Home-based rehabilitation in Multiple Sclerosis: Impact on exercise capacity?

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Diest and Heusden-Zolder, 10th of June 2015 D.M & W.B.

Research Context

This pilot study focussing on the effects of home-based rehabilitation for people with mild to moderate Multiple Sclerosis (MS) contributes to the domain of neurological rehabilitation. In young to middle aged persons, MS is one of the most common neurological diseases worldwide. As such, a better understanding of the impact of rehabilitation may improve overall treatment of this disease.

The goal of this study was to investigate whether home-based rehabilitation is an effective tool to improve cardiovascular exercise capacity in MS. In laboratory controlled settings, this has been studied extensively. In fact, a wide variety of such studies have indicated that exercise therapy is a beneficial component in the overall rehabilitation of MS. Interestingly, studies performed in home-based settings have not yet found similar results. Therefore and because home-based rehabilitation might be an important part in the overall rehabilitation of MS, the present pilot study explored the impact of home-based rehabilitation on exercise capacity related parameters (workload effects and heart rate effects).

This Master thesis is the first part of a larger research project investigating the impact and role of home-based rehabilitation in MS. We initiated this study last year with a literature search (Master thesis part 1). The study protocol was proposed by Prof. Dr. B. Op 'T Eijnde (promotor). Subject recruitment was performed by his research group in close collaboration with the Hasselt University Sports medical Center ADLON.

The present study was performed in the REVAL Rehabilitation Center (cardiological screening and maximal graded cycle ergometer test), in the home-based setting (rehabilitation) and included a two-week walking trip in the Jordan desert.

Prof. Dr. B. Op 'T Eijnde guided all participants during the entire study and performed data-acquisition. Data-extraction was performed by both authors of this Master thesis, followed by the data-analysis which was performed by M. Debecker. Writing the abstract, introduction, methods, results and conclusion was performed together, whereas the discussion was mainly written by B. Willems. Everything has been revised and complemented by both authors together.

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Appendix

1. Abstract

PURPOSE: The present project explores the effects of a 20-week home-based training programme on exercise capacity in people with mild to moderate multiple sclerosis (PwMS) (Expanded disability status scale score (EDSS) range 2.5 ±1.04).

METHODS: Whereas eight PwMS were included in the intervention group (MS_{TR}), seven PwMS were recruited from a previously performed study and served as the control group (MS_{SED}). Before and after a 20-week individualised home-based training programme (2-5 training sessions/week) a maximal graded cycle ergometer exercise test was performed. Primary outcomes included resting heart rate (HR_{rest}), maximal exercise intensity (W_{max}), relative maximal exercise intensity (W_{maxrel}) and time until exhaustion (Time). Secondary outcomes included maximal heart rate (HR_{max}) and peak blood lactate concentration ($Lactate_{peak}$).

RESULTS: At baseline, HR_{rest} and $Lactate_{peak}$ were respectively 31.6% ($p<.01$) and 52.1% ($p<.05$) higher in MS_{TR} compared to MS_{SED}. Twenty weeks of training increased W_{max} by 15.5% ($p<.001$), W_{maxrel} by 21% ($p<.001$) and Time by 19.1% ($p<.01$) in MS_{TR} compared to MS_{SED}. Home-based training had no effect on HR_{rest}, HR_{max}, $Lactate_{peak}$.

CONCLUSION: Twenty weeks of individualised home-based training improves maximal exercise intensity, relative maximal exercise intensity and time until exhaustion in people with mild to moderate multiple sclerosis.

Keywords: Multiple Sclerosis, Home-Based, Rehabilitation, Exercise Capacity

2. Introduction

Multiple Sclerosis (MS) is an immune-mediated neurological disease that affects the central nervous system (CNS) [14, 24, 26]. Even though several risk factors for MS have been identified, the precise aetiology remains unknown [29]. Worldwide, two and a half million people are affected by MS. As such, MS has become the most prevalent neurological disease in young to middle aged people. The average age of onset is between 28 and 30 years and women are twice as likely to have the disease than men [14, 18, 28, 34]. Several types of MS exist. Eighty-five percent of people with MS (PwMS) suffer from relapsing remitting MS (RRMS), making it the most prevalent type of MS. Usually RRMS will progress into secondary progressive MS. Other types include primary progressive MS, progressive-relapsing MS, benign MS and malign MS [23, 34].

