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The Relationship between Fatigue and Subsequent Physical Activity among Older Adults with Symptomatic Osteoarthritis

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Abstract

Objective—Although it has been well established that fatigue is a common complaint among older adults with osteoarthritis (OA), relatively little is known about how fatigue in daily life affects physical activity. The purposes of this study were to examine the relationship between momentary fatigue and subsequent physical activity among people with OA who report clinically relevant levels of fatigue and to examine moderators of this relationship.

Methods—People with knee or hip OA and clinically relevant fatigue participated in physical performance assessments, completed questionnaires, and underwent a home monitoring period in which fatigue severity was measured 5 times per day over 5 days (N = 159). Physical activity was concurrently measured via a wrist-worn accelerometer. Multilevel modeling was used to examine the relationship of momentary fatigue and subsequent activity controlling for other factors (e.g., age, body mass index, pain, depression).

Results—Fatigue was the strongest predictor of reduced subsequent activity. Only functional mobility (TUG) moderated the relationship between fatigue and activity. The relationship between fatigue and activity was strongest for people with high functional mobility.

Conclusions—Momentary fatigue is a robust and important variable associated with decreased physical activity. Further, the moderating effect of functional mobility suggests this is a factor that should be considered when intervening on fatigue. While people with better functional mobility may benefit from an activity-based treatment approach (such as learning activity pacing techniques to reduce fatigue's impact on activity), those with worse functional mobility may benefit from treatment focusing on underlying impairments.

Among people with osteoarthritis (OA), pain is the main reason cited for difficulty in performing daily tasks [1] and for seeking treatment. While the main focus of treatment is on pain relief, this approach may be too narrow for optimal OA management. Fatigue, for instance, is also recognized as a symptom that has a substantial impact on many aspects of life among people with OA [2]. Although fatigue is not as well studied in OA as pain, it is prevalent. Approximately 40% of people with OA aged 65 years and older reported clinically meaningful levels of fatigue [3]. In another study of people with knee and hip OA who were referred to an OA outpatient clinic, 66% reported moderate to severe fatigue [4]. Fatigue is a predictor of adverse outcomes, particularly among older adults. In fact, fatigue (described as self-reported exhaustion) is one of five clinical indicators in a common model of frailty [5], a condition of impaired strength, endurance, balance, and increased vulnerability to trauma or other stressors [6]. When fatigue in older adults was measured as tiredness in daily activity performance, it predicted the development of mobility problems

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[7], dependence in daily living tasks [8], and mortality [9]. In another study, tiredness ‘most of the time’ was associated with lower functioning that persisted for 3 years and mortality [10, 11].

There is a clinical assumption that OA pain causes fatigue and that relief of pain will cause a commensurate reduction in fatigue; however, this assumption is likely flawed as these two symptoms may have different etiologies and a more complex interaction, especially in older adults. Fatigue among people with OA may result from a variety of factors or their combination, not only disease-specific factors like OA, but also psychological issues and sleep problems that can be difficult to disentangle. Instead of focusing on causes of fatigue, another way to potentially impact fatigue in OA is to mitigate its effects, particularly on activity. Fatigue was cited as the primary reason that older adults in a large population-based cohort limited their activity [12], and the fatigue-activity relationship is thought to be particularly important to examine to better understand physical fatigue among older adults [13]. In our previous studies in which we assessed symptoms within and across days (i.e. momentary fatigue and pain) and concurrent physical activity, we found that fatigue was related to reduced physical activity more so than pain in women with OA [14]. In another analysis of these data, women with OA were 4 times more likely to experience increased fatigue after a high bout of physical activity compared to age-matched controls [15].

It is particularly important to examine how fatigue is associated with subsequent physical activity levels in daily life. A better understanding of how people behave and adjust their activity levels in the presence of fatigue can inform the development and refinement of behavioral interventions. Further, the characteristics that moderate this relationship become particularly important to consider when targeting treatments to particular subgroups. Although there has not been much work done in this area, in a sample of people with knee or hip OA that were 50 and older, the use of different coping strategies moderated the relationship between fatigue and activity which provides information on how behavioral strategies work on a moment to moment basis as people engage in activity with fatigue (35). Other than this study, little remains known about other moderators of the relationship between fatigue and activity.

