

Periodized home-based training: A new strategy to improve high intensity exercise therapy adherence in mildly affected patients with Multiple Sclerosis

Peer-reviewed author version

KEYTSMAN, Charly; VAN NOTEN, Pieter; SPAAS, Jan; NIESTE, Ine; VAN ASCH, Paul & OP 'T EIJNDE, Bert (2019) Periodized home-based training: A new strategy to improve high intensity exercise therapy adherence in mildly affected patients with Multiple Sclerosis. In: Multiple Sclerosis and Related Disorders, 28, p. 91-97.

DOI: 10.1016/j.msard.2018.12.018

Handle: <http://hdl.handle.net/1942/30312>

# **Periodized home-based training: a new strategy to improve high intensity exercise therapy adherence in mildly affected patients with Multiple Sclerosis.**

**Charly Keytsman<sup>1</sup>, Pieter Van Noten<sup>1</sup>, Jan Spaas<sup>1</sup>, Ine Nieste<sup>1</sup>, Paul Van Asch<sup>2\*</sup>,**

**Bert O Eijnde<sup>1\*</sup>**

(1) REVAL Rehabilitation Research Center, BIOMED Biomedical Research Institute, Faculty of  
Medicine and Life Sciences, Hasselt University, Agoralaan Building A, Diepenbeek, Belgium

(2) Move to Sport Foundation, Mechelsesteenweg, Kontich, Belgium

\*shared last author

Corresponding author:

Charly Keytsman

REVAL Rehabilitation Center – Biomedical Research Institute (BIOMED) – Hasselt University

Agoralaan Building A

B-3590 Diepenbeek, Belgium

Email: charly.keytsman@uhasselt.be

Tel: +32477/61 11 22

## ABSTRACT

**Introduction.** Although high intensity interval therapy (HIT) in Multiple Sclerosis (MS) induces substantial effects, longer term compliance to such a training program is not evident. When embedded in a periodized, home-based training strategy, high intensity exercise therapy adherence may improve. This is explored first in mildly affected persons with MS.

**Methods.** Exercise capacity (maximal exercise test) and body composition (DEXA) of healthy controls (n=22) and persons with MS (n=23, EDSS: 1.9±1.1) were assessed at baseline (PRE). Next and within the context of an MS awareness project (climbing the Mont Ventoux, France), all participants were enrolled in a 6m home-based periodized HIIT oriented cycling program with remote (Polar® M200 activity tracker) supervision. Hereafter, POST measurements were performed similar to baseline.

**Results.** Six months of periodized and home-based HIT oriented training induced improvements in body weight (-3%, p=0.008), BMI (-3%, p=0.01), total mass (-2%, p=0.023),  $VO_{2max}$  (+5%, p=0.016), workload (+11%, p=0.001), time until exhaustion (+14%, p=0.001), recovery heart rate (+4%, p=0.04), lactate peak (+16%, p=0.03) and RER (+4%, p=0.04) in MS. Furthermore, all persons with MS safely reached the top of the Mont Ventoux, except for two.

**Conclusion.** The applied 6m periodized, home-based and HIIT-oriented cycling program provided good therapy adherence with similar improvements in exercise capacity compared to healthy controls. Furthermore, this exercise regimen trained mildly-affected persons with MS adequately to climb the Mont Ventoux.

## INTRODUCTION

Exercise therapy and increased physical activity in persons with Multiple Sclerosis (MS) improves mobility, muscular strength, physical fitness and fatigue<sup>1,2</sup> without increasing relapse rate<sup>3</sup>. As such, physical activity and more particular exercise therapy has become an important complementary part of MS rehabilitation. In particular, high intensity interval training/rehabilitation (HIT) in MS has gained much attention. Although and in contrast to lower intensity exercise that has shown good long-term therapy adherence, it appears to be less effective to improve health-related variables such as body composition, blood pressure and blood lipid profiles<sup>4</sup>. It substantially enhances functionally (daily life) relevant variables such as exercise capacity (+22%) and muscle strength (+44%)<sup>4,5</sup> however and in this population it is also associated with improvements of various quality of life<sup>6,7</sup> measures as well as cognitive performance (+8%)<sup>8</sup>. Because this exercise mode appears to be safe and well-tolerated in MS<sup>4,5,8,9</sup>, further optimization of high intense exercise therapy and especially its effective longer-term implementation in actual rehabilitation programs in this population, is highly warranted. Consequently, any HIT-oriented exercise therapy strategy that improves longer-term compliance (therapy adherence) is worthwhile investigating. Periodized, home-based training within an awareness of increased physical activity in MS context could be such a strategy.

In sports settings, conditioning and strength training programs are usually periodized into sequential phases and cyclical periods to achieve specific performance goals and maximize optimal long-term training/performance stimuli while minimizing overtraining and/or injuries. Here, training is not based on single progressive linear training stimuli for a prolonged period but is divided in periodically alternating blocks of e.g. 1-4 weeks<sup>10</sup> that include different training goals, varying exercise modalities (e.g. high volume/duration and low intensity vs. low volume/duration and high intensity) and periods of rest/recovery<sup>11-15</sup>. Many rehabilitation programs in various populations however still mainly use continuous linear progression models that use single stimuli and training modalities. This in fact results in suboptimal training/rehabilitation outcomes<sup>12, 14, 15</sup> and may also lead to overtraining. Therefore, and because as described above HIT in MS has only minor effects on health-related variables, the use of periodized repetitive alterations of high volume / low intensity and low volume / high intensity training sessions and adequate recovery periods during MS rehabilitation possibly not only allows longer-term exercise compliance but may also affect health outcome.

