Activity patterns in response to symptoms in patients being treated for chronic fatigue syndrome: an experience sampling methodology study

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Running head: *Activity management in CFS*

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**Abstract**

**Objective:** Cognitive-behavioral models of Chronic Fatigue Syndrome (CFS) propose that patients respond to symptoms with two predominant activity patterns, activity limitation and all-or-nothing behaviors, both of which may contribute to illness persistence. The current study investigated whether activity patterns occurred at the same time as, or followed on from, patient symptom experience and affect.

**Methods:** Twenty-three adults with CFS were recruited from UK CFS services. Experience sampling methodology (ESM) was used to assess fluctuations in patient symptom experience, affect and activity management patterns over 10 assessments per day for a total of six days. Assessments were conducted within patients’ daily life and were delivered through an app on touchscreen Android mobile phones. Multi-level model analyses were conducted to examine the role of self-reported patient fatigue, pain and affect as predictors of change in activity patterns at the same and subsequent assessment.

**Results:** Current experience of fatigue-related symptoms and pain predicted higher patient activity limitation at the current and subsequent assessments, while subjective wellness predicted higher all-or-nothing behavior at both times. Current pain predicted less all-or-nothing behavior at the subsequent assessment. In contrast to hypotheses, current positive affect was predictive of current activity limitation, while current negative affect was predictive of current all-or-nothing behavior. Both activity patterns varied at the momentary level.

**Conclusions:** Patient symptom experiences appear to be driving patient activity management patterns, in line with the cognitive-behavioral model of CFS. ESM offers a useful method for examining multiple interacting variables within the context of patients’ daily life. **Keywords:** Chronic Fatigue Syndrome; Experience sampling methodology; Activity; Behaviours.

Chronic fatigue syndrome (CFS) is characterized by the experience of persistent and severe fatigue, in addition to other symptoms such as pain, sleep disturbance and reported cognitive deficits ([Fukuda et al., 1994](#_ENREF_11)). Cognitive-behavioral models propose that patient cognitions and behaviors interact in a complex fashion with patient symptom experience and affect in the perpetuation of CFS ([Chalder, Tong, & Deary, 2002](#_ENREF_8); [Deary, Chalder, & Sharpe, 2007](#_ENREF_9); [Surawy, Hackmann, Hawton, & Sharpe, 1995](#_ENREF_29)). It is suggested that patients beliefs about their symptoms (for example, that they are indicative of damage) and about appropriate responses to symptoms (for example that they should avoid activity to avoid exacerbating symptoms) drive their symptom management behavior ([Knoop, Prins, Moss-Morris, & Bleijenberg, 2010](#_ENREF_13)). Focusing on symptoms, catastrophizing about symptoms, and the belief that symptoms mean harm are suggested to lead to two predominant forms of behavioral response to symptoms, “all-or-nothing behavior” and “activity limitation”, which themselves contribute to dysregulation and the maintenance of symptoms ([Moss-Morris, 2005](#_ENREF_15)).

There is evidence that “all-or-nothing” behavior, in which bursts of intense activity when feeling relatively well are interspersed with periods of extended rest in response to symptoms, is associated with the initial persistence of fatigue symptoms and onset of CFS after glandular fever ([Moss-Morris, Spence, & Hou, 2011](#_ENREF_17)). There is less evidence that “all-or-nothing” behavior is involved in the maintenance of symptoms, although reduced “all-or-nothing” behavior did mediate a small proportion of the effects of cognitive behavior therapy and graded exercise therapy on fatigue in one study ([Cella, White, Sharpe, & Chalder, 2013](#_ENREF_5); [Chalder, Goldsmith, White, Sharpe, & Pickles, 2015](#_ENREF_7)). Therefore all-or-nothing behavior is regarded as a potentially unhelpful management strategy.