In this study, we examined how momentary fatigue relates to subsequent physical activity in a sample of older adults with OA who reported clinically relevant levels of fatigue and explored what factors moderated this relationship. We hypothesized that higher fatigue would be related to lower subsequent activity levels.

Patients and Methods

Participants

Community-living older adults aged > 65 years were recruited through newspaper and online advertisements, radio advertisements, and through flyers distributed in senior centers, senior housing sites, and hospitals. Participants were included if they had knee or hip pain of mild to moderate severity on the WOMAC pain scale [16]. They also needed to have OA in the corresponding knee or hip joint(s) according to the American College of Rheumatology (ACR) clinical criteria [17, 18] which was ascertained through physical exam by a rheumatologist-trained nurse practitioner. Further, participants needed to meet the fatigue criteria [two questions from the Center for Epidemiological Studies Depression Scale (CES-D)] [19] which is part of the frailty phenotype in older adults [5]. To meet the criteria, participants needed to report a frequency of at least “a moderate amount of the time” for 1 of 2 questions: “How often in the past week did you feel like everything you did was an effort?” and “How often in the past week could you not get going?” Other eligibility criteria included acceptable cognition (score of > 5 on the Six-Item Screener [20]) and ability to enter

symptom ratings into the study accelerometer), and a normal sleep schedule (usual wake-up time before 11 am and bedtime before 2 am). Participants were excluded if they were unable to walk with or without an assistive device, experienced a period of bed-rest > 2 days within the past month, or changed their medications within the past two weeks. Medical conditions that could impact symptom ratings or accelerometer data also deemed people ineligible including rheumatoid arthritis, cancer or cancer treatment within the last year, lung disease, heart failure, fibromyalgia, chronic fatigue syndrome, lupus, multiple sclerosis, or sleep apnea. Lastly, participants were ineligible if they had other known medical causes of fatigue (i.e., abnormal TSH or low hemoglobin determined via blood test).

Procedure

Research personnel met with participants who were initially eligible from the phone screening for a clinic visit. After informed consent was obtained, participants met with a nurse practitioner for further screening (i.e., blood draw, OA clinical criteria, health history), and completed questionnaires. Participants eligible from the in-person screening returned for a second clinic visit in which physical performance and aerobic function testing was performed. Participants then took part in a tutorial on the Actiwatch-Score (Actiwatch-S; Philips Respironics, Mini Mitter, Bend, OR) accelerometer with an accompanying logbook for use in the home monitoring period. They were instructed to wear the Actiwatch-S on their non-dominant wrist for a five day period (Monday through Friday) and only to take it off when there was a possibility of the device becoming wet (e.g., showering/swimming). Participants were instructed to input symptom ratings 5 times per day and to record ratings in the logbook along with their wake and bedtimes each day. Participants returned the Actiwatch-S and logbook after the home monitoring period by mail in a prepaid envelope which concluded study participation.

Measures

Demographics and Health Status—Demographics included age, gender, race/ethnicity, and marital status. Health status variables included pain severity in each joint with OA, body mass index (BMI), and number of health problems (out of a list of 41) from different body symptoms (e.g., stomach pain, headaches, daytime sleepiness), which we refer to illness burden. Depressive symptomatology was measured using the CES-D [19]; a score of 16 or greater has been associated with clinically significant depressive symptoms [21].

Baseline Fatigue and Pain—Fatigue was measured using the Brief Fatigue Inventory, in which 9 items reflecting fatigue severity or fatigue interference in daily life are rated on a scale of 0 – 10 (“no fatigue” to “fatigue as bad as you can imagine”) over the past week and averaged to generate a total score [22]. Pain was also measured using the WOMAC, which has three subscales that measure pain, stiffness, and physical functioning [23]. To measure physical function on the WOMAC, the short-form was administered [24].

Sleep—The Pittsburgh Sleep Quality Index (PSQI) was used to determine participants' sleep quality, including sleep duration, sleep efficiency, sleep latency and disruption of daytime activities [25]. The sleep efficiency subscale was used in this study.

