19.39	6.57**	19.96	8.07**
Level 1 (within-person)								
Intercept variance	233.64	6.36***	289.37	7.87***	155.66	4.29***	223.00	6.06***
Osteoarthritis[a]	.02	.05	.04	.05	−.09	.05	−.15	.06**
BDI–depression	.13	.03***	–		.07	.03**	.20	.05***
STAI–anxiety	–		–		–		.04	.05

Dashes indicate that a predictor was not entered in the final models.
BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Scale.
* $P < .05$.
** $P < .01$.
*** $P < .001$.
[a] Osteoarthritis versus other rheumatological illness.

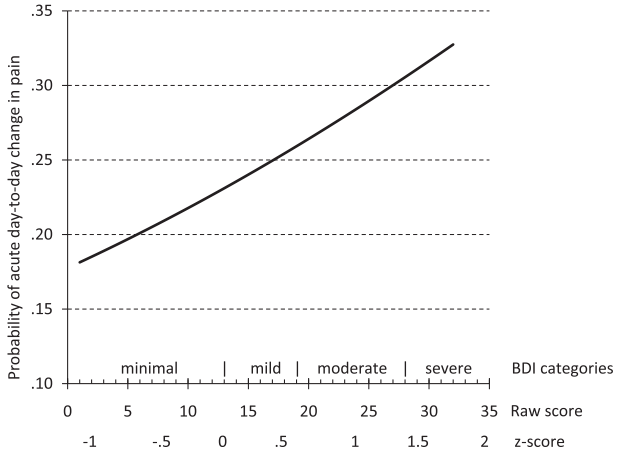

Fig. 2. Study 1: estimated probability of acute change in pain intensity as a function of Beck Depression Inventory II depression scores.

depression, and the estimated odds of an acute shift in frustration increase by 34%per SD higher depression (the effect of depression on acute shifts in frustration is significantly stronger than the effect on acute shifts in happiness, $P < .01$).

3.1.5. The 1-month temporal stability of individual differences in within-person variability

Finally, we examined the test-retest reliability of individual differences in the magnitude of within-person variability. Specifically, we obtained the within-person residual SD for each person separately for the first 14 days and for the second 14 days of the 28-day period from multilevel models, controlling for weekend effects. We then estimated the intraclass correlation coefficients (ICC) for the within-person SDs between the 2 periods as a measure of test-retest reliability. The resulting ICCs with 95% confidence limits were .67 for pain (CL = .55 to .76), .65 for fatigue (CL = .53 to .75), .53 for happiness (CL = .38 to .65), and .40 for frustration, (CL = .23 to .55), indicating moderate test-retest stability across the two 14-day periods.

3.2. Study 2

3.2.1. Participants and missing data

Participants were 194 osteoarthritis (OA) patients with chronic pain entering a clinical trial for coping skills training for pain management. The average age was 66 years (range 36 to 88 years, SD = 9.4), and participants were predominantly female (78%), white (86%), and married (62%). Most were high school graduates (94%), and 41% had graduated from college. The average duration of OA was 13 years (range 1 to 55 years, SD = 10.1), and 15% of the patients were currently receiving disability compensation. The daily ratings (pain intensity, fatigue, interference with walking, interference with work, interference with social activities, quality of day, satisfaction with accomplishments) were collected over 7 consecutive days. Across all 194 participants and 7 days, a total of 112 (8.2%) of 1358 days were missing.

At baseline, the mean BDI depression score was 9.79 (SD = 7.19), with 75.3% of the sample showing minimal (scores 0 to 13), 13.9% mild (scores 14 to 19), 8.8% moderate (scores 20 to 28), and 2.1% severe (scores 29+) depression. The mean score for AIMS tension was 13.23 (SD = 3.66), for ASES self-efficacy 6.09 (SD = 1.83), and for CSQ catastrophizing 7.05 (SD = 6.48).

3.2.2. Individual differences in within-person variability

Table 3 shows the means and the variances (displayed as SD) between and within people for each of the daily variables. The amount of within-person variability was significant and pronounced for all variables, accounting for between 34% (for interference with social relationships) and 54% (for quality of day ratings) of the total variance. As shown in Table 3, the between-person SDs, which represent individual differences in mean levels across the week, ranged from 13.6 points (for quality of days) to 18.7 points (for interference with walking). The within-person SDs, which roughly represent the magnitude of day-to-day fluctuation on a 0 to 100 scale, were not much smaller than the between-person SDs, and ranged from 13.0 points (for social interference) to 16.8 points (for interference with work).