Barriers for persons with MS to engage in long-term exercise interventions include lack of time, distance, transportation, neurological disability, specialist availability and insurance coverage<sup>16-18</sup>. Consequently, rehabilitation programs tend to be short (4-8 weeks), are often purely reactive to exacerbations and very often only address acute disability/symptoms<sup>17</sup>, without focussing on long-term benefits of consistent adequate physical activity and life-style changes. Possibly, addressing some of these barriers such as lack of time (by low-volume / high intensity training sessions) and both distance and transportation difficulties using home-based exercise programs, may have the potential to improve longer-term adherence to HIT. In this respect it is important to note that although home-based rehabilitation is safe and effective to improve functionality and symptoms in MS<sup>19, 20</sup>, unsupervised training programs in a home- or community setting were reported to be less effective compared to (remotely) supervised home-based training<sup>21</sup>. Consequently, home-based exercise programs in MS should include remote supervision.

Finally, the increasing awareness of the MS population of the positive impact of exercise therapy may also improve long-term therapy adherence/compliance and exercise therapy participation. In this respect, we previously successfully conducted several MS exercise therapy studies that were embedded in awareness to physical activity projects (*Machu Picchu*<sup>22</sup> and *MSRUN*<sup>23</sup> project). These projects included physical challenges such as mountain climbing, walking in the heat and running the Antwerp 10 miles, that increased awareness in both the participating subjects as well as the entire MS community.

Therefore, the present study explores whether a HIT oriented periodized home-based exercise intervention strategy, that is implemented in an awareness project, may be able to induce longer-term exercise therapy adherence and improves fitness and health-related parameters such as exercise capacity and body composition. Because this is the first time such a strategy will be applied, this was tested in mildly affected MS patients first.

## METHODS & MATERIALS

### *Participants*

Mildly affected persons with MS (all phenotypes, EDSS<4) and healthy controls (aged>18y), were included after recruitment through regional announcements via the Rehabilitation Research Center of Hasselt University (REVAL) and the Belgian-based MovetoSport foundation (Kontich, Belgium) networks, after which written informed consent was collected. Subjects were excluded if they participated in another study, had (in case of MS) an acute exacerbation in the preceding 6 months prior to the start of the project, experienced contraindications to participate in moderate to high intensity exercise, or in the presence of cardiovascular/orthopaedic diseases. Furthermore, subjects were asked to provide/use their own bicycle to participate in the awareness project (see below). The study was approved by the Ethical Committee of the Jessa hospital and Hasselt University, was performed in accordance with the Declaration of Helsinki and was registered at ClinicalTrials.gov (NCT03418376).

### *Study design*

Following heart function evaluation by an experienced medical doctor, exercise capacity (maximal graded exercise test) and body composition (DEXA scan) were assessed at baseline (PRE). Next and to monitor therapy adherence, all participants received an activity tracker (Polar® M200) and were enrolled in a 6-month home-based exercise program. Each training cycle (3w, see below), participants received personalized periodized home-based training instructions by mail. Training involved cycling on their own personal bicycle with remote supervision using the Polar® Coach module. Participants continuously had the possibility to communicate with the researchers by phone or email in case of problems. Following the 2<sup>nd</sup> and 5<sup>th</sup> training cycle, a group cycling tour was organized to improve group dynamics and motivation. Following 8 training cycles (~6m) POST measurements were performed similar to baseline and one week later subjects climbed the Mont Ventoux by bicycle (awareness project, see below).

Throughout the study course part of participants in both groups used an ergogenic supplement (beta-alanine). This did not induce additional effects and is not further discussed in the present study.

### *Therapy adherence*

The online Polar® Coach module allowed online monitoring/supervision of each training session and thus adherence to the prescribed training sessions. As such, adherence was defined as the number of completed training sessions compared to the number of prescribed sessions (%). As described by Feys et al.<sup>23</sup> therapy adherence was considered good when at least 90% or more of the prescribed training sessions were effectively executed. Furthermore, training duration, total cycling distance, percentage in target heart rate training zones and caloric expenditure throughout the intervention period (6 months) were monitored.

### *Exercise capacity*

During the exercise test to volitional fatigue, an electronically braked cycle ergometer (eBike Basic®, General Electric GmbH, Bitz, Germany) with pulmonary gas exchange analysis (Metalyzer II® 3B Cortex, Leipzig, Germany) was used. Female and male persons with MS started at 20W and 30W, respectively, during the first minute. Hereafter, workload increased, respectively, 10W and 15W per minute<sup>9</sup> and were asked to bicycle at >70rpm throughout the test. Oxygen uptake ( $\text{VO}_2$ ), expiratory volume (VE), and respiratory exchange ratio (RER) were collected breath-by-breath and averaged every minute. Using a 12-lead ECG device, heart rate (HR) was monitored every minute. At the end of the test RER values (>1.1) were evaluated to verify whether the test was maximal. In addition, maximal cycling resistance ( $W_{\text{max}}$ ), maximal heart rate ( $\text{HR}_{\text{max}}$ ), test duration and  $\text{VO}_{2\text{max}}$ , defined as the corresponding load, heart rate, minutes and oxygen uptake measured at the level of exhaustion, were reported. Capillary blood samples were obtained from the earlobe to analyze blood lactate concentrations (mmol/l) at maximal exhaustion (lactate max) and after recovery (lactate peak), using a portable lactate analyzer (Accutrend Plus, Roche Diagnostics Limited, Sussex, UK), which has previously shown to be accurate and reliable<sup>24</sup>.