Physical Performance and Aerobic Function—Two objective physical performance tests were performed. Functional mobility was measured using the Timed Up and Go (TUG) test [26] in which participants are timed as they get up from a chair, walk 3 meters, return to the chair, and sit down. Walking endurance was tested using the 6 minute walk test (6MWT) [27] in which people walk for 6 minutes at their usual pace while timed. During the 6MWT, aerobic function was measured using the CosMed K4 b² portable metabolic measurement

system, a valid and reliable device measuring oxygen uptake during exercise of varying intensities [28]. Aerobic function was operationalized as the peak oxygen uptake (V_{O_2}) and measured in milliliters of oxygen per kilogram of bodyweight per minute (ml/kg/min). The measurement of aerobic function during a submaximal test, such as the 6MWT, has been performed in a previous study by members of our study team and found to be associated with functional disability [29]. A lower V_{O_2} denotes decreased aerobic function.

Measures from the Actiwatch Accelerometer

Momentary Fatigue and Pain: Participants input symptom ratings into the Actiwatch-S 5 times a day (wake-up, 11am, 3pm, 7pm, and bedtime) for 5 days. Fatigue and pain were rated on a 0-10 scale (0 = “no fatigue/pain,” - 10 = “fatigue/pain as bad as you can imagine.”).

Physical Activity: Physical activity was measured using the Actiwatch-S. Even though the accelerometer is worn on the wrist, the device measures activity related to whole-body movements [30]. Studies support its reliability and criterion validity [31] as well as its ability to discriminate between activity levels of controls versus disease groups [14, 32]. The accelerometer recorded activity over 15-second epochs. The activity counts per minute (ac/min) were used in the analysis which was aggregated for each time interval between symptom reporting periods during each day (greater ac/min indicates a higher activity level). A subsequent physical activity bout as defined in this study is the period (which was typically 4 hours, but varied for participants at the beginning and end of the day) that followed a fatigue rating that occurred at wake-up, 11am, 3pm, or 7pm.

Data Analysis

For descriptive purposes, correlations (Pearson's r) were computed between variables of interest at the subject level. For some variables, (activity level, momentary fatigue and pain), there were many observations per participant, while for others (e.g., BMI, WOMAC pain), there was only observation per participant. Therefore, multilevel modeling (MLM) was used with activity level as the outcome variable in order to separately model variation that occurs both between and within subjects.

For the multilevel modeling, an “empty” model was first performed using only activity level with no predictor variables. This allowed for a determination of how much variability in activity level can be attributed to within subject variation (that is, changes in activity level that occur within persons from interval to interval) versus between subject variation (that is, the overall differences in activity level across persons). In MLM terms, the within subject variation occurs at level 1, while the between subjects variation occurs at level 2. As recommended in multilevel models, within subject variables (momentary fatigue and pain) were person-centered so that values indicate change from the person's average [33]).

After the empty model, a predictive model of activity level was built that included both level 1 variables (momentary fatigue and pain) and level 2 variables (averaged fatigue and pain levels, BMI, age, TUG, etc). To examine the relationship of fatigue and subsequent activity, the data were structured such that the fatigue rating occurred prior to the activity interval in the model. As in previous work [14], pain and fatigue were included in both the fixed and random parts of the model. This allowed testing of whether magnitudes of the relationships between momentary pain, momentary fatigue, and activity level differed across participants.

Finally, to see if the relationship between fatigue and activity level was moderated by other participant characteristics, interaction terms were added to the fixed part of the model. All covariates in the model were tested as potential moderators. Significant interactions were

graphed using the simple slopes between fatigue and subsequent activity at low (-1SD), mean, and high (+1SD) values of the moderating variables [34].