Expanding the multilevel models with weekday–weekend differences showed that for the average patient (i.e., fixed effects), interference with social relations was greater on weekends (estimate = 2.26, SE = .93, $P < .05$) and satisfaction with accomplishments was lower on weekends (estimate = −1.96,

Table 3
Study 2 (7 days)—means and variance components for daily variables.

	Mean	SD		Within-person variance (%)
		Between-person	Within-person	
Pain	47.05	17.10	14.56	42
Fatigue	46.31	17.32	15.22	44
Interference with walking	44.36	18.74	15.99	42
Interference with work	40.37	18.44	16.82	45
Interference with social relations	19.14	18.02	13.03	34
Quality of day	62.69	13.63	14.70	54
Satisfaction with accomplishments	63.56	14.85	15.11	51

n = 194; between-person and within-person variances are statistically significant ($P < .0001$) for all variables.

SE = .99, $P < .05$) than on weekdays. In addition, the random effects estimates showed that the magnitude of weekend effects varied significantly ($P < .05$) across people for fatigue, interference with social relations, and satisfaction with accomplishments. Thus, weekday–weekend differences were controlled in the further analyses.

Tests for individual differences in the amount of day-to-day variability were highly significant ($P < .001$) for all variables: pain intensity, $\chi^2(193) = 421.74$; fatigue, $\chi^2(193) = 475.14$; interference with walking, $\chi^2(193) = 478.91$; interference with work, $\chi^2(193) = 483.37$; interference with social relations, $\chi^2(193) = 802.58$; quality of day, $\chi^2(193) = 433.70$; and satisfaction with accomplishments, $\chi^2(193) = 455.50$ (The χ^2 test for significant individual differences in variability should be used cautiously when the number of observations per person is small, given that the null distribution may not be assumed to be a χ^2 value in these cases. Comparisons of the sums of squared dispersion scores with the correct null distribution (as described in Snijders et al., p. 127) [36], did not change the results, with all $P < .001$.). Thus, examining predictors of day-to-day variability was justified.

3.2.3. Psychological factors as predictors of within-person variability

Table 4 shows the results for the final multilevel models, which included BDI depression, AIMS anxiety, ASES self-efficacy, and CSQ catastrophizing scores as simultaneous predictors of a person's average level (fixed effects in Table 4) and day-to-day variability (within-person random effects in Table 4) for each of the outcome variables.

3.2.3.1. Prediction of a person's mean level. When entered separately in initial models, each of the predictors significantly predicted symptom intensity levels for all outcomes, with the exception of anxiety not being predictive of interference with walking (see Table 4). In the final models, higher depression scores uniquely predicted higher levels of fatigue ($P < .01$), more interference with work ($P < .05$), more interference with social relations ($P < .05$), and less satisfaction with accomplishments ($P < .01$). Higher self-efficacy predicted greater average quality of days ($P < .01$) and greater satisfaction with accomplishments ($P < .05$). Higher catastrophizing predicted higher levels of pain intensity ($P < .001$) and more interference with walking ($P < .01$), work ($P < .05$), and interference with social relations ($P < .01$).

3.2.3.2. Prediction of within-person variability. No significant effects were found in the prediction of within-person variability in pain, fatigue, and interference with walking (see Table 4). Higher depression levels predicted greater day-to-day variability in social interference ($P < .001$; estimated within-person SD = 10.87 at low depression and SD = 13.93 at high depression), and in satisfaction with daily accomplishments ($P < .06$; SD = 13.93 at low and

Table 4
Study 2 (7 days)—multilevel models for psychological predictors of mean levels and within-person variability.