### *Body composition*

Whole body fat mass and percentage, body mass index (BMI), total and fat free mass were obtained using Dual Energy X-ray Absorptiometry scan (DEXA) (Hologic Series Delphi-A Fan Beam X-ray Bone Densitometer, Vilvoorde, Belgium). A calibrated analogue scale (Seca®) was used to measure total body weight and height.

### *Home-based, periodized exercise*

Training cycles are presented schematically in Table 1. The exercise training program (6 months) involved 8 recurrent 3-week cycles (week I-III) involving Polar® M200 exercise intensity monitoring (% of HR<sub>max</sub>). During week I, subjects performed moderate to high intensity bicycle training (3/w). Twice a week, subjects performed longer training sessions (2→3h, 60-80% HR<sub>max</sub>) and once a week a more intense, shorter (1→1.5h, 75-90% HR<sub>max</sub>) training session was executed. During week II, subjects performed maximum intensity interval cycle training (3/w). High intensity interval cycle training (HIT) consisted of 3-5 maximal sprints (90-100% HR<sub>max</sub>) of 60-90s, interspersed by 1-3min rest intervals. A 10min standardized warming up and 10min cooling down was performed before and after each training session. In week III subjects performed one short high intense interval training session and one optional endurance session of 2-3h (70-90% HR<sub>max</sub>). During the last week of each 3-week cycle, subjects received training instructions for the next training cycle.

### *Awareness project*

The awareness project involved climbing the Mont Ventoux (France) by bicycle following the above described periodized home-based training program, and was used to improve therapy adherence throughout the intervention period. As such, it was possible to observe whether the applied periodized, home-based training program enabled these patients to perform a challenging sports performance. On September 16, 2017, subjects climbed the Mont Ventoux by bicycle starting from Sault. The climb included a distance of 25.70 km, whilst climbing 1152m (peak altitude: 1912m) with an average gradient of 4.5% (range 1%→10.5%). For safety reasons, every person with MS was accompanied by a HC buddy throughout the challenge. Carbohydrate and water



provision was provided after eight and 16 km. Performance of persons with MS was monitored using their Polar® M200 activity tracker and all practical arrangements were covered by the organizing foundation.

### *Statistical analysis*

All data were analyzed using SPSS v. 22.0 (IBM). Normality of data distribution was evaluated using the Shapiro-Wilk test. Baseline differences and parameters of training volume (number of completed sessions, total training duration, cycling distance, percentage in target heart rate training zones and caloric expenditure) between groups were analysed using an unpaired student's t-test (Mann Whitney U test). Parameters of body composition and exercise capacity within groups were analysed using a paired student's t-test (Wilcoxon signed-rank test). Difference scores (delta's, POST-PRE) were calculated for both groups and analysed using an unpaired student's t-test (Mann Whitney U test). All data are presented as means  $\pm$  SD's and the threshold for statistical significance was set at  $p < 0.05$ .

## **RESULTS**

### *Subject characteristics*

Thirty-three persons with MS and an equal amount of HC attended an information session at Hasselt University, after which ten persons with MS and 11 HC declined to participate in the project for reasons not related to the study (e.g. no support from social environment). The remaining twenty-three mildly affected persons with MS (mean EDSS  $1.9 \pm 1.1$ , range 0  $\rightarrow$  3.5) and twenty-two HC were included in present study. Throughout the 6-month home-based training intervention, five persons with MS and three HC dropped out. Reasons were musculoskeletal injuries not related to the intervention program (2 persons with MS, 1 HC), motivational issues (1 persons with MS, 1 HC), one exacerbation in the MS group, and personal reasons (1 person with MS, 1 HC). Eighteen persons with MS and nineteen HC underwent the full clinical analysis (PRE-POST measurement). Eventually, 17 persons with MS and 17 HC participated in the Mont Ventoux climb. Baseline subject characteristics are shown in Table 2 including all subjects that performed the full clinical analysis (MS,  $n=18$ ; HC,  $n=19$ ). No significant differences were found between groups.

### *Therapy adherence*

All MS patients who completed the 6-month training program showed high training adherence with 61/64 (~95%) of the prescribed training sessions performed. Healthy controls performed 57/64 sessions (~90%) with no difference between groups ( $p=0.225$ ). Furthermore, eight subjects with MS and six HC regularly performed the extra optional training session in Week III. Missed trainings sessions were due to personal reasons, musculoskeletal injury, holidays or one MS-related exacerbation, but were not related to the training program. Furthermore, no differences were found between groups (data shown in Figure 1) for total training duration ( $p=0.97$ , Figure 1A), total cycling distance ( $p=0.45$ , Figure 1B), caloric expenditure ( $p=0.70$ , Figure 1C) and time spent (percentage) in the different target heart rate training zones (Figure 2).