Patient avoidance of activity has been shown to be directly linked with patient beliefs about the physical origin of symptoms, and increased fatigue severity ([Vercoulen et al., 1998](#_ENREF_30)), in addition to patient beliefs about pain, and increased pain intensity ([Nijs, Van de Putte, Louckx, Truijen, & De Meirleir, 2008](#_ENREF_22)). There is evidence to suggest that both pain and fatigue decrease simultaneously in response to treatment ([Bloot, Heins, Donders, Bleijenberg, & Knoop, 2015](#_ENREF_2); [Bourke, Johnson, Sharpe, Chalder, & White, 2014](#_ENREF_3); [Knoop, Stulemeijer, Prins, van der Meer, & Bleijenberg, 2007](#_ENREF_14)), although the dynamic relationship between pain, fatigue and other perpetuating variables is not currently well understood ([Nijs et al., 2012](#_ENREF_21)). vidence for the role of avoidance or activity limitation in the maintenance of fatigue comes from treatment studies. Reduced self-reported “activity limitation”, has been shown to mediate improvement in fatigue symptoms after treatment ([Heins, Knoop, Burk, & Bleijenberg, 2013](#_ENREF_12); [Wearden & Emsley, 2013](#_ENREF_32)), and we also now know that change in the beliefs underlying activity limitation (“fear avoidance beliefs”) mediates change in fatigue following cognitive behavioral and graded exercise treatment ([Chalder et al., 2015](#_ENREF_7)). We therefore have some evidence that over time, activity patterns are associated with perpetuation of symptoms, and that, with treatment, change in activity patterns are associated with reduction in fatigue. However, little is known about what initiates and maintains these activity patterns on a moment-to-moment or day-to-day basis. For example, we do not know whether, during the course of a day, patients rest in response to symptoms, are intensely active when they are feeling well (that is, “all-or-nothing” behavior) or whether they avoid activity more generally over the course of the day.

The present study therefore aimed to concurrently examine aspects of the cognitive-behavioral model to further understanding of the factors predicting patient activity patterns in CFS. A mobile phone-based app ([Ainsworth et al., 2013](#_ENREF_1)), was used to examine interrelationships between short-term fluctuations in fatigue-relatedsymptoms, pain and affect (both positive and negative) and concomitant and subsequent activity patterns.

**Hypotheses**

We hypothesized that higher fatigue-related symptom reporting would be associated with self-reported activity limitation at both the current assessment and at the subsequent assessment; that is that participants would demonstrate more activity limitation in response to fatigue. To assess the independent contribution of pain in driving patient activity management strategies, both activity limitation and all-or-nothing behavior was examined in association with pain. We predicted that higher pain would be associated with higher activity limitation and lower all-or-nothing behavior at current and subsequent assessments. In line with cognitive-behavioral models, it was also predicted that higher negative affect and lower positive affect would be associated with activity limitation. We hypothesized that subjectively feeling well would be associated with self-reported all-or-nothing behavior at both the current assessment and at the subsequent lagged assessment; that is, the participant would report higher activity when they were feeling well. In addition, it was predicted that higher levels of positive affect and lower levels of negative affect would be associated with more all-or-nothing behavior.

**Method**

**Participants**

Participants with a clinical diagnosis of CFS/ME were recruited from specialist UK National Health Service (NHS) CFS/ME services; the final sample included 23 patients ranging from 17 to 58 years old, with a mean age of 35.5 (SD = 13.96) years. Upon entry in the study, patients had been ill for a median of 5 years (Interquartile range (IQR) = 10) and had recently been enrolled in specialist treatment programs, delivering either cognitive behavior therapy based on the cognitive behavioral model, or pragmatic rehabilitation, a therapy which combines elements of cognitive behavior therapy and graded exercise therapy ([Wearden et al., 2010](#_ENREF_31)).

**Procedure**

Participants were loaned an Android Smartphone with a modified CFS-specific version of the Clintouch App ([Ainsworth et al., 2013](#_ENREF_1)) installed. A standard ESM protocol was followed ([Myin-Germeys, Delespaul, & van Os, 2003](#_ENREF_18)), whereby participants received ten assessments per day for a period of six days. The assessments were signaled by an alert, and scheduled according to an identical semi-random schedule for all participants. One assessment occurred within each 90 minute period throughout the day between 7:30am and 10:30pm; the time elapsed between assessments ranged from 29-162 minutes (M = 88.52, SD = 34.03 minutes). Participants were instructed that an alert would signal a momentary assessment, and that there would be a 15-minute period in which to begin the assessment before the questions expired.

**Measures**

All items were measured on a momentary basis (i.e. “Before the beep went off I was…” or “Right now I am…”) and were rated on a 7-point Likert scale anchored with *Not at all* to *A lot* (scored from 1-7).

### Patient activity management (cognitive-behavioral) strategies.

Items assessing patient activity management strategies were modified for ESM from the Cognitive-Behavioral Response Questionnaire ([Skerrett & Moss-Morris, 2006](#_ENREF_26)). Activity limitation was assessed by two items, ‘resting to control my symptoms’ and ‘avoiding activities that might make my symptoms worse’; the alpha coefficient for these items was α =.80. Two further items were included to assess all-or-nothing behaviors. These items were ‘rushing to get things done whilst I feel able’ and ‘doing things whilst I can’, and loaded on to a single factor solution (α =.87).