	Pain intensity		Fatigue		Interference with walking		Interference with work		Interference with social relations		Quality of day		Satisfaction with accomplishments	
	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Fixed effects														
Intercept	46.79	1.26***	45.83	1.30***	44.21	1.38***	40.12	1.37***	18.46	1.23***	62.73	1.01***	64.39	1.09***
Weekend	1.07	1.01	1.53	1.08	.75	1.03	.42	1.14	2.33	.92*	.86	.98	−2.01	1.07†
BDI–depression	1.67	1.87	4.96	1.93**	1.84	1.78	4.12	2.02*	3.77	1.87*	−2.38	1.48	−4.31	1.62**
AIMS–anxiety	−.86	1.60	.78	1.65	–		−2.01	1.73	.18	1.58	−2.27	1.27	−1.37	1.38
ASES–self-efficacy	−1.13	1.41	.66	1.45	−.88	1.54	−2.85	1.52	−1.65	1.39	3.21	1.11**	3.07	1.21*
CSQ–catastrophizing	5.72	1.52***	2.01	1.56	5.55	1.67**	3.86	1.64*	4.57	1.50**	−.79	1.20	−0.13	1.30
Random effects														
Level 2 (between-person)														
Intercept variance	250.26	30.09***	263.91	31.84***	307.35	36.40***	287.95	35.16***	248.57	29.70***	142.57	18.60***	172.62	22.07***
Weekend	26.09	20.34	38.24	22.89*	.49	20.96	29.14	24.83	41.52	16.55**	13.82	18.70	44.37	21.65*
Level 1 (within-person)														
Intercept variance	208.80	9.99***	225.41	10.83***	255.93	12.10***	273.63	12.96***	153.28	7.36***	211.58	10.14***	214.59	10.37***
BDI–depression	–		–		–		–		.26	.06***	–		.10	.05†
AIMS–anxiety	–		–		–		−.08	.05	–		–		–	
ASES–self-efficacy	–		–		–		.09	.05†	–		−.13	.05**	−.15	.05**
CSQ–catastrophizing	–		–		–		–		.12	.06†	–		–	

Dashes indicate that a predictor was not entered in the final models.
AIMS = Arthritis Impact Measurement Scale; ASES = Arthritis Self-Efficacy Scale; BDI = Beck Depression Inventory; CSQ = Coping Strategies Questionnaire.
† $P < .06$.
* $P < .05$.
** $P < .01$.
*** $P < .001$.

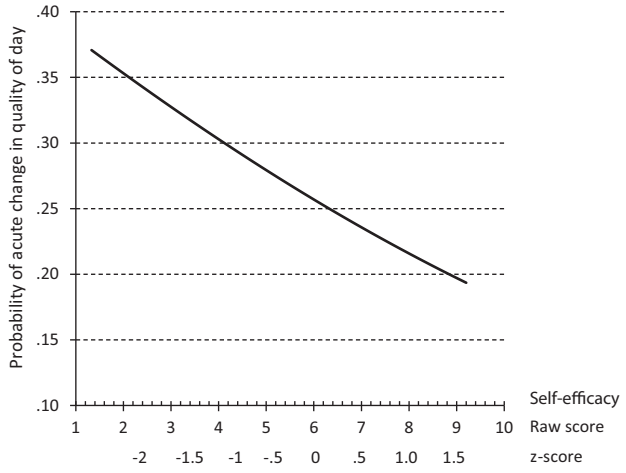

Fig. 3. Study 2: estimated probability of acute change in pain intensity as a function of Arthritis Self-Efficacy Scale scores, where higher scores indicate more self-efficacy.

SD = 15.40 at high depression). Higher self-efficacy predicted less variability in the quality of days ($P < .01$; SD = 15.52 at low and SD = 13.63 at high self-efficacy) and in satisfaction with accomplishments ($P < .01$; SD = 15.79 at low and SD = 13.59 at high self-efficacy). In addition, there was a trend for greater catastrophizing to predict more variability in interference with social relations ($P < .06$; SD = 11.66 at low and SD = 13.14 at high catastrophizing). These effects were all in the hypothesized direction, indicating more variability among patients with greater psychological distress and poorer coping resources. Contrary to expectation, there was a trend for greater self-efficacy to predict more variability in interference with work ($P < .06$; SD = 15.81 at low and SD = 17.30 at high self-efficacy).

3.2.4. Supplemental results based on the PAC

We conducted analyses based on the PAC to further illustrate the magnitude of the effects. Fig. 3 exemplifies the PAC in quality of days predicted from ASES self-efficacy scores. At low levels of self-efficacy (a raw score <4 on the 10-point scale, 1SD or more below the sample average score), the predicted chance of acute shifts in the quality of days exceeds 30%, whereas at high levels (raw score >8, 1 SD above the average score), the chance of acute shifts is 19% to 22%. The odds of acute shifts in the quality of days decrease by 19% ($P < .01$) per SD higher self-efficacy. Furthermore, the odds of an acute shift in daily satisfaction with accomplishments decreased by 15% ($P < .05$) per SD higher self-efficacy, and the odds of acute shifts in social interference increased by 39% ($P < .001$) per SD higher depression.