### *Exercise capacity*

Similar to HC, the applied training program improved  $VO_{2max}$  (HC: +6%,  $p=0.03$ ; MS: +5%,  $p=0.016$ ), workload (HC: +11%,  $p<0.0001$ ; MS: +11%,  $p=0.001$ ) and time until exhaustion (HC: +11%,  $p=0.001$ ; MS: +14%,  $p=0.001$ ) of mildly affected persons with MS. Furthermore, six months of home-based exercise improved recovery heart rate (+4%,  $p=0.0017$ ), lactate peak (+16%,  $p=0.03$ ) and RER (+4%,  $p=0.04$ ) in MS and in HC lactate max (+30%,  $p=0.005$ ) and maximal heart rate (-2%,  $p=0.03$ ) were affected (Table 4). With the exception of recovery heart rate ( $p=0.03$ ) PRE-POST changes did not differ between groups.

### *Body composition*

Six months of home-based training (Table 3) induced significant reductions in body weight (-3%,  $p=0.008$ ), BMI (-3%,  $p=0.01$ ) and total mass (-2%,  $p=0.023$ ) of mildly affected MS patients. Fat mass, fat percentage and fat free mass did not differ over time ( $p>0.05$ ) in MS. The applied home-based training program did not affect body composition in HC. No differences were found for PRE-POST changes between groups ( $p>0.05$ ).

### *Awareness project*

All persons with MS (and HC) that successfully completed the training program safely reached the top of the Mont Ventoux, (25.7 km, average slope: 4.5%) except for two (termination at 2km and 1km from the top because of exhaustion). The group reached the top of the mountain in a mean time of 2h48min, an average speed of 9.8 km/h, a mean heart rate of 133bpm and maximal heart rate of 175 bpm. No injuries or adverse events (physical complications or exacerbations) occurred during the challenge. Healthy controls were asked to accompany one MS patient throughout the challenge, for safety reasons.

## **DISCUSSION**

The investigation of strategies to improve long-term high intensity exercise therapy adherence in MS is highly warranted and represents a major topic of interest in the supportive care and rehabilitation of these patients. Improving therapy adherence in these patients leads to prolonged physical activity participation that may result in to long-term effects on clinical outcomes, such as exercise capacity and health-related parameters. In an attempt to improve therapy adherence and to further optimize HIT-oriented rehabilitation in MS, the present study investigated the impact of a combined periodized home-based exercise intervention strategy, implemented in an awareness project, in mildly affected relatively fit persons with MS. The applied program provided good adherence to the prescribed HIT-oriented training sessions (~95% of the sessions completed) and should therefore be further investigated in larger studies, with even longer (>6 months) exercise interventions. Moreover, the exercise program induced similar significant improvements in exercise capacity between healthy controls and MS patients. Furthermore and in the context of an awareness project, this periodized home-based exercise training strategy allowed persons with MS to successfully climb the Mont Ventoux by bicycle.

Recent studies clearly show that HIT is a very efficient rehabilitation strategy to enhance exercise capacity<sup>4</sup>, muscle strength<sup>5</sup> and cognitive performance<sup>8</sup>. Hereby, it also improves functionality and quality of life of persons with MS. Next to these clinical improvements<sup>9, 25</sup> HIT is less time-consuming (total session duration ~20-30min) compared to classic moderate intensity endurance training (total session duration ~40-60min)<sup>25</sup> and because this is often a barrier for engagement in (longer term) physical activity<sup>16</sup> it is therefore probably better integrable in to everyday life. Because as described above HIT in MS does not substantially affects important health-related

variables whereas moderate intensity training (MIT) does<sup>26, 27</sup>, the combination of HIT and MIT implies the potential to enhance both functional (exercise capacity) and health (body composition) parameters. As such, we attempted to further optimize high intense rehabilitation in MS and explored the potential of a HIT-oriented exercise strategy that involved periodized training with week by week (week I-III) variations in exercise intensity (high vs. low), session duration (long vs. short) and rest/recovery. This allowed the application of short sessions that were not only alternated with recovery periods but also with moderate intensity longer duration training sessions<sup>11-15</sup>. In mildly affected relatively fit person with MS, this program appeared to be feasible (personal communication by subjects) during longer training periods and significantly improved exercise capacity ( $VO_{2\max}$  +5%, workload +11%) and some parameters of body composition (weight -3%, BMI -3%, total mass -2%) with similar effects between MS and HC. This shows that this training program induces similar training effects in mildly affected persons with MS (EDSS:  $1.8 \pm 1.1$ ) compared to HC. Unfortunately, we were not able to significantly improve health-related parameters such as fats mass in the present study. It is difficult to speculate why the moderate intensity training component did not affect this. Therefore, other training methods to improve health-related parameters in MS should be explored.

Another part of the applied training strategy included home-based exercise therapy that has been described as an efficient approach to remove barriers for engagement in physical activity such as lack of time and distance to rehabilitation centres, and hereby it may improve therapy adherence in persons with MS<sup>16-18</sup>. As such, home-based exercise could lead to persistent increased levels of physical activity and improved functioning in this population. Indeed, it was already shown that performing home-based exercise programs in MS (3/w, strength/aerobic training, 12w to 23w) improves walking speed, aerobic capacity, functional mobility and cognitive parameters<sup>19, 23</sup>. Although we assessed different functional parameters, the results of the present study are consistent with these findings. Here and compared to healthy controls, a 6-month home-based cycling program induced similar improvements in exercise capacity and some parameters of body composition in mildly affected relatively fit persons with MS. Interestingly and similar to Feys et al<sup>23</sup> the applied training strategy resulted in a very high adherence with 95% of the training sessions completed over a training period of six months.

