

DISSERTATION REPORT

ENERGY CONSERVATION MANAGEMENT AND PHYSICAL BEHAVIOUR IN FATIGUED PEOPLE WITH MULTIPLE SCLEROSIS

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On February 14, 2018, Lyan Blikman, defended her PhD thesis: *Energy conservation management and physical behavior in fatigued people with Multiple Sclerosis* at the Erasmus University Rotterdam, The Netherlands. Supervisors: Henk J. Stam, Jetty van Meeteren, Johannes B.J. Bussmann.

Main findings

- Detailed analyses of physical behaviour showed that ambulatory fatigued persons with multiple sclerosis (MS) do differ from healthy controls not only in physical activity level, but also in other physical behaviour dimensions (e.g. day patterns, intensity of activities and distribution of periods of activity).
- In ambulatory persons with MS-related fatigue, a weak association was found between physical fatigue and several physical behaviour dimensions (i.e., the amount, the intensity and the day pattern of activities).
- The individual Energy Conservation Management (ECM) format used in this study did not reduce MS-related fatigue and restrictions in participation more than an information-only control condition. Our study does not support the implementation of our individual ECM format as a treatment for MS-related fatigue.
- Energy conservation strategies given in ECM were appreciated by participants and perceived as useful for fatigue, so ECM seems to have a subjective good effect for fatigued persons with MS.
- Resulting from a responder study: fatigued people with MS who are more severely fatigued, have a less negative perception of fatigue, perceive fewer disease benefits, and who perceive a higher discrepancy in social support show the best response to ECM treatment.

Fatigue is a frequent, frustrating, overwhelming and often disabling symptom that affects the majority of people with multiple sclerosis (MS), resulting in severely limited activities of daily living and restricted participation (e.g. in performance of social roles). Fatigue is also related to changes in the physical behaviour of people with MS, in which both motor and sensory disorders play a role. Relieving the effects of severe fatigue on daily life is an important treatment goal in MS. The broader objective of the studies included in this thesis was to assess the effectiveness of energy conservation management (ECM) in reducing fatigue and improving societal participation in fatigued people

with MS. ECM is a type of occupational treatment applied in the context of rehabilitation, and is based on the Packer group course “Managing fatigue”. ECM aims to create a positive attitude towards active decision-making, to stimulate the optimum use of available energy, to increase a patient’s use of energy-conserving strategies, and to improve their confidence in their ability to manage fatigue. Another important objective was to study in greater detail the physical behaviour in fatigued people with MS and the association between fatigue and physical behaviour.

This thesis is a part of the “Treating Fatigue in Multiple sclerosis: Aerobic Training, Cognitive Behavioral Thera-

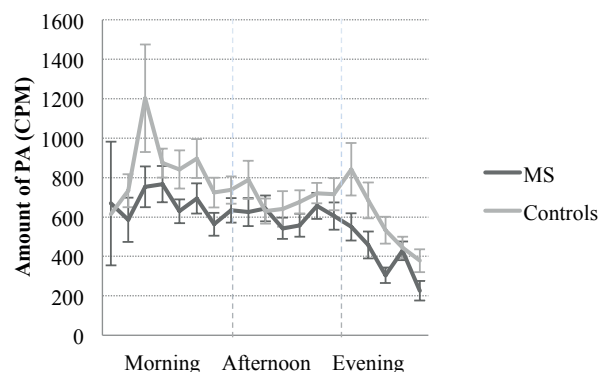


Fig. 1. Amount of physical activity per period of the weekday. Expressed in mean counts per minute (CPM) per hour, with the standard error of the mean (SEM). Persons with MS had significantly lower amounts of physical activity levels per day periods, except for the afternoon. Day pattern outcomes were based on weekdays. This figure is taken from Figure 1 in Ref 3; after permission from the Publisher.

py and Energy Conservation Management” (TREFAMS-ACE) multicentre programme. The 2 main objectives of the TREFAMS-ACE study were: (i) to assess the effectiveness of 3 different rehabilitation treatment strategies in reducing fatigue and improving societal participation in fatigued people with MS; and (ii) to study the neurobiological mechanisms of action that underlie treatment effects and MS-related fatigue in general. The extended study protocol is described in Chapter 2 of this thesis. The programme included 3 single-blinded randomized controlled trials (RCTs), all with the same 2-parallel-arms design. In all RCTs the control arm consisted of an information-only condition. The only differences between the RCTs were the experimental treatment, some specific treatment-related outcomes, and the locations in which the studies took place. Patients were randomized to either the trial-specific treatment, consisting of 12 therapist sessions over 4 months, or an information-only control condition provided by an experienced MS nurse, and consisting of 3 consultations over 4 months. All measurements were carried out one week prior to randomization and at 8, 16 (i.e. post-intervention), 26 and 52 weeks after starting the treatment, and included self-reported questionnaires, visits to the rehabilitation centre, and saliva tests and activity monitoring at home.