**Patient affect.**

Standard ESM affect items were used to assess patient affect ([Myin-Germeys et al., 2003](#_ENREF_18)). Positive affect was assessed by five items, excited, happy, satisfied, relaxed, and cheerful (α =.87). A further five items were included to assess negative affect, these included sad, annoyed, irritated, anxious, lonely, guilty (α =.87)

**Symptoms.**

Symptom items were adapted from the well-validated Chalder Fatigue Questionnaire ([Chalder, Berelowitz, Pawlikowska, Watts, & et al., 1993](#_ENREF_6)). Four items were used to assess fatigue-related symptom severity in the moment. These included feeling weak, tired, experiencing mental fog, and being sleepy (α = .73). Patient pain was assessed by a single item relating to the extent to which pain was being experienced in the moment. It is recommended that both positively and negatively phrased items are included within ESM assessments ([Palmier-Claus et al., 2011](#_ENREF_24)), and previous exploration of patient daily experiences of living with a chronic condition has suggested that feeling ‘well’ is not simply an absence of symptom experience ([Olsson, Skär, & Söderberg, 2010](#_ENREF_23)). Therefore to assess the extent to which they felt ‘well’ in the moment, two items, ‘feeling well’ and ‘feeling active’ were included (α = .74).

**Participant compliance**

A total of 1380 assessments were delivered across the sample, and of these, 893 were initiated within 15 minutes of an alert (65% compliance). Participants completed between 15 and 60 assessments (M = 38.83, SD = 14.83). The average number of daily assessments completed by participants was 6.47. Traditionally, participants who complete less than 20 momentary assessments are excluded from analyses ([Palmier-Claus et al., 2011](#_ENREF_24)); three participants within the current sample completed 15, 15 and 16 assessments respectively. Preliminary analyses were conducted excluding these participants. However, in order to exploit all of the available data all of the participants were retained in the final analyses.

**Statistical Analysis**

Multi-level models were used to examine study hypotheses, taking in to account the hierarchal structure of ESM data. The XTMIXED command was used in Stata ([StataCorp, 2009](#_ENREF_28)) for all continuous outcome variables, with a random intercept for each participant and for each day within participant; betas, 95% CI and p-values are reported for all associations between independent and dependent variables. Predictor variables included patient affect and symptoms at the same (t) and previous (t-1) assessment. These were grand mean centered before inclusion as predictor variables in all models. Patient activity management strategies were included as the dependent variables (t). Intraclass correlation coefficients (ICC) were calculated for each of the predictor variables to enable the proportion of variability in each level of the data (i.e. assessment, day and person levels) to be explored.

**Results**

**Predicting Patient Activity Limitation**

As predicted, patient symptom severity was associated with increased self-reported activity limitation at both the concomitant and subsequent assessments (Table 1). In addition, higher levels of current and previous pain predicted increased activity limitation at the current assessment. In contrast to study hypotheses, patient reported negative affect did not significantly predict patient activity limitation on a momentary basis. Greater patient reported positive affect approached significance in predicting increased activity limitation at the current assessment (p=.056); the direction of this relationship was opposite to that hypothesized.

**Predicting All-or-nothing behaviors**

Patient reports of feeling well were associated with higher levels of reported all-or-nothing behaviors at the current assessment (Table 1). In addition, feeling well at the current assessment significantly predicted increased all-or-nothing behavior at the subsequent assessment. Higher levels of pain at the current assessment did not predict all-or-nothing behavior at the current assessment, but was predictive of less all-or-nothing behavior reported at the subsequent assessment. Patient reports of positive affect were not found to significantly predict patient all-or-nothing behavior, and in further contrast to study hypotheses, higher negative affect predicted more all-or-nothing behavior at the current assessment.

**[insert Table 1 here]**

**The variability of activity management strategies across the different levels of data**

When examining the ICC analyses, it was identified that the majority of the unexplained variation in patient activity management strategies was at the current assessment level for all predictor variables (Table 1). For example, all-or-nothing responses showed 82% variance from one assessment to another, within the same patient and across the same day when feeling well was the predictor variable, whereas 15% of the variance was due to differences between individual participants.