### *Limitations*

Because this was the first time a HIT oriented periodized home-based training strategy was applied in MS patients, and for safety reasons, the present project only included mildly affected relatively fit persons with MS (EDSS:  $1.8 \pm 1.1$ ). As such, we cannot extrapolate these results to other persons with MS. However, the obtained good training adherence and significant improvements in exercise capacity warrant future studies investigating this training strategy in more severely affected less fit persons with MS. In the present study we have chosen to combine several training methods in to one periodized home-based strategy. As such, the sole impact of either periodized or home-based HIT oriented training was not investigated. Given the above described results periodized and homed-based HIT training should now be investigated separately in larger (powered) controlled trials (randomized) and be compared to more conventional, linear progressive training programs. Furthermore, it should be noted that the high therapy adherence in the present project may be partly attributed to enhanced motivation by goal setting at the end of the study, implemented in the project ('Mont Ventoux Challenge'). Therefore, future studies that are implemented in awareness projects should include objective measurements of motivational aspects.

### **CONCLUSION**

We conclude that a 6-month HIT oriented periodized and home-based training strategy allowed good therapy adherence and improved exercise capacity in mildly affected persons with MS similar to healthy controls. Furthermore, this exercise program trained MS patients to successfully climbing the Mont Ventoux by bicycle.

## Reference List

1. Latimer-Cheung AE, Pilutti LA, Hicks AL, et al. Effects of exercise training on fitness, mobility, fatigue, and health-related quality of life among adults with multiple sclerosis: a systematic review to inform guideline development. *Archives of physical medicine and rehabilitation*. 2013; 94: 1800-28.e3.
2. Dalgas U, Stenager E and Ingemann-Hansen T. Multiple sclerosis and physical exercise: recommendations for the application of resistance-, endurance- and combined training. *Mult Scler*. 2008; 14: 35-53.
3. Pilutti LA, Platta ME, Motl RW and Latimer-Cheung AE. The safety of exercise training in multiple sclerosis: a systematic review. *J Neurol Sci*. 2014; 343: 3-7.
4. Keytsman C, Hansen D, Wens I and B OE. Impact of high-intensity concurrent training on cardiovascular risk factors in persons with multiple sclerosis - pilot study. *Disabil Rehabil*. 2017: 1-6.
5. Wens I, Dalgas U, Vandenabeele F, et al. High Intensity Exercise in Multiple Sclerosis: Effects on Muscle Contractile Characteristics and Exercise Capacity, a Randomised Controlled Trial. *PLoS One*. 2015; 10: e0133697.
6. Karlsen T, Aamot IL, Haykowsky M and Rognmo O. High Intensity Interval Training for Maximizing Health Outcomes. *Progress in cardiovascular diseases*. 2017; 60: 67-77.
7. Guiraud T, Nigam A, Gremeaux V, Meyer P, Juneau M and Bosquet L. High-intensity interval training in cardiac rehabilitation. *Sports Med*. 2012; 42: 587-605.
8. Zimmer P, Bloch W, Schenk A, et al. High-intensity interval exercise improves cognitive performance and reduces matrix metalloproteinases-2 serum levels in persons with multiple sclerosis: A randomized controlled trial. *Mult Scler*. 2017: 1352458517728342.
9. Wens I, Dalgas U, Vandenabeele F, et al. High Intensity Aerobic and Resistance Exercise Can Improve Glucose Tolerance in Persons With Multiple Sclerosis: A Randomized Controlled Trial. *Am J Phys Med Rehabil*. 2017; 96: 161-6.
10. Issurin VB. Benefits and Limitations of Block Periodized Training Approaches to Athletes' Preparation: A Review. *Sports Med*. 2016; 46: 329-38.
11. Breil FA, Weber SN, Koller S, Hoppeler H and Vogt M. Block training periodization in alpine skiing: effects of 11-day HIT on VO<sub>2</sub>max and performance. *Eur J Appl Physiol*. 2010; 109: 1077-86.
12. Issurin VB. New horizons for the methodology and physiology of training periodization. *Sports medicine (Auckland, NZ)*. 2010; 40: 189-206.
13. Storen O, Bratland-Sanda S, Haave M and Helgerud J. Improved VO<sub>2</sub>max and time trial performance with more high aerobic intensity interval training and reduced training volume: a case study on an elite national cyclist. *Journal of strength and conditioning research*. 2012; 26: 2705-11.
14. Issurin V. Block periodization versus traditional training theory: a review. *J Sports Med Phys Fitness*. 2008; 48: 65-75.
15. Ronnestad BR, Hansen J and Ellefsen S. Block periodization of high-intensity aerobic intervals provides superior training effects in trained cyclists. *Scand J Med Sci Sports*. 2014; 24: 34-42.
16. Asano M, Duquette P, Andersen R, Lapierre Y and Mayo NE. Exercise barriers and preferences among women and men with multiple sclerosis. *Disability and Rehabilitation*. 2013; 35: 353-61.
17. Conroy SS, Zhan M, Culpepper WJ, 2nd, Royal W, 3rd and Wallin MT. Self-directed exercise in multiple sclerosis: Evaluation of a home automated tele-management system. *J Telemed Telecare*. 2017: 1357633x17702757.
18. Stroud N, Minahan C and Sabapathy S. The perceived benefits and barriers to exercise participation in persons with multiple sclerosis. *Disabil Rehabil*. 2009; 31: 2216-22.
19. Romberg A, Virtanen A, Ruutiainen J, et al. Effects of a 6-month exercise program on patients with multiple sclerosis: a randomized study. *Neurology*. 2004; 63: 2034-8.
20. Khan F and Amatya B. Rehabilitation in Multiple Sclerosis: A Systematic Review of Systematic Reviews. *Archives of physical medicine and rehabilitation*. 2017; 98: 353-67.