The studies included in this thesis focus primarily on the ECM component of the research programme (Chap-

ters 5, 6 and 7); furthermore, 2 studies used baseline data of physical behaviour and fatigue from the RCT (Chapters 3 and 4).

Fatigue limits activities of daily living and affects physical behaviour. Conversely, physical behaviour can also affect fatigue. Previous studies have shown that the relationship between fatigue and physical behaviour is complex, and the results of studies have often conflicted. Thus far, the effects of MS and MS-related fatigue on physical behaviour have been studied primarily from the perspective of physical activity levels (e.g. total number of activity counts), which is just one dimension of physical behaviour, and perhaps not the most clinically relevant or most responsive physical behaviour parameter in MS. Possible other dimensions of physical behaviour that can be considered are day patterns, the frequency and intensity of activities, and the distribution of activity and rest.

To study the effects of MS and MS-related fatigue on physical behaviour in greater detail, in Chapter 3 we compared various aspects of physical behaviour in fatigued people with MS and healthy controls. The results showed that, besides physical activity level (i.e. fewer activity counts per day and per minute), fatigued people with MS also differed from matched healthy controls in other PB dimensions: those in the MS group spread their activities differently over the day (less physically active in the morning and evening, but not in the afternoon), they

Table I. Physical behaviour (PB) outcomes

Outcomes PB	MS Group (n=23)	Controls (n=23)	p-value	Mean Difference (95% CI)	Cohen d Effect Size
Length of day (min)	907±84	943±51	0.085	-36 (-77 to 5)	0.52
Amount of physical activity					
CPD (±103)	520±173	676±218	0.010*	-156 (-273 to -39)	0.78
Day CPM	577±198	712±209	0.030*	-135 (-256 to -14)	0.66
Morning CPM	661±304	861±332	0.039*	-200 (-389 to -11)	0.63
Afternoon CPM	610±239	699±248	0.223	-89 (-234 to 56)	0.36
Evening CPM	467±203	642±324	0.034*	-175 (-336 to -14)	0.65

CPD: counts per day; CPM: counts per minute.

This Table is taken from part of Table 2 in Ref 3; after permission from the Publisher.

spent a higher percentage of their time sedentary, and they spent less time in the moderate-to-vigorous physical activity (MVPA) category. Furthermore, people with MS showed fewer MVPA periods and a different distribution of sedentary and MVPA periods, respectively longer and shorter periods over the day. The study showed that fatigued people with MS not only differ from healthy controls in general activity outcomes, such as total amount of activity, but also in several other physical behaviour outcomes.

In Chapter 4 of this thesis, we examined the association between physical behaviour and fatigue accounting for the multi-dimensionality of both constructs. To study the association, we used 4 dimensions of fatigue (subjective, physical, cognitive and psychological fatigue) and the more detailed physical behaviour outcomes of Chapter 3. We concluded that the physical fatigue dimension was significantly and negatively associated with the physical behaviour dimensions “amount of activity”, “intensity categories”, and “day pattern”, although the relationships were weak. These relationships indicate that persons who are more physically fatigued have a physical behaviour pattern that diverges considerably from that of healthy people. None of the other fatigue dimensions were associated with any of the physical behaviour outcomes. These results underlined the importance of considering specific fatigue and PB dimensions in addition to the total scores.

Prior to the ECM RCT, we systematically reviewed the evidence for the effectiveness of ECM in people with MS (Chapter 5). Based on 6 studies and a meta-analysis, we concluded that the ECM group programme by Packer et

al. is effective in treating MS-related fatigue and improving quality of life over the short-term (at 8 weeks) in comparison with a waiting-list control condition. However, although the differences were statistically significant, they were small from a clinical perspective. Furthermore, the review concluded that there was a lack of literature evidence related to long-term effectiveness, clinically relevant changes in fatigue, well-designed control groups, and participation outcomes, and that evidence supporting ECM was restricted to a group format.

In Chapter 6, we describe the results of our RCT concerning the effects of ECM. As primary outcomes, the short and long-term effects of ECM on fatigue (Checklist Individual Strength; CIS20r) and participation (Impact on Participation and Autonomy questionnaire; IPA) in fatigued persons with MS were assessed. Several other fatigue measures (CIS20r remaining subscales, Modified Fatigue Impact Scale (MFIS), Fatigue Severity Scale (FSS)), as well as daily functioning measures (Health survey Short-Form (SF-36), Rehabilitation Activities Profile (RAP)) were included as secondary outcomes and a treatment-specific Energy Conservation Strategies Survey (ECSS) was included. Analysis was based on 76 randomized ambulatory fatigued people with MS. The results showed that ECM was no more effective in reducing MS-related fatigue and improving societal participation than an information-only control condition: no statistically significant or clinically relevant differences were found. However, additional analyses showed that persons with MS did implement the provided ECM strategies in daily life and that they experienced these strategies as useful.