Results

After phone screening, 221 potential participants underwent an in-person screening visit which resulted in 172 eligible participants (see Figure 1). People who were ineligible had less pain (7.5 + 3.4 versus 8.6 + 3.6; $p = .04$) and greater WOMAC physical function (i.e., less disability) compared to eligible participants (9.4 + 3.8 versus 10.9 + 4.2; $p = 0.4$ respectively). Baseline characteristics of eligible participants are shown in Table 1. Over half of participants were married women and most were Caucasian. Thirty-seven participants met the ACR clinical criteria for both knee and hip OA, but when asked to identify the most painful joint with OA, the knee was most common. The mean body mass index was considered obese (BMI = 30.5). Participants reported moderate levels of fatigue on the BFI, and mild to moderate involvement of WOMAC pain, stiffness, and physical function. In physical performance, the sample had worse scores than norms for healthy older adults on functional mobility [35] and walking endurance [35, 36]. During the home monitoring period, fatigue and pain were experienced at mild to moderate levels when averaged across 5 days.

Table 2 presents the between-subject correlations between all of variables of interest. As noted in Table 2, activity level averaged over the home monitoring period (mean ac/min) was most strongly and positively associated with walking endurance (6MWT; $r = .26$) and was negatively associated with functional mobility (TUG), age, and sleep efficiency. Average fatigue and pain from the home monitoring period were highly correlated ($r = .81$), and both symptoms were most strongly associated with WOMAC physical function and pain. Additional associations reaching statistical significance were observed between symptoms during the home monitoring period and TUG, illness burden, depression, and aerobic function.

The relationship between fatigue and subsequent activity was examined using MLM (see Table 3). From 172 eligible participants, data from 140 participants were analyzed. Most people were excluded from the analysis due to missing data on the aerobic function test ($n = 16$), and others were excluded for missing data on random predictor variables. In the 'empty' model, most of the variability in activity occurred within subjects, with only 35% of variability in activity occurring between subjects (ICC = .35, $p < .001$). The results show a strong negative relationship between fatigue and subsequent activity. As fatigue increased by one unit, subsequent activity counts/minute decreased by 14 units (in the model without the interaction). No other variables were significantly independently associated with activity level. However, greater sleep efficiency was marginally associated with higher subsequent activity ($p = .07$).

Interaction terms were added to the model to examine what variables moderated the relationship between fatigue and subsequent activity. Of all variables in the model tested, only functional mobility moderated this relationship which is presented in the final model in Table 3 ($b = 1.2$, $p = .05$). Examination of the simple slope between momentary fatigue and subsequent activity at high, mean, and low levels of functional mobility indicates that with higher levels of functional mobility, the relationship between fatigue and subsequent activity is more negative (slopes for high, mean, and low groups were -18, -14, and -10 respectively, see Figure 2). People with the lowest functional mobility have the lowest association between fatigue and subsequent activity.

In comparing the variability in intercepts between this model and the empty model, the between subject variables accounted for 7% of the explainable between subject variation in activity level. Similarly, in comparing the residual variability, the within subject variables (pain, fatigue, and the interaction with TUG) accounted for 8% of the explainable within subject variability in activity level.

Because functional mobility was highly correlated with walking endurance on the 6MWT ($r = .7$), in a post-hoc analysis, we ran two separate MLM with TUG and 6MWT in each exclusively along other variables in Table 3. While each of these physical performance variables was significantly associated with activity level in these models, still only functional mobility moderated the fatigue/activity relationship.

Discussion

In this study we examined the relationship of fatigue on subsequent physical activity in people with OA who reported clinically-relevant levels of fatigue. For the sample, increased momentary fatigue was associated with reduced subsequent activity, which supported our hypothesis. Fatigue was more strongly associated with activity when compared to pain, which showed no association with activity. These findings are generally consistent with previous studies where we examined the relationship between fatigue and activity using these same measures in slightly younger adult OA samples [14, 37]. In addition, in the current study, we recruited older people who had baseline fatigue levels thought to be clinically relevant. Despite moderate baseline levels of fatigue among people with OA, the daily experience of fatigue remains strongly related to physical activity levels and therefore is a potentially important therapeutic target among all people with symptomatic knee or hip OA.