21. Snook EM and Motl RW. Effect of exercise training on walking mobility in multiple sclerosis: a meta-analysis. *Neurorehabil Neural Repair*. 2009; 23: 108-16.
22. D'Hooghe M B, Feys P, Deltour S, et al. Impact of a 5-day expedition to machu picchu on persons with multiple sclerosis. *Multiple sclerosis international*. 2014; 2014: 761210.
23. Feys P, Moumdjian L, Van Halewyck F, et al. Effects of an individual 12-week community-located "start-to-run" program on physical capacity, walking, fatigue, cognitive function, brain volumes, and structures in persons with multiple sclerosis. *Mult Scler*. 2017: 1352458517740211.
24. Baldari C, Bonavolonta V, Emerenziani GP, Gallotta MC, Silva AJ and Guidetti L. Accuracy, reliability, linearity of Accutrend and Lactate Pro versus EBIO plus analyzer. *Eur J Appl Physiol*. 2009; 107: 105-11.
25. Wens I, Hansen D, Verboven K, et al. Impact of 24 Weeks of Resistance and Endurance Exercise on Glucose Tolerance in Persons with Multiple Sclerosis. *Am J Phys Med Rehabil*. 2015.
26. Petajan JH, Gappmaier E, White AT, Spencer MK, Mino L and Hicks RW. Impact of aerobic training on fitness and quality of life in multiple sclerosis. *Ann Neurol*. 1996; 39: 432-41.
27. Petajan JH and White AT. Recommendations for physical activity in patients with multiple sclerosis. *Sports Med*. 1999; 27: 179-91.

## Tables

**Table 1. Home-based periodized cycling training program**

	Week I	Week II	Week III
<b>Cycle 1</b>	<b>S1:</b> 1h, 60-80% HR <sub>max</sub> <b>S2:</b> 1.5h, 60-80% HR <sub>max</sub> <b>S3:</b> 1h, 60-80% HR <sub>max</sub>	<b>S1:</b> 3x60s (90-100% HR <sub>max</sub> ) with 3min recovery intervals <b>S2:</b> 3x60s (90-100% HR <sub>max</sub> ) with 3min recovery intervals <b>S3:</b> 3x60s (90-100% HR <sub>max</sub> ) with 3min recovery intervals	<b>S1:</b> 3x70s (90-100% HR <sub>max</sub> ) with 3min recovery intervals.  <b>Optional:</b> 1x, 2-3h, 70-90% HR <sub>max</sub>
<b>Cycle 2</b>	<b>S1:</b> 1.5h, 70-80% HR <sub>max</sub> <b>S2:</b> 1h, 60-70% HR <sub>max</sub> <b>S3:</b> 2h, 60-80% HR <sub>max</sub>	<b>S1:</b> 3x70s (90-100% HR <sub>max</sub> ) with 3min recovery intervals. <b>S2:</b> 3x60s (90-100% HR <sub>max</sub> ) with 60s recovery intervals <b>S3:</b> 3x70s (90-100% HR <sub>max</sub> ) with 3min recovery intervals.	<b>S1:</b> 3x80s (90-100% HR <sub>max</sub> ), with 3min recovery intervals.  <b>Group session:</b> 40km, 60-80% HR <sub>max</sub> , including 235m ascent.
<b>Cycle 3</b>	<b>S1:</b> 1.5h, 70-80% HR <sub>max</sub> <b>S2:</b> 1h, 60-70% HR <sub>max</sub> <b>S3:</b> 2h15min, 60-80% HR <sub>max</sub>	<b>S1:</b> 3x80s (90-100% HR <sub>max</sub> ) with 3min recovery intervals. <b>S2:</b> 3x70s (90-100% HR <sub>max</sub> ) with 60s recovery intervals. <b>S3:</b> 3x80s (90-100% HR <sub>max</sub> ) with 3min recovery intervals.	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ), with 3min recovery intervals.  <b>Optional:</b> 1x, 2-3h, 70-90% HR <sub>max</sub>
<b>Cycle 4</b>	<b>S1:</b> 2h, 70-80% HR <sub>max</sub> <b>S2:</b> 1h, 60-70% HR <sub>max</sub> <b>S3:</b> 2.5h, 65-80% HR <sub>max</sub>	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ) with 3min recovery intervals. <b>S2:</b> 3x80s (90-100% HR <sub>max</sub> ) with 3min recovery intervals. <b>S3:</b> 3x90s (90-100% HR <sub>max</sub> ) with 3min recovery intervals.	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ), with 3min recovery intervals.  <b>Optional:</b> 1x, 2-3h, 70-90% HR <sub>max</sub>
<b>Cycle 5</b>	<b>S1:</b> 2h, 70-80% HR <sub>max</sub> <b>S2:</b> 1h, 60-70% HR <sub>max</sub> <b>S3:</b> 3h, 65-80% HR <sub>max</sub>	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ) with 3min recovery intervals. <b>S2:</b> 3x90s (90-100% HR <sub>max</sub> ) with 60s recovery intervals. <b>S3:</b> 3x90s (100% HR <sub>max</sub> ) with 3min recovery intervals.	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ), with 3min recovery intervals.  <b>Group session:</b> 55km, 70-90% HR <sub>max</sub> , including 985m ascent.
<b>Cycle 6</b>	<b>S1:</b> 2h, 70-80% HR <sub>max</sub> <b>S2:</b> 1h15min, 60-70% HR <sub>max</sub> <b>S3:</b> 3h, 70-80% HR <sub>max</sub>	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ) with 3min recovery intervals. <b>S2:</b> 3x90s (90-100% HR <sub>max</sub> ) with 60s recovery intervals. <b>S3:</b> 3x90s (90-100% HR <sub>max</sub> ) with 3min recovery intervals.	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ), with 3min recovery intervals.  <b>Optional:</b> 1x, 2-3h, 70-90% HR <sub>max</sub>
<b>Cycle 7</b>	<b>S1:</b> 2h, 70-80% HR <sub>max</sub> <b>S2:</b> 1.5h, 60-70% HR <sub>max</sub> <b>S3:</b> 3h, 75-85% HR <sub>max</sub>	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ) with 150s recovery intervals. <b>S2:</b> 3x60s (90-100% HR <sub>max</sub> ) with 60s recovery intervals. <b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ) with 150s recovery intervals.	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ), with 3min recovery intervals.  <b>Optional:</b> 1x, 2-3h, 70-90% HR <sub>max</sub>
<b>Cycle 8</b>	<b>S1:</b> 2h, 70-80% HR <sub>max</sub> <b>S2:</b> 1.5h, 65-75% HR <sub>max</sub> <b>S3:</b> 2.5h, 75-90% HR <sub>max</sub>	<b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ) with 2min recovery intervals. <b>S2:</b> 3x60s (90-100% HR <sub>max</sub> ) with 60s recovery intervals. <b>S1:</b> 3x90s (90-100% HR <sub>max</sub> ) with 2min recovery intervals.	<b>S1:</b> 3x60s (90-100% HR <sub>max</sub> ), with 60s recovery intervals.  <b>Optional:</b> 1x, 2-3h, 70-90% HR <sub>max</sub>