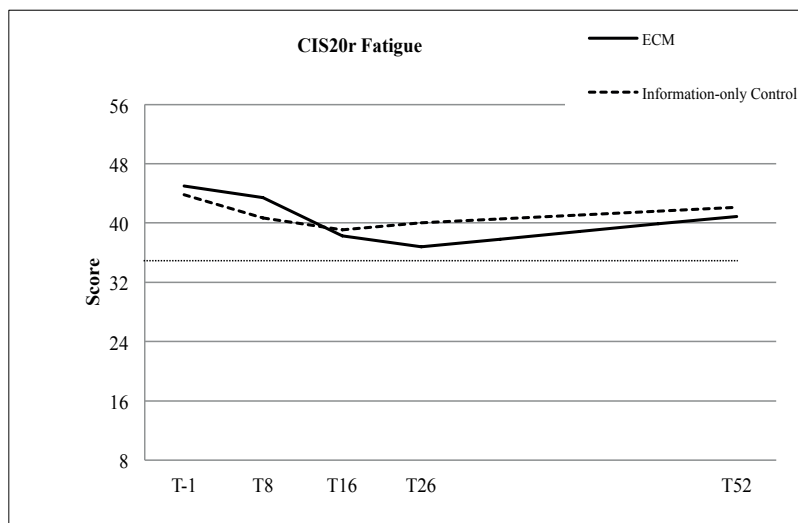


Fig. 2. Graph of the observed data on the primary outcome CIS20r fatigue. Solid line: energy conservation management (ECM) intervention group; dashed line: Information-only control group; small dotted line: value of severe fatigue CIS20r ≥ 35 . On the horizontal axis the measurements are represented, t-1 is baseline and then 8, 16, 26 and 52 weeks after start of EC; or on Information only Control treatment by an MS nurse. CIS20r – Checklist Individual Strength, subscale subjective fatigue: higher scores reflect worse fatigue; IPA – Impact on Participation and Autonomy: higher scores reflect more barriers to participation and autonomy. The figures is taken from part of Figure 2 in Ref 1; after permission from the Publisher.

Although there was no significant difference between the intervention group and the control group, the RCT showed within-group effects of ECM on fatigue. Identification of fatigued people with MS who show a better response to ECM is important. Therefore, in Chapter 7 we examined whether baseline demographic, disease-related and personal determinants can identify responders to the ECM intervention and how these determinants are distinct from those in the controls. In total, 69 participants were included (ECM 34; MS nurse 35). The participants who had clinically-relevant reductions in fatigue, a difference of ≥ 8 on the CIS20r, were labelled as responders. In the ECM group, 4 determinants (baseline fatigue, fatigue perception, Illness Cognitions Questionnaire (ICQ) subscale disease benefits, and social discrepancies) were related to the probability of being a responder. Two determinants (fatigue perception, ICQ disease benefits) were distinctive for the ECM group. The results suggest that fatigued people with MS who show the greatest response to ECM treatment are more severely fatigued at the start, have a less negative perception of fatigue, perceive fewer disease benefits and perceive serious discrepancies in social support.

Finally, Chapter 8 provides a general discussion of the results of this thesis. The main conclusion of our RCT is that ECM does not have significant added value for fatigued people with MS. Our results also underline the multidimensionality of fatigue and physical behaviour. The general discussion examines possible explanations for the negative findings of the RCT, for the differences with the systematic review, and the complex relation between physical behaviour and fatigue. Finally, the thesis

considers the clinical implications and possible directions for future research.

LIST OF ORIGINAL PUBLICATIONS

1. Blikman LJ, van Meeteren J, Twisk JW, de Laat FA, de Groot V, Beckerman H, et al. Effectiveness of energy conservation management on fatigue and participation in multiple sclerosis: A randomized controlled trial. *Mult Scler* 2017; 23: 1527–1541. Available from: <https://dx.doi.org/10.1177/1352458517702751>.
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6. Blikman LJ, van Meeteren J, Twisk JW, de Laat FA, de Groot V, Beckerman H, Stam HJ, Bussmann JB, TREFAMS-ACE study group. Energy Conservation Management for fatigued people with MS: who benefits? *Am J Occup Ther* (in press).