MS is characterized by the presence of sclerotic plaques in the brain and spinal cord resulting in inflammation, demyelisation and axonal degeneration [4, 11], which, in turn, results in long-term disability [8, 35]. Symptoms include pain, fatigue, visual impairment, spasticity, cognitive dysfunction, bladder dysfunction, bowel dysfunction and sexual dysfunction. Decreases in muscle strength, cardiovascular endurance and balance are also common [6]. Furthermore, PwMS tend to be less physically active than healthy adults [21] which, in turn, further decreases muscle strength, balance and cardiovascular endurance. The lower levels of physical activity might also increase the risk for secondary problems like cardiovascular disease [32, 36]. Therefore, physical rehabilitation of PwMS might be an important component of overall treatment of MS.

To date, physical rehabilitation of decreased muscle strength and cardiovascular endurance has been widely studied in PwMS. In his review, Dalgas et al. clearly showed improvements in cardiovascular endurance (up to 22% increased VO_{2max}) following a low to moderate intensity endurance training programme [8]. This was confirmed in other studies [1, 17, 37]. Furthermore, improvements up to 32% in one repetition maximum (1RM) have also been demonstrated following resistance training in MS [8, 17, 31]. Similar increases in strength were also found in other studies [3, 37]. However, these studies focused predominantly on rehabilitation performed in ‘controlled’ laboratory and/or rehabilitation centre settings.

Research in less controlled settings however, is scarce. Only a few studies examined the effects of home-based rehabilitation on muscle strength and cardiovascular endurance in PwMS. Although marked improvements in muscle strength and walking speed following home-based rehabilitation were shown [5, 9, 27], results regarding cardiovascular endurance remain unclear [5, 20, 27]. Also, there might be fewer barriers to exercise participation when comparing home-based rehabilitation with rehabilitation performed in more controlled research settings. Therefore, home-based rehabilitation might be an interesting tool in overall MS rehabilitation.

In keeping with the above line of reasoning, the present study examines the effects of a home-based rehabilitation programme on cardiovascular endurance in people with mild to moderate MS. We hypothesize that home-based rehabilitation will have a positive effect on cardiovascular endurance.

3. Methods

3.1 Subjects

Fifteen participants with mild to moderate MS (Expanded Disability Status Scale [EDSS] 2.6 ± 1.13) were recruited.

Subjects were included if they (1) were aged between 18 and 65 years, (2) had an EDSS score of four and a half or less, (3) were relapse-free in the 30 days prior to the start of this study and (4) had a sedentary lifestyle defined by at most 150 minutes of physical activity per week (American College of Sports Medicine). Subjects were excluded if they (1) had an EDSS score of more than four and a half, (2) experienced a relapse in the 30 days prior to the start of the study, (3) had contra-indications for increased physical activity diagnosed by a medical professional, (4) participated in a physical exercise programme in the last six months or (5) were physically active for more than 150 minutes per week. Participants were also excluded if they experienced an exacerbation during the course of the exercise programme.

Individual participant characteristics can be viewed in ***Table 1.***

All participants were informed in detail on all experimental procedures and signed an informed consent in accordance with the ethical guidelines of good clinical practice from the declaration of Helsinki.

Table 1: Baseline characteristics

MS_{TR}	Gender	Age	EDSS	Type MS	Length (m)	Weight (kg)	BMI
154	F	48	2	RR	1.66	64	23.23
155	F	46	2	RR	1.56	75	30.82
156	F	28	2.5	RR	1.68	66	23.38
157	F	27	2	RR	1.68	71.1	25.19
158	M	59	3	RR	1.73	84	28.07
159	M	54	2.5	RR	1.88	84	23.77
160	M	47	4.5	RR	1.87	90	25.74
161	F	45	4.5	RR	1.63	55	20.70
MS_{SED}	Gender	Age	EDSS	Type MS	Length (m)	Weight (kg)	BMI
304	M	36	4	RR	1.85	73	21.33
311	F	56	2	RR	1.67	69	24.74
313	F	42	1	RR	1.67	67.5	24.20
318	F	60	4	SP	1.68	70.3	24.91
326	F	40	1.5	RR	1.62	64.4	24.54
332	F	54	2.5	RR	1.58	66.5	26.64
334	F	33	1.5	RR	1.60	71	27.73