The home-based cycle training program (6m) involved 8 recurrent 3-week cycles (week I-III) involving 1-3 training sessions (S1-S3) and Polar®M200 exercise intensity monitoring (% of HR<sub>max</sub>). During week I, subjects performed moderate to high intensity bicycle training (3/w). During week II, subjects performed maximum intensity interval cycle training (3/w). Week III involved one interval training session and one optional endurance session.



**Table 2. Baseline subject characteristics**

	MS	HC
Age (years)	41.7 ± 8.5	41.5 ± 9.9
Height (m)	1.73 ± 0.1	1.75 ± 0.1
Gender (f/m)	6/12	5/14
EDSS	1.9 ± 1.1	/

Data are expressed as means (SD's) and represent baseline characteristics healthy controls (HC, n=19) and multiple sclerosis subjects (MS, n=18). Abbreviations: f, female; m, male; BMI, Body Mass Index; EDSS, Expanded Disability Status Scale.

**Table 3. Body composition**

	MS		HC	
	PRE	POST	PRE	POST
Weight (kg)	74.2 ± 11.2	71.9 ± 10.9*	75.2 ± 11.2	74.1 ± 10.2
BMI	24.8 ± 3.9	24.1 ± 3.9*	24.6 ± 2.8	24.3 ± 2.7
Fat mass (kg)	16.6 ± 8.3	15.7 ± 8.5	15.6 ± 5.3	14.9 ± 5.4
Fat percentage (%)	23.8 ± 9.6	23.1 ± 10.1	22.7 ± 7.5	22.1 ± 8.1
Fat free mass (kg)	51.1 ± 7.4	50.5 ± 7.9	53.3 ± 9.8	53.1 ± 9.8
Total mass (kg)	67.7 ± 10.9	66.2 ± 10.7*	68.9 ± 10.6	68 ± 9.6

Data are expressed as means (SD's) and represent parameters of body composition before (PRE) and after (POST) a 6-month home-based cycling intervention of healthy controls (HC, n=19) and multiple sclerosis subjects (MS, n=18). \*p<0.05 compared to PRE within group.