3.2.5. Longer-term temporal stability of individual differences in within-person variability

We were able to examine the longer-term test-retest reliability of individual differences in variability in this study, given that the data was from a randomized clinical trial and patients completed the daily ratings for 7 days at posttreatment in addition to the baseline daily ratings. The average interval between baseline and posttreatment assessments was 4.0 months (mean 121 days, SD = 20.3). We estimated the within-person SDs separately for the baseline and posttreatment assessment periods from multilevel models, and then computed the ICCs between the periods as a measure of test-retest reliability. Only patients from the usual care control group of the clinical trial were included in these analyses (n = 81). The ICCs (with 95% confidence limits) were .38 for pain (CL = .18 to .55), .08 for fatigue (CL = −.13 to .29), .31 for interference with walking (CL = .10 to .49), .53 for interference with work (CL = .36 to .67), .16 for social interference (CL = −.06 to .36), .23 for quality of day (CL = .02 to .42), and .32 for satisfaction with accomplishments (CL = .11 to .50). These correlations are low to moderate in magnitude.

4. Discussion

With the advent of electronic diary methods that capture the dynamic nature of symptom levels, it is becoming increasingly evident that a patient's average or usual level of pain, interference, or affect represent only one dimension of persistent pain [41]. In this report, we focus on individual differences in the magnitude of fluctuations in pain and other daily measures across multiple days in 2 studies. Several results are noteworthy. First, day-to-day fluctuations are sizeable in patients with persistent pain. Second, the magnitude of variability is similar in both studies using different rheumatology diagnostic groups. In both samples, day-to-day fluctuations range on average from 13 to 17 points (100-point scale) across all daily measures. Indeed, variability in daily pain and other variables has been found across patients with rheumatoid arthritis [38], OA [2], chronic pain [21,27], and fibromyalgia [15]. This documents the need to understand day-to-day symptom fluctuation in a variety of persistent pain conditions, including OA, which has been assumed to be a more stable disease [2]. Taken together, these findings suggest that such fluctuations are an important feature of the pain experience and deserve more attention from pain clinicians and researchers.

Furthermore, substantial individual differences in the magnitude of the variability are observed in both studies. Whereas some patients experience little fluctuation in the intensity of daily pain and other measures, other patients' reports show pronounced day-to-day shifts. Across our 2 studies, we were able to examine several constructs with the potential to explain these individual differences in day-to-day variability: depression, anxiety, self-efficacy, and pain catastrophizing, though not all variables were available in both studies. Depression emerges as a significant predictor of greater variability in pain intensity in Study 1. Depression predicts more frequent acute day-to-day changes in pain, that is, daily shifts exceeding a threshold that has been considered clinically meaningful [13]. Specifically, patients with low levels of depression experienced these acute daily shifts in pain intensity on every fifth day, whereas patients with moderate or severe depression experienced them approximately every third day.

Depression also predicts daily variations in ratings of happiness and frustration in Study 1, consistent with depression being viewed as a mood regulation problem. The effect is stronger for daily shifts in frustration than for happiness, in line with cognitive theory suggesting that depression involves biased attention and processing, particularly of negative emotional information [4]. Previous studies have similarly documented greater affective instability in patients during depressive episodes [7]. In Study 2, depression is a significant predictor of daily variations in how much arthritis interfered with social relationships and how satisfied patients were with their daily accomplishments. However, depression does not predict pain variability in Study 2. This may be due to the fact that Study 2 patients were less depressed, with only 11% in the moderate to severe range of depression on the BDI (compared with 22% in Study 1), thus attenuating a possible relationship. Anxiety does not predict variability in either study for any of the patient ratings. These results are consistent with prior research in which depression is a more consistent predictor of adjustment to pain than anxiety [27]. Considered overall, these findings suggest that patients who have persistent pain and who

have higher levels of depression are more likely to have highly variable day-to-day experiences in pain and wellbeing with more frequent highs and lows.