Abbreviations: BMI: Body Mass Index ; EDSS: Expanded Disability Status Scale ; F: Female; kg: Kilogramme; M: Male; m: Metre: RR: Relapsing-Remitting; SP: Secondary Progressive

3.2 Study design

Eight participants were referred from several neurologists, previous studies performed in the REVAL Rehabilitation Research Center of Hasselt University (REVAL) and from MS-Liga Flanders and were included in the intervention group (MS_{TR}). Seven participants were recruited from a similar study previously performed by Dra. I. Wens at REVAL and were used as the control group (MS_{SED}) [Wens et al., personal communication, unpublished data].

Following recruitment, all participants received a standardized sport medical screening including a 12-Lead electrocardiogram (ECG) performed by an experienced physician. Furthermore, body weight, body height and blood pressure were assessed.

Subjects then performed a maximal graded exercise test on a cycle ergometer (PRE-test). MS_{TR} subjects were enrolled in a twenty-week custom made home-based rehabilitation programme focussing on improving cardiovascular endurance (exercise capacity), whereas MS_{SED} subjects remained sedentary throughout the study course. Participants included in MS_{TR} were divided into three groups based on their exercise capacity at baseline. This distinction was made to ensure optimal training workload for each subject. Group one, two and three included subjects with a low, moderate and good basic fitness level, respectively. Exercise modalities used in each group consisted of walking, running and cycling. Groups differed between initial exercise intensity. The low basic fitness group started exercising below the aerobic threshold (AT). The moderate basic fitness group initially exercised at AT while the good basic fitness group started exercising above AT. We refer to ***Appendix 1*** for an example of a training schedule.

Intensity during exercise was monitored using hearth monitoring (Polar®). Following 18 weeks of training, MS_{TR} participated in a two-week walking trip in the Jordan desert (10 days, 265 kilometres, 4,8 kilometres/hour average pace).

After the twenty-week intervention period, all subjects performed a second maximal graded exercise test similar to baseline (POST-test).

3.3 Measurements

3.3.1 Maximal graded exercise testing

Graded exercise testing was performed using a cycle ergometer (eBike Basic, General Electric GmbH, Blitz, Germany). After completion of the medical screening, seat and steering wheel height were adjusted according to the participant's biometry. Exercise intensity (Watt, W) was based on the participant's sex. Following a 10-min warming up (♂: 30W; ♀: 20W), exercise testing started at a workload of 30W and 20W for male and female subjects, respectively. Every minute and until voluntary exhaustion, exercise intensity increased with 15W for men and with 10W for women. Minimal cycle frequency was set at 75 rounds per minute (RPM). Heart rate (HR) was assessed using heart monitoring (Polar®). Capillary blood lactate levels (Analox® lactate analyser, earlobe puncture) were measured every two minutes. Recovery heart rate and peak capillary blood lactate were measured two minutes following test completion. Upon test completion, HR at AT (HR_{AT}) and anaerobic threshold (AnT; HR_{AnT}) were determined. These measures were used to determine the exercise intensity of the individualised training programme.

3.3.2 Primary and secondary outcome measures

Primary outcome measures included (1) resting heart rate (HR_{rest}), (2) maximal exercise intensity (W_{max}), (3) relative maximal exercise intensity (W_{maxrel}) and (4) time until exhaustion (Time). Secondary outcome measures included (1) maximal hearth rate (HR_{max}) and (2) peak lactate ($lactate_{peak}$).