**Discussion**

This study aimed to examine the interrelations between short-term fluctuations in patient self-reported fatigue-related symptoms, pain and affect, and concomitant and subsequent activity patterns in CFS. The main findings show that patient activity patterns arise in response to patient symptom experience, the effects of which were found to extend beyond the immediate context in which the symptoms were being experienced. In line with study hypotheses, patients reported limiting their activity more (that is, resting) when they were experiencing higher levels of fatigue-related symptoms and higher pain. In addition, patients reported more all-or-nothing type activity strategies when they were feeling subjectively well, and less following high levels of pain. These results support the cognitive-behavioral maintenance model for CFS ([Chalder et al., 2002](#_ENREF_8); [Deary et al., 2007](#_ENREF_9); [Surawy et al., 1995](#_ENREF_29)), by demonstrating that patient activity management is, at least to some extent, driven by symptom experiences. Patients in our study had recently been enrolled onto a course of either CBT or pragmatic rehabilitation. Over time, both of these treatments will help patients to understand that activity limitation and all-or-nothing behavior are not helpful responses to symptoms, and both will encourage a gradual, programmed increase in activity levels based on collaboratively agreed goals rather than driven by symptoms. It is a limitation of our study that we do not know exactly how much treatment, if any, each patient had received at the time of completing the ESM measures. However, as patients participated either prior to or early in the course of their treatment, it is likely that had not yet started to benefit from the changes in beliefs and behavior that treatment would be expected to bring about. Cognitive-behavioral and graded-exercise therapies are recommended treatments for CFS in the UK ([NICE, 2007](#_ENREF_20)), and demonstrate small to moderate effects in improving patient illness outcomes ([Castell, Kazantzis, & Moss-Morris, 2011](#_ENREF_4); [White et al., 2011](#_ENREF_33)). Both of these therapies involve a gradual and programmed increases in activity and may result in breaking the link between experiencing symptoms and activity levels, thus modifying patient beliefs and behavioral responses that are thought to perpetuate CFS ([Moss-Morris et al., 2013](#_ENREF_16)).

Cognitive-behavioral maintenance models for CFS have previously been criticized for lacking specificity ([Knoop et al., 2010](#_ENREF_13)), with evidence accumulated for the role of individual perpetuating factors in isolation ([Moss-Morris, 2005](#_ENREF_15)). Little empirical research has focused on the interaction of several factors thought to be important in symptom perpetuation and maintenance (Deary et al., 2007). By using ESM to facilitate data collection we were able to simultaneously examine the impact of both symptom experience, including both fatigue-related symptoms and pain, as well as patient affect in predicting activity management patterns. The current results indicate that activity limitation was predicted by both pain and fatigue-related symptoms, suggesting that it in order to develop theory and understanding of these complex processes the relationship between pain, fatigue and patient cognitive-behavioral variables needs further investigation ([Nijs et al., 2012](#_ENREF_21)). Interestingly, our analyses indicate that at a momentary level at least, patient affect is predictive of an activity pattern opposite to that we originally hypothesized. This finding was applicable to both activity limitation and all-or-nothing responses, as, contrary to our predictions, higher levels of positive affect was significantly associated with activity limitation and higher levels of negative affect were associated with all-or-nothing behavior. Whilst this at first sight seems counterintuitive, we speculate that these findings may reflect patient beliefs about the meaning of the relationship between symptoms and activity management strategies. The association between positive affect, fatigue-related symptom severity, pain and activity limitation, may potentially reflect underlying patient beliefs that limiting activity, that is resting, is a beneficial strategy for coping with increased symptom severity or pain. Likewise, we speculate that feeling well may provide patients with an opportunity to engage in increased activity but may be accompanied by patient beliefs that subsequent worsening symptoms are inevitable, beliefs which may then be associated with negative affect.

However, we acknowledge the limitations associated with some of the items included within the current study. Firstly, pain was assessed by a single item at each assessment, and while fatigue-related severity was assessed using four items relating to common experiences of fatigue we did not include fatigue as an item. Secondly, those items relating to activity limitation required patients to report on their behavior (for example, are they limiting activity in that moment) and also make a judgement relating to that behavior (for example, is this to control their symptoms), thereby confounding beliefs about symptoms and symptom management with reports of activity. This was a design fault of our study, which arose because we chose to use items from the cognitive-behavioral response questionnaire items as a measure of patient activity management, in order to provide some comparability with other studies using that questionnaire. Future studies would benefit from including objective measures of activity, which are separate from measures of patient beliefs about activity. Including pure activity measures would assist us in to further develop a theoretical understanding of the dynamic relationships between symptoms and activity. In addition, utilization of m-health capabilities, such as incorporating ESM studies alongside established treatment programs would also enable assessment of the potential mechanisms of change during treatment ([Ritterband, Thorndike, Cox, Kovatchev, & Gonder-Frederick, 2009](#_ENREF_25)). For example, it would be possible to examine whether hypothesized changes in cognitions are responsible for changes in activity management behaviors ([Knoop et al., 2010](#_ENREF_13)).