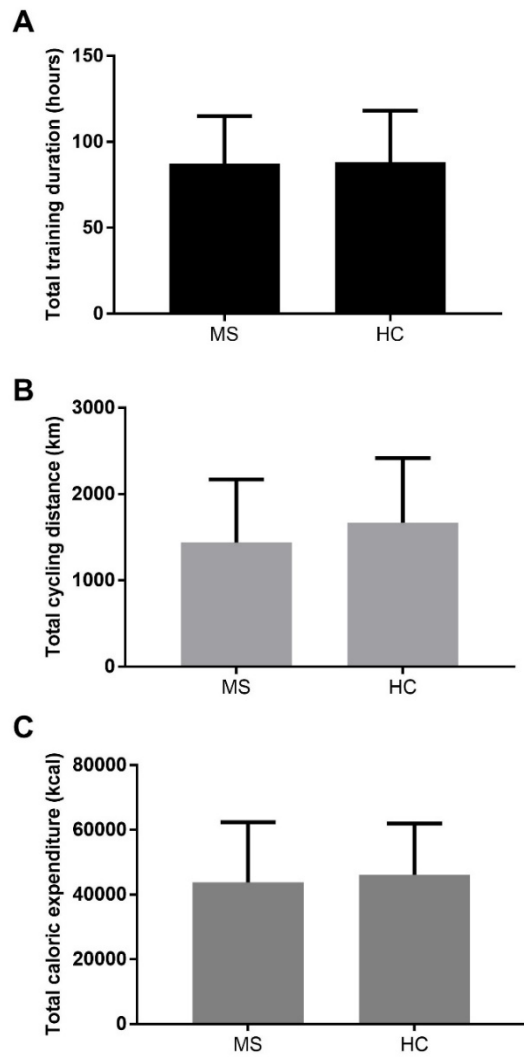
**Table 3. Exercise capacity**

	MS		HC	
	PRE	POST	PRE	POST
VO2 max	40.8 ± 6.6	42.9 ± 7.1*	44 ± 8.2	46.8 ± 7.6*
Workload	213.3 ± 43.2	237.2 ± 47.4*	244.7 ± 53.2	270.8 ± 53.1*
Time (min)	15 ± 2.5	17.1 ± 2.9*	17.3 ± 2.7	19.2 ± 2.6*
HR max (bpm)	180 ± 9	179.1 ± 9.8	181.4 ± 10.8	178.2 ± 11.8*
HR recovery (bpm)	128 ± 17	133.3 ± 15.1*	131.1 ± 13.7	129.5 ± 14.7
Lac max (mmol/l)	4.5 ± 1.6	5.9 ± 1.8	5.3 ± 1.3	6.9 ± 2.1*
Lac peak (mmol/l)	8.9 ± 2.3	10.3 ± 3.1*	9.7 ± 2.4	10.7 ± 2.2
RER	1.13 ± 0.1	1.18 ± 0.1*	1.12 ± 0.1	1.15 ± 0.1

Data are expressed as means (SD's) and represent parameters of exercise capacity before (PRE) and after (POST) a 6-month home-based cycling intervention of healthy controls (HC, n=19) and multiple sclerosis subjects (MS, n=18). \*p<0.05 compared to PRE within group.

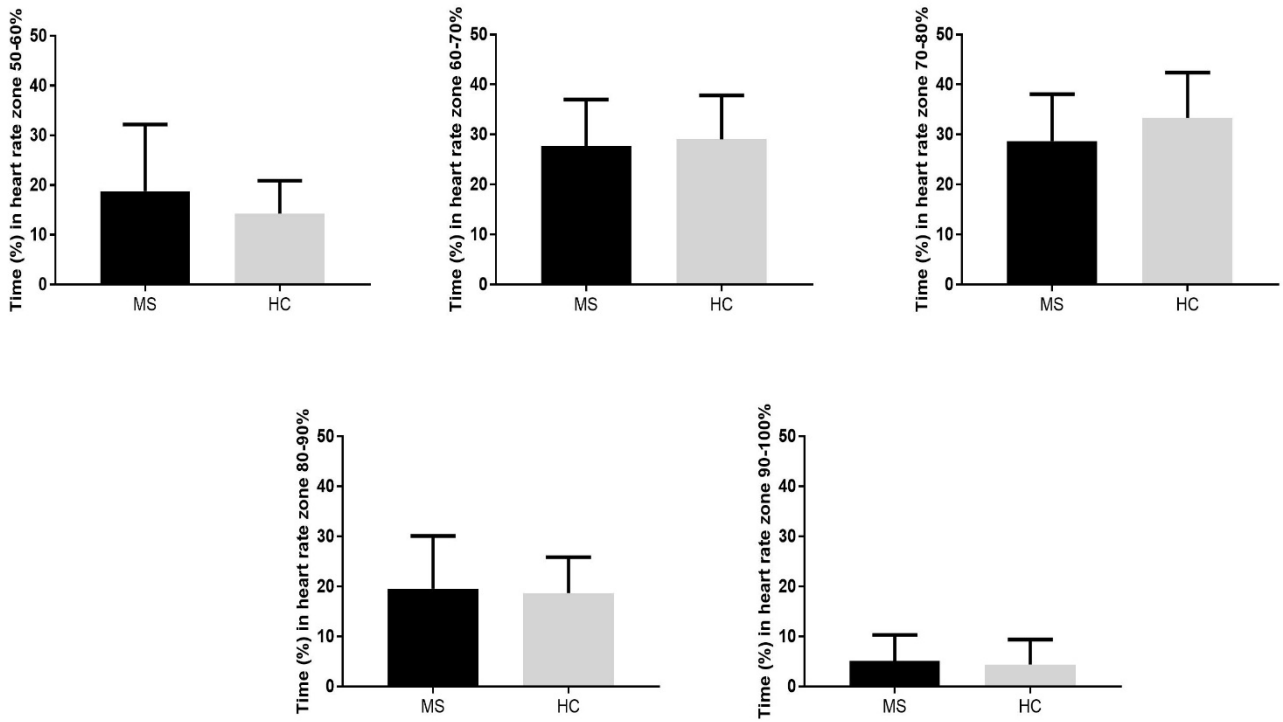
## Figures

**Figure 1. Training parameters**



Data are expressed as means (SD's) and represent total training duration (A), total cycling distance (B) and total caloric expenditure (C) of the home-based cycle training program (6m) healthy controls (HC, n=19) and multiple sclerosis subjects (MS, n=18).

**Figure 2. Heart rate training zones of the exercise intervention**



Data are expressed as means (SD's) and represent time (%) spent in the different heart rate training zones (50-60%, 60-70%, 70-80%, 80-90%, 90-100%) during the prescribed exercise sessions of the home-based cycle training program (6m) in healthy controls (HC, n=19) and multiple sclerosis subjects (MS, n=18).