We examined a large array of potentially relevant covariates and found that none were significant in the model of the relationship between fatigue and activity, and only functional mobility (measured by TUG) moderated this relationship. For all functional mobility subgroups, there was a negative relationship between fatigue and subsequent physical activity. However, people who had higher functional mobility (i.e., faster TUG time) had stronger relationships between fatigue and physical activity than people with lower functional mobility. This suggests different underlying causes of fatigue by functional mobility. It may be that the momentary fatigue reported by those with higher functional mobility is more of a physical nature and activity-dependent compared to the fatigue reported by those with worse functional mobility. Thus, those with worse functional mobility may have different underlying causes of fatigue that extend beyond peripheral OA disease and symptoms. Further, it could be that people with lower functional mobility are engaging less in activities that are fatiguing compared to those with higher functional mobility. Decreased physical performance (measured by usual gait speed) is strongly associated with reduced physical activity measured by accelerometer [38].

These findings provide some implications for OA treatment, particularly that it may be important to tailor non-pharmacological treatment for fatigue based on functional mobility level. Given that those with the highest functional mobility had the strongest effects of fatigue on subsequent activity, optimal interventions for this subgroup may need to include activity-based strategies such as activity pacing. While self-pacing may be problematic because people titrate activity in the presence of symptoms or to avoid symptoms, if used appropriately, time-based activity pacing, taught as a self-management tool, is thought to lead to sustained or increased activity levels [39] and has been shown to positively impact fatigue in a pilot study [40]. For people who have lower functional mobility, it may be more important to focus on improving physical function to decrease fatigue.

This study has some limitations. The generalizability of our findings is limited to the characteristics of our sample who were mainly Caucasian and had mild to moderate pain and fatigue symptoms. Although we tried to sample people with clinically relevant levels of fatigue, the inclusion criteria of fatigue using the frailty phenotype [5] may not have adequately identified people with OA for whom fatigue was already a problem. In a study of the prognostic significance of this phenotype, the 2 questions from the CES-D did not independently predict any adverse outcome (i.e., injurious falls, nursing home admission, disability, death) examined over 6 years [41]. In our sample, participants had difficulty answering one of these questions: “How often in the past week could you not get going?” Many participants reported that it was a necessity to get up and accomplish tasks everyday limiting the usefulness of that question. Although the wrist-worn accelerometer is a reliable and valid measure of activity patterns, as with any activity monitor, it is most sensitive at capturing movement at the site where it is worn. Therefore, this could have contributed to error in the measurement of physical activity that relates to functional mobility as upper-extremity, sedentary activities may be better captured (contributing to higher activity counts) than some lower extremity activities. We also did not have a measure of activity intensity which may provide additional insight into the fatigue-activity relationship. In addition, because the model explained only a small amount of variance in activity level within and across participants, the relationship between fatigue and activity may be better explained by other factors not assessed in this study. Coping strategy use is one factor that may be useful to include in future models as it moderated the relationship between fatigue and activity in a previous study [37]. Given that there were few studies to guide hypotheses, our approach to studying moderators was necessarily exploratory. We tested a number of potential moderators and found support only for functional mobility as a moderator. This finding needs to be replicated in additional studies.

In conclusion, this study examined how fatigue in daily life related to subsequent physical activity among fatigued people with knee and hip OA. Daily experiences of fatigue were negatively and robustly related to subsequent physical activity. Further analyses revealed that the effect was strongest for people with the highest functional mobility, providing some support for a tailored approach to fatigue management in OA based on functional mobility.

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Significance and Innovation

- Among older adults with knee or hip osteoarthritis (OA) who reported fatigue considered clinically relevant, momentary fatigue was independently and strongly related to reduced subsequent physical activity.
- Only the level of functional mobility moderated the relationship between fatigue and activity. Fatigue was more strongly related to subsequent physical activity for those with high functional mobility compared to those with low functional mobility
- The results provides preliminary support for tailoring different non-pharmacological treatment strategies for people with knee and hip OA based upon their functional mobility level.