3.4 Data analysis

All data was analysed using Statistical Package for the Social Sciences v.22 (SPSS). Baseline comparison was performed using the Mann-Whitney U Test. Within-Group and Between-group normality was assessed using box-plots and the Shapiro-Wilk test. A two-factor (Group and Time) Mixed ANOVA was performed. When a significant Time x Group effect was present, a simple-effect analysis using Between-Group and Within-Group one-way ANOVA's was performed to assess the nature of this effect. Results with a p-value < 0,05 will be significant.

4. Results

4.1 Drop-out and side-effects

Following baseline measures, one participant (number 161, ***Table 1***) in the intervention group was excluded due to exacerbation. This participant was not included in the baseline comparison or the statistical analysis. No side-effects following intervention were reported.

4.2 Baseline comparison

For gender, age, length, weight, BMI and EDSS score no differences at baseline were found (***Table 2***).

Table 2: Baseline comparison

	MS_{TR} Mean ± SD	MS_{SED} Mean ± SD	p-value*
Gender (M/F)	3/4	1/6	0.38
Age	43.29 ± 12.27	45.86 ± 10.65	0.81
Length (m)	1.72 ± 0.12	1.67 ± 0.09	0.26
Weight (kg)	76.3 ± 9.94	67.83 ± 3.16	0.1
BMI	25.74 ± 2.81	24.51 ± 1.95	0.71
EDSS	2.64 ± 0.90	2.36 ± 1.21	0.38

* Performed with the Mann-Whitney U Test
Abbreviations: BMI: Body Mass Index; EDSS: Expanded Disability Status Scale; F: Female; kg: Kilogramme; M: Male; m: Metre

4.3 Primary outcome measures

4.3.1 Resting heart rate

Significant differences between baseline measures were found ($p < .01$). Significant main effects exist for Group, $F(1,12) = 5.19$, $p < .05$ and Time x Group, $F(1,12) = 17.66$, $p < .01$. Simple-effects analyses showed a 15% increase in HR_{rest} in MS_{SED} from PRE- to POST-test ($p = .000$). ***(Figure 1a)***

4.3.2 Maximal exercise intensity

No differences in baseline measurements were found. Significant main effects exist for Time, $F(1,12) = 13.65$, $p < .05$, Group, $F(1,12) = 4,85$, $p < .05$ and Time x Group, $F(1,12) = 24.48$, $p < .001$. Simple-effects analysis showed a 15,5% increase in W_{max} in MS_{TR}($p = .000$). ***(Figure 1b)***

4.3.3 Relative maximal exercise intensity

No differences in baseline measurements were found. Significant main effects exist for Time, $F(1,12) = 17.68$, $p < .01$ and Time x Group, $F(1,12) = 27.60$, $p < .001$. Simple-effects analysis showed a 21% increase in W_{maxrel} in MS_{TR} ($p = .000$). ***(Figure 1c)***

4.3.4 Time until exhaustion

No differences in baseline measurements were found. Significant main effects exist for Time, $F(1,12) = 13.07$, $p < .01$ and Time x Group, $F(1,12) = 21.06$, $p < .01$. Simple-effects analysis showed a 19,1% increase in Time until exhaustion in MS_{TR} ($p = .000$). ***(Figure 1d)***