Our findings demonstrated that both all-or-nothing behavior and activity limitation varied most at the individual assessment level, indicating that patients were reporting high variability in the extent to which they were engaging in both activity patterns across assessments within the course of each day. In contrast, the results indicated little variation in the activity management patterns between different days (within the same person), with some variation observed between individual patients. These findings are in line with previous findings demonstrating that objective activity levels in CFS patients are also variable at the individual level ([Evering, Tonis, & Vollenbroek-Hutten, 2011](#_ENREF_10)). Furthermore, the results indicate that symptom severity, pain and affect are independently predicting activity management strategies across different timeframes, although it is important to note that the time between assessments varied across the study, from approximately 30 to 160 minutes Our study drew upon previous ESM sampling schedules in designing the frequency of the assessments ([Myin-Germeys et al., 2003](#_ENREF_18)) yet this could be further strengthened by taking account of the advances in m-health, for example, by using sensing capabilities to prompt individualized, tailored assessments in real time ([Spruijt-Metz & Nilsen, 2014](#_ENREF_27)). Combining this with clearly defined cognitive behavioural components could form the basis for building an interactive digital intervention ([Nahum-Shani et al., 2015](#_ENREF_19)), to help patients to understand their activity patterns and disassociate activity from symptom experiences or affect. For example, in response to current reports of symptom severity, such an intervention might guide patients to address unhelpful activity beliefs using cognitive-behavioural strategies ([White et al., 2011](#_ENREF_33)) before they engage in prolonged periods of activity limitation. Similarly, prompts could be delivered to engage patients in graded activities in accordance with a predetermined, agreed and acceptable activity schedule, with additional alerts and reminders programmed using algorithms for “all-or-nothing” or “activity limitation” type activity patterns.

**Conclusions**

The current findings suggest that two unhelpful activity management patterns in CFS arise as a result of patient symptom experience and affect. Although the results reported here must be interpreted tentatively given the small sample size; combining experience sampling methodology with m-health enabled us to demonstrate that it is feasible to examine these complex associations between known perpetuating factors in CFS in the context of daily life. We suggest that in further developing a complex understanding of the interrelations between these variables, it may be possible to pinpoint when the unhelpful behavioral patterns begin. Future studies may utilize m-health capabilities to not only develop theoretical understanding of maintenance of CFS symptoms, but to work towards interactive digital interventions to enact symptom improvement.

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**Table 1:** Theassociation between patient affect, symptom experience variables and cognitive-behavioral strategies in current (t) and lagged (t-1) analyses, and the Intraclass correlation coefficients (ICC) for individual patient predictor variables

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| **Predictor variables** | **Activity Limitation** | | | **ICC** | | |
|  | **β** | **SE** | **p** | **Person** | **Day** | **Beep** |
| **Symptom severity** |  |  |  |  |  |  |
| Current | **.155** | **.013** | **<.001** | .09 | .08 | .83 |
| Lagged (t-1) | **.030** | **.009** | **.001** | .15 | .08 | .77 |
| **Pain** |  |  |  |  |  |  |
| Current | **.298** | **.046** | **<.001** | .09 | .06 | .85 |
| Lagged (t-1) | **.310** | **.052** | **<.001** | .10 | .09 | .81 |
| **Negative affect** |  |  |  |  |  |  |
| Current | .043 | .065 | .513 | .17 | .08 | .75 |
| Lagged (t-1) | .038 | .075 | .610 | .16 | .09 | .75 |
| **Positive affect** |  |  |  |  |  |  |
| Current | .102 | .054 | .056 | .18 | .08 | .74 |
| Lagged (t-1) | .011 | .062 | .863 | .16 | .09 | .75 |
|  | **All-or-nothing behavior** | | |  | **ICC** |  |
| **β** | **SE** | **p** | **Person** | **Day** | **Beep** |
| **Feeling well** |  |  |  |  |  |  |
| Current | **.700** | **.025** | **<.001** | .14 | .03 | .83 |
| Lagged (t-1) | .218 | .033 | **<.001** | .15 | .03 | .82 |
| **Pain** |  |  |  |  |  |  |
| Current | .023 | .084 | .784 | .12 | .05 | .83 |
| Lagged (t-1) | **-.252** | **.094** | **.008** | .15 | .02 | .83 |
| **Positive affect** |  |  |  |  |  |  |
| Current | .152 | .094 | .104 | .12 | .05 | .73 |
| Lagged (t-1) | .032 | .107 | .762 | .14 | .02 | .84 |
| **Negative affect** |  |  |  |  |  |  |
| Current | **.312** | **.113** | **.006** | .11 | .06 | .83 |
| Lagged (t-1) | .090 | .127 | .480 | .14 | .02 | .84 |

*Note*. p<.05 is in boldface.