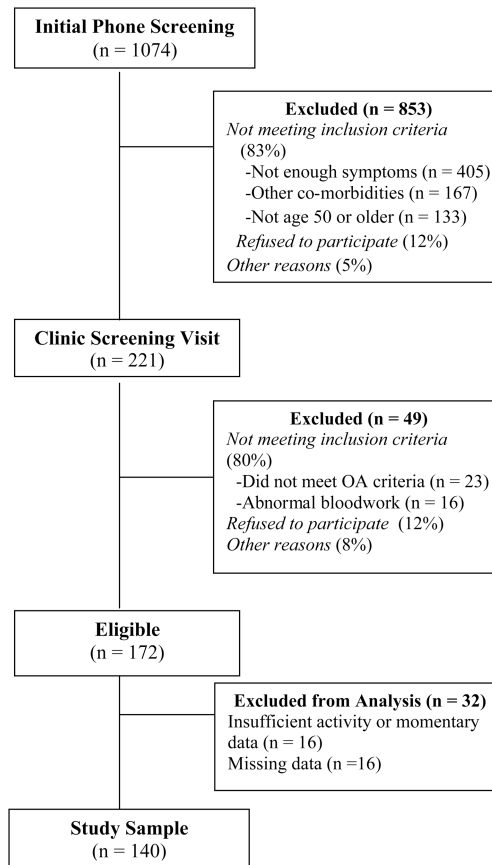


Figure 1. Study Flow Chart

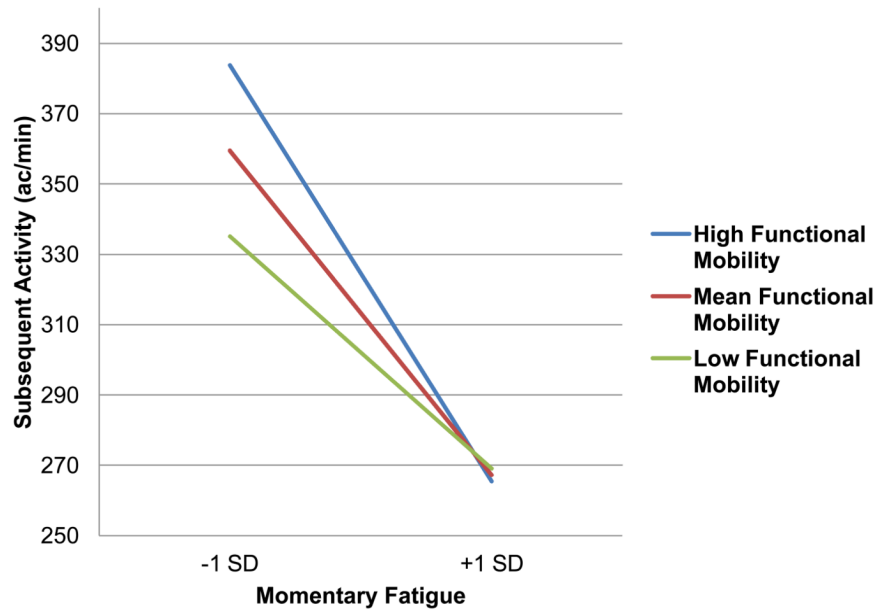


Figure 2. The Simple Regression Slopes for Centered Momentary Fatigue and Levels of Subsequent Physical Activity for Low, Mean, and High Functional Mobility on the Timed Up and Go (TUG) Test.

Note. High and Low functional mobility groups are + 1 SD and -1 SD from the mean respectively. Functional mobility is inversely related to TUG score (i.e., people with high functional mobility have the lowest walking times on the TUG test). The simple slopes for the high, mean, and low functional mobility groups are -18, -14, and -10 respectively.