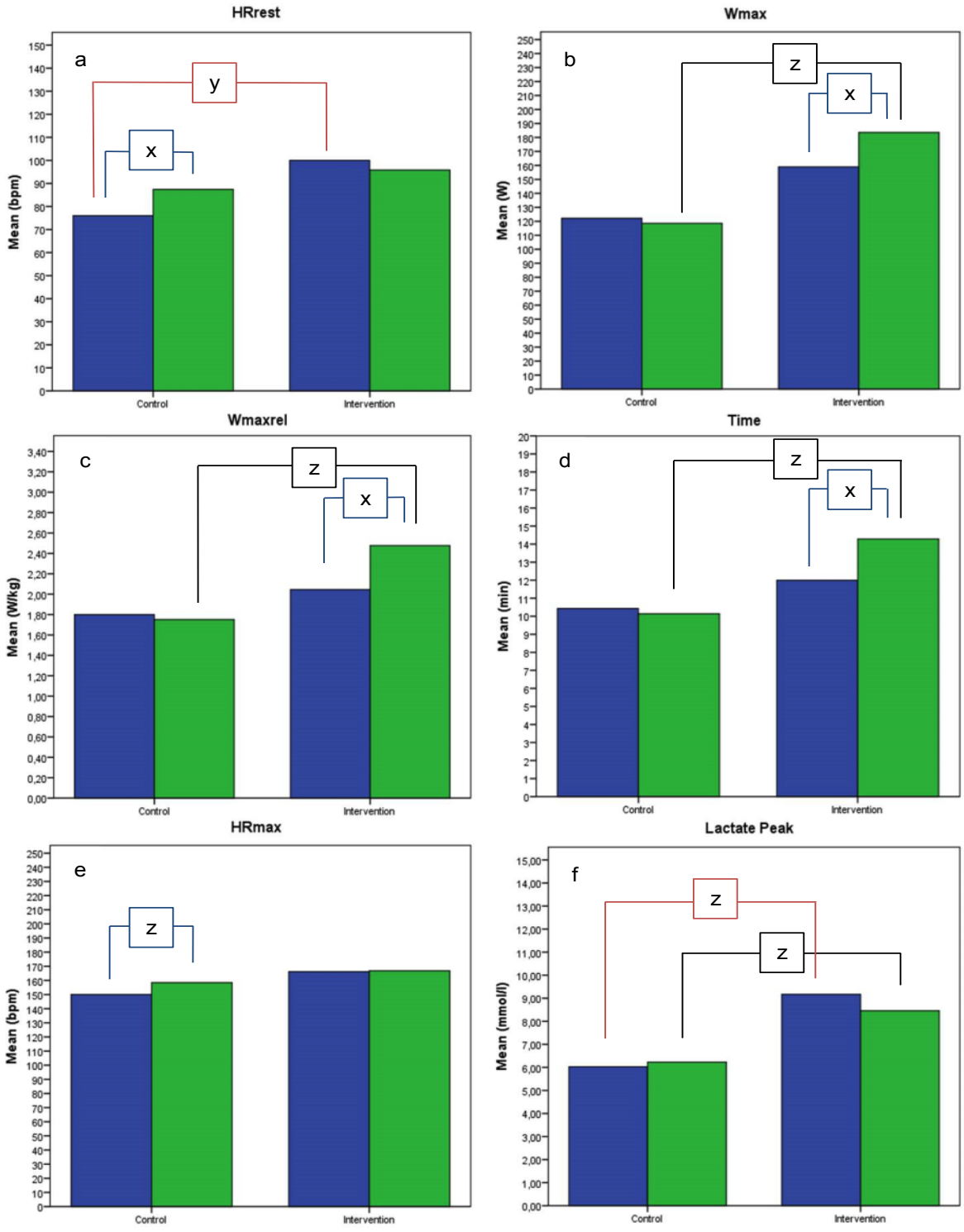
4.4 Secondary outcome measures

4.4.1 Maximal heart rate

No differences in baseline measurements were found. There was a significant effect for time, $F(1,12) = 4.87$, $p < .05$. The maximal hearth rate in MS_{SED} increased significantly with 5,6% ($P = .014$). ***(Figure 1e)***

4.4.2 Peak lactate

Significant differences between baseline measures were found ($p < .05$). Significant main effects exist for Group, $F(1,12) = 7.06$, $p < .05$. Further statistical analysis showed there was no significant difference between PRE- and POST-test results in MS_{TR} or in MS_{SED}. ***(Figure 1f)***



= Significant difference in baseline measures

= PRE-test

= POST-test

X: p = .000
Y: p < .01
Z: p < .05

Figure 1 Results

5. Discussion

The present study explored the impact of home-based rehabilitation on various exercise capacity related outcome measures in PwMS. Under the conditions of the present study, we demonstrated that home-based exercise is able to improve maximal workload and time until exhaustion during a maximal graded cycle ergometer test. Home-based training did not change resting heart rate and peak blood lactate concentration.