In Study 2, we examine 2 indexes of pain coping (self-efficacy and pain catastrophizing) that might explain variability. First, patients who are more confident about their ability to control pain (self-efficacy) display more stability in their satisfaction with daily accomplishments and quality of their day. Thus, self-efficacy may serve as a buffer that prevents frequent vacillation in patients' perceived quality of life and daily accomplishments. These results are consistent with findings that self-efficacy buffers the effects of stressful events on emotion and well-being [31]. Second, pain catastrophizing predicts more variability of interference with social relations. The dominant theory of pain catastrophizing is a communal model that maintains that catastrophizing initially develops because it helps patients to maintain proximity and support from others [42]. However, the communal model and research studies further suggest that, when pain persists over time, catastrophizing has a detrimental impact on support and social relationships [9]. Our finding that catastrophizing predicts more variability in interference with social relations thus fits both theory and prior research.

Our results have several clinical implications. First, they suggest that fluctuations in pain and other pain-related measures are a common experience for patients, even those with stable disease. Thus, to best capture how patients are adjusting to pain, clinical assessments should go beyond asking patients to report their usual or average pain level and include assessment of how their pain varies from day to day and how this variability impacts them. Second, clinicians might consider targeting a reduction in variability as an important treatment target. For example, patients may find the pain experience to be more predictable and manageable if it varies less from day to day. Our results suggest that individual differences in variability are moderately stable over 4 weeks (Study 1). The 4-month stability estimate (Study 2) is moderate to low, but comparison of these reliabilities must be interpreted cautiously because fewer observations were available and a different methodology was used in Study 2. Third, clinicians need to recognize that patients with certain characteristics (e.g., depression) are more likely to experience daily fluctuations. Thus, a treatment focus on depression may also mitigate variability in pain and related variables.

There are several important future directions for research in this area. First, there is a need to explore additional factors that might explain daily variability. The current study focused on several psychological factors, but future studies should examine biological factors (e.g. genetic background, disease severity, medications) as well as social and environmental factors (social support, cultural background, activity level) that may be important. Second, future studies should examine the degree to which fluctuations in pain and related experiences are, in and of themselves, predictive of treatment outcome. Along these lines, there is evidence that people who show greater symptom fluctuations may be more likely to respond to drugs and placebos. For example, Harris et al. [15] reported that fibromyalgia patients with larger pain variability (defined by within-person SD) were more responsive to a placebo intervention than patients with smaller pain variability. Similarly, Scott-Lennox et al. [35] reported that patients with initially more intense pain flares were more responsive to placebo.

There are several strengths of these studies. First, the daily ratings of pain and related variables were collected electronically with time and date stamping to ensure the internal validity of the measurements [40]. Second, the hypotheses were examined in 2 somewhat different samples of rheumatology patients, increasing generalizability of the findings. Third, the samples were relatively large (N = 106, N = 194), increasing the reliability of the findings. Fourth, the analytic strategies used in this report are especially suited to understand individual differences in symptom variability. Importantly, the described multilevel models can readily be expanded to research questions involving longitudinal change in variability, for example, to analyze the extent to which patients exhibit increasing stability over time in response to medical or psychological treatment [16].

There are also limitations of these studies. The samples are predominantly female as would be expected in rheumatology samples, white, and well educated; thus, the results may not generalize to other demographic and diagnostic groups. Second, the analyses are based on end-of-day diaries. The results may not generalize to fluctuations that occur within days, such as moment-to-moment instability. Third, the relatively small number of observations per person (7 days) in Study 2 may have limited the statistical power to detect significant effects of person-level predictors in this study, and may also have attenuated the test-retest reliability estimates of individual differences in variability. Fourth, the analyses are cross-sectional and cannot establish whether depression and coping appraisals are a cause or a consequence of fluctuations in pain and daily adjustment, or whether both have reciprocal effects on each other.

In conclusion, fluctuations in pain, interference in activities, and mood are observed to be a fundamental aspect of the daily experience of patients with persistent pain. However, little is still known about the clinical importance of these fluctuations as an individual-difference marker. Whereas this research was focused on associations of variability with psychological factors, future research will be necessary to examine more closely the clinical utility of measuring individual differences in variability. This requires more understanding, for example, about the role of symptom variability in the frequency of medication usage or healthcare utilization, and about the patient's overall view of the manageability of the disease. It is conceivable that optimal treatment effects, as perceived by patients, may require reductions in both level and variability in pain.

Conflict of interest statement

Broderick and Stone have a financial interest in Invivodata, Inc. The other authors have no conflict of interest to declare.

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