Table 1
Baseline Characteristics of Eligible Participants (N = 172)

Variable	Mean (SD)	Range	N
Age	72.0 (6.0)	65-90	172
Women (%)	62.2%		172
Caucasian (%)	83.7%		172
Married (%)	57.6%		171
Most Painful OA Joint (Knee, %)	63.7%		171
Body Mass Index (BMI)	30.5 (5.8)	21-52	169
Illness Burden (# health problems--0 – 41)	9.5 (4.5)	0-24	170
CES-D Total Score	11.6 (8.4)	0-48	172
Brief Fatigue Inventory –Total Score	4.6 (2.0)	0 - 9	171
WOMAC Pain Scale	8.6 (3.2)	2-20	171
WOMAC Stiffness Scale	3.7 (1.6)	0-8	170
WOMAC Physical Disability (short form)	10.8 (4.2)	0-22	169
Pittsburgh Sleep Quality Index--Sleep Efficiency (%)	81.5% (15.6)	36-100	168
Timed Up and Go Test (TUG)	11.3 (3.5)	5.5-30	172
Six Minute Walk (total feet)	1130.2 (251.0)	265-1770	170
Aerobic Function [(Vo ₂) ml/kg/min]	12.0 (3.3)	3.9 – 20.5	154
Average Weekly Fatigue	4.0 (1.8)	0-8.5	162
Average Weekly Pain	3.2 (1.7)	0-8.9	162
Average Weekly Activity (ac/min) *	321.4 (101.5)	78-561.7	163

* ac/min = activity counts per minute

Table 2

Correlations (Pearson's r) Among Study Variables at the Subject Level.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Average Activity	--												
2. Average EMA Fatigue	.00	--											
3. Average EMA Pain	-.01	.81	--										
4. TUG	-.18	.19	.23	--									
5. 6 Min Walk	.26	.16	-.15	-.70	--								
6. Age	-.20	-.06	-.04	.09	-.21	--							
7. BMI	-.08	.08	.15	.07	-.20	-.26	--						
8. Illness Burden	.02	.31	.29	.17	.08	-.02	.02	--					
9. WOMAC Pain	.07	.34	.49	.12	-.21	-.15	.18	.35	--				
10. WOMAC Phys Function	-.03	.48	.62	.24	-.33	-.02	.24	.39	.72	--			
11. PSQI sleep efficiency	.20	-.02	-.17	-.21	.12	-.07	-.02	-.26	-.18	-.14	--		
12. Depression	-.03	.32	.29	.19	-.03	.00	.01	.47	.24	.28	-.28	--	
13. Aerobic function (Vo2)	.08	-.26	-.22	-.36	.47	.07	-.08	-.14	-.18	-.26	.04	-.15	--

* bolded correlations, p < .05

Table 3
The Relationship of Momentary Fatigue and Subsequent Activity (N = 140)

Covariance parameter estimates	Subject	estimate	Std. error	Z	P
<i>Random effects: prediction of activity level by interval</i>					
Intercept	ID	8797.94	1211.01	7.26	<.01
Fatigue slope	ID	263.75	97.78	2.70	<.01
Fatigue slope × intercept	ID	-143.28	262.37	-0.55	0.59
Pain slope	ID	283.36	127.30	2.23	0.01
Pain slope × intercept	ID	-22.93	306.66	-0.07	0.94
Pain slope × Fatigue slope	ID	-203.72	96.01	-2.12	0.03
Residual		15826	469.75	33.69	.01
<hr/>					
Predictor variables control variables					
		Std. error	DF	t	P
<i>Fixed effects</i>					
Age	-2.16	1.52	128	-1.42	0.16
BMI	-1.09	1.60	128	-0.68	0.50
Illness Burden	2.52	2.50	128	1.01	0.32
WOMAC pain score	4.42	3.88	128	1.14	0.26
WOMAC function score	-0.40	3.43	128	-0.12	0.91
Sleep efficiency	1.06	0.59	128	1.81	0.07
CES-D score	0.06	1.25	128	0.05	0.96
Aerobic function (V02)	3.46	2.82	128	1.23	0.22
Timed up and Go	-3.40	2.89	128	-1.18	0.24
<i>Level 2 Symptoms</i>					
Mean fatigue	4.24	8.67	128	0.49	0.63
Mean pain	-3.82	9.83	128	-0.39	0.70
<i>Level 1 Symptoms</i>					
Fatigue score in previous interval	-13.97	2.53	2496	-5.53	<.0001
Pain score in previous interval	0.39	2.80	2496	0.14	0.89
<i>Level 1 × Level 2</i>					
Fatigue × Timed up and go	1.20	0.62	2496	1.95	0.05