5.1 Heart rate effects

Interestingly, both HR_{max} and HR_{rest} were unaffected by the 20-week home-based intervention programme. Although surprising, the absence of an exercise effect on HR_{rest} following exercise training was supported by Hansen et al [12]. They suggested that this might be caused by an impaired cardiac autonomic control often seen in PwMS [12].

5.2 Workload effects

Our results suggest that home-based rehabilitation is able to increase W_{max} and W_{maxrel}. We could not find other studies examining the effects of a home-based intervention on W_{max} and W_{maxrel}. However, studies examining the effect of rehabilitation on W_{max} and W_{maxrel} in controlled research settings were more abundant. For example, studies performed by Bjarnadottir et al., Petajan et al., and Rampello et al., reported an increase in W_{max} up to 48% [2, 25, 30]. It was also suggested by Motl et al. [22] that these effects might be more beneficial for PwMS who are still ambulatory and are still able to perform training at higher volumes. Also, Bjarnadottir et al. found increases in W_{maxrel} following rehabilitation [2]. These findings might have important implications. Firstly, PwMS can potentially perform their activities of daily living (ADL) and sport related activities at higher intensity. Secondly, this might also mean that PwMS can perform low-level intensity tasks for a longer period of time. Thus, making them more independent in their ADL.

5.3 Time

Subjects within the intervention group were able to perform the POST-test maximal graded exercise test for a significantly longer period of time compared with the control group. This finding corresponds with the increase in W_{max} found following intervention. Therefore, PwMS might be able to perform more strenuous tasks for a longer period of time. This could also mean that they are able to complete a task more effectively when getting fatigued. As far as we know, this was the first study examining time until voluntary exhaustion.

5.4 Peak lactate

At baseline, there was a significant difference between MS_{TR} and MS_{SED}. However, the intervention had no effect on $lactate_{peak}$ in MS_{TR}. A possible explanation is that participants never crossed the anaerobic threshold, therefore not meeting the requirements needed to induce changes in lactate metabolism. No other home-based studies examining $lactate_{peak}$ were available. However, several studies investigating changes in $lactate_{peak}$ following completion of an exercise programme in controlled settings found a significant decrease in $lactate_{peak}$ favouring the intervention group [12, 13, 33]. It has to be noted that studies performed by Hansen et al. combined aerobic training with resistance training. Therefore, we cannot clearly state the effect of cardiovascular training on $lactate_{peak}$.

5.5 Limitations

One of the major limitations of the present pilot study was the small sample size. Another limitation of the study was lack of randomisation. Both mean that inter-individual differences can have a major impact on results as shown by our findings from HR_{rest} and $Lactate_{peak}$. The next limitation was the fact that the golden standard (maximal oxygen uptake (VO_2max)) was not used as an outcome measure [15, 16]. A similar study reported the required oxygen-measuring mask as uncomfortable and no results on VO_{2max} were found [7]. Another limitation was that the data for HR_{rest}, HR_{max}, Time and $lactate_{peak}$ were not normally distributed. Therefore it was not methodologically correct to perform a mixed ANOVA. However, Donaldson and Lunney found that when sample sizes are equal, the power of the F-ratio is not affected in data that are not normally distributed [10, 19]. A final limitation is that one participant performed the PRE-test using a different test protocol compared to other participants. For this participant, exercise intensity increased every three minutes while for the other participants exercise intensity increased every minute.

6. Conclusion

Participants were recruited to examine the effects of a 20-week home-based rehabilitation programme on several cardiovascular outcome parameters. Our results suggest that this type of rehabilitation is effective for increasing maximal exercise intensity, relative maximal exercise intensity and time until exhaustion. However, more research is needed to understand the full extent of the effects of home-based rehabilitation in MS.

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Appendix

Appendix 1: example training schedule

Training schedule MS

	Day	Activity
4/11	Mon	4km running (P1+5)
	Tue	-
	Wed	5km running (P1)
	Thu	-
	Fri	-
	Sat	4km running (P1+5)
	Sun	-
11/11	Mon	1h cycling extensive duration (P1)
	Tue	-
	Wed	4km running (P1+5)
	Thu	-
	Fri	-
	Sat	6km walking (P1+5)
	Sun	4km running (P1)
18/11	Mon	1h cycling extensive duration (P1+5)
	Tue	-
	Wed	8km walking (P1+5)
	Thu	-
	Fri	-
	Sat	6km running (P1)
	Sun	8km walking (P1)
25/11	Mon	1h cycling extensive duration (P1+10)
	Tue	-
	Wed	5km running (P1)
	Thu	-
	Fri	-
	Sat	10km walking (P1+5)

	Sun	10km walking (P1) **Contact Prof. Dr. B. Op 't Eijnde with trainingsfeedback**
2/12	Mon	-
	Tue	-
	Wed	8km walking (P1)
	Thu	-
	Fri	-
	Sat	-
	Sun	10km walking (P1)
9/12	Mon	1h cycling extensive duration (P1+15)
	Tue	-
	Wed	6km running (P1+5)
	Thu	-
	Fri	-
	Sat	12km walking (P1)
	Sun	14km walking (P1)
16/12	Mon	1h cycling extensive duration(P1+5)
	Tue	-
	Wed	6km running (P1+10)
	Thu	-
	Fri	-
	Sat	8km running (P1)
	Sun	4km running (P1+10)
23/12	Mon	1h cycling extensive duration (P1+15)
	Tue	-
	Wed	8km walking (P1+5)
	Thu	-
	Fri	-
	Sat	12km walking (P1)
	Sun	14km walking (P1)
30/12	Mon	1,5h cycling extensive duration (P1+10)
	Tue	-
	Wed	4km running (P2-5)
	Thu	-

	Fri	-
	Sat	10km walking (P1+5)
	Sun	14km walking (P1)
6/1	Mon	1h cycling extensive duration (P1+10)
	Tue	-
	Wed	-
	Thu	4km running (P2-5)
	Fri	-
	Sat	10km walking (P1+5)
	Sun	10km walking (P1+5)
13/1	Mon	-
	Tue	-
	Wed	5km running (P1+15)
	Thu	-
	Fri	-
	Sat	9km walking (P1+5)
	Sun	**Walking trip in the dunes of Zeeland**
20/1	Mon	7km walking (P1)
	Tue	-
	Wed	-
	Thu	6km running (P1+15)
	Fri	-
	Sat	8km walking (P1+10)
	Sun	10km walking (P1+5)
27/1	Mon	8km walking (P1)
	Tue	-
	Wed	6km running (P1+15)
	Thu	-
	Fri	8km walking (P1+5)
	Sat	8km walking (P1+10)
	Sun	10km walking (P1+5)
27/1	Mon	8km walking (P1)
	Tue	-
	Wed	-

	Thu	-
	Fri	-
	Sat	5km running (P2-5)
	Sun	-
3/2	Mon	8km walking (P1)
	Tue	-
	Wed	-
	Thu	-
	Fri	-
	Sat	5km running (P2-5)
	Sun	10km walking (P1+5)
10/2	Mon	7km walking (P1)
	Tue	-
	Wed	-
	Thu	6km running (P1+15)
	Fri	-
	Sat	9km walking (P1+10)
	Sun	11km walking (P1+5)
17/2	Mon	6km walking (P1)
	Tue	-
	Wed	6km running (P1+15)
	Thu	-
	Fri	10km walking (P1+5)
	Sat	8km walking (P1+10)
	Sun	10km walking (P1+5)
24/2	Mon	6km walking (P1)
	Tue	-
	Wed	6km running (P1+15)
	Thu	-
	Fri	-
	Sat	6km walking (P1+5)
	Sun	**Walking trip through the hills of Wavre**
		Two-week walking trip in the Jordan desert

Abbreviations:

- Mon=Monday; Tue= Tuesday; Wed= Wednesday; Thu= Thursday; Fri= Friday; Sat= Saturday; Sun= Sunday
- P1= Aerobic threshold heart rate; P2= Anaerobic threshold heart rate
    - -5, +5, +10, +15 = Heart rate under or above P1/P2
- km= kilometre; h= hour

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Richting: **master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen**
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