Sport Sci Health (2016) 12:437–442
DOI 10.1007/s11332-016-0310-0

ORIGINAL ARTICLE

Effects of a combined aerobic and resistance exercise program in people with multiple sclerosis: a pilot study

Erica Gobbi[1] · Attilio Carraro[1]

Received: 2 June 2016 / Accepted: 21 August 2016 / Published online: 30 August 2016

Abstract

Purpose Exercise training and social support have been reported to counteract the disabling symptoms of multiple sclerosis (MS). The purpose of this study was to pilot test a combined aerobic and resistance exercise program, performed in pairs, on functional abilities, fatigue, and health-related quality-of-life (HRQOL) in people with MS.

Methods Eight patients with MS aged between 35 and 59 years were involved in a pre–post-pilot study. The intervention consisted of 20 combined aerobic and strength training sessions carried out by two participants simultaneously over a 7-week period. The Functional Independence Measure was used to assess activity limitation, and the Short Form-36 to evaluate the HRQOL. Fatigue perceptions were assessed by the Fatigue Severity Scale (FSS) and Fatigue Descriptive Scale (FDS). Overall, peak oxygen consumption test, 6-Minute Waking Test, T25-Foot Walk, and 9-Hole Peg Test were administered to evaluate functional abilities.

Results Role-physical and Vitality HRQOL subscales significantly increased by 120 % ($p = 0.026$) and by 33.85 % ($p = 0.012$), respectively, over the training. Fatigue perception significantly decreased in both the scales: FDS changed by -12.20 % ($p = 0.049$) and FSS by -12.85 % ($p = 0.034$). No changes were reported for functional measures over the training period.

Conclusions The full adherence of participants and the absence of detrimental effects sustain the feasibility of the training program. Findings suggest possible beneficial effects of a combined exercise program with social support on HRQOL and fatigue.

Keywords Combined exercise · Multiple sclerosis · Fatigue · Quality-of-life · Peer support

Abbreviations

MS	Multiple sclerosis
HRQOL	Health-related quality-of-life
EDSS	Expanded Disability Status Scale
FIM	Functional Independence Measure
FSS	Fatigue Severity Scale
FDS	Fatigue Descriptive Scale

Introduction

Multiple sclerosis is the most common chronic neurological disease affecting young adults who are at the peak of their career and family development, worldwide [1]. It is a progressive disease characterized by many symptoms, including muscle weakness, fatigue, loss of balance, impaired speech, double vision, declining cognitive function, and paralysis [2]. The symptoms widely vary across individuals with MS; however, similar progress in reduced ability to perform activities of daily living and compromised quality-of-life have been reported [3, 4].

Although a definitive treatment for MS is yet to be found, new therapeutic options provide symptom management and mitigate the detrimental effects of the disease. Moreover, exercise training and physical activity have been reported to counteract the disabling symptoms of MS [5–7]. Four main types of exercise have been studied (aerobic exercise, resistance exercise, yoga, and stretching), with interventions durations ranging from 3 weeks to

✉ Erica Gobbi
erica.gobbi@unipd.it

1 Department of Biomedical Sciences, University of Padua, via F. Marzolo 3, 35131 Padua, Italy

6 months, frequency from 1 to 5 times/week, and with sessions lasting from 30 to 60 min, at different levels of intensity [8]. Latmier-Cheung et al. [9], starting from a pool of 4362 studies, reviewed findings of 54 studies and showed evidence for the effectiveness of exercise training on the improvement of both aerobic capacity and muscular strength. In addition, improvements in mobility, fatigue, and health-related quality-of-life (HRQOL) have been reported [9, 10].

Despite the fact that several studies have explored exercise effects, it is not possible to recommend a specific exercise dose and type regarding what is safe and effective for people with MS [8]. Currently, exercise training in MS can be referred to several general recommendations [11–13]; however, no univocal consensus or robust methodologies have been found. The most recent guidelines for exercise prescriptions in MS are provided by the Canadian Society for Exercise Physiology and recommend 30 min of moderate intensity aerobic activity, two times per week, and strength training exercises for major muscle groups, two times per week [12].

In addition to the lack of evidence-based and MS-specific physical activity guidelines, the promotion of regular physical activity participation among people with MS is needed. Most people with MS are physically inactive [14], with an average activity level more than 0.5 standard deviations below that of the general population [15]. Increases of fatigue, fear of symptom exacerbation, negative feelings, and social barriers hamper participation in physical activity, and are the most reported perceived barriers among MS patients [16].

Strategies to increase physical activity among people with MS and persuade them that exercise can be beneficial in coping with the disease are still needed. Social support was found to be a potential facilitator for the intention to exercise and the execution of exercise among people with MS [17]. In particular, peer support is one of the most commonly identified perceived facilitators of physical activity among MS patients [16]. Exercising in pairs or in small groups, sharing similar problems and feelings, was found to be a good strategy to let people feel more comfortable and sustain exercise participation [18, 19].

Assuming this ground, the purpose of this study was to pilot test a combined aerobic and resistance exercise program, performed in pairs, on functional abilities, endurance, fatigue, and HRQOL in a group of people with MS. We hypothesized that both functional and psychological measures would report improvements further supported by the presence of a "partner in exercise" that can sustain the short-term participation of people with MS.

Methods

Participants

Eight people with MS (4 men and 4 women), aged between 35 and 59 years, participated voluntarily in this study. They were screened from a list of outpatients who were being followed at a neurorehabilitation centre. The inclusion criteria consisted of clinically or laboratory definite diagnosed MS [20] and a score between 2.0 and 5.0 on the Expanded Disability Status Scale (EDSS) [21]. Subjects using MS disease-modifying drugs (immunomodulators or amantadine) were included, across the study period, none of them made use of antispasmodic drugs and medication regimen did not change. Individuals were excluded if they had suffered from acute exacerbation throughout the 2 months before entering the study or if they received acute corticosteroid treatment. Participants' characteristics are presented in Table 1. Written informed consents were obtained from all the participants prior the enrollment in the study.

Procedures

The present pilot study was designed as a pre–post-trial of a combined aerobic and strength exercise program with social support and the supervision of the exercise therapist and researcher. Participants were paired on the basis of their time availability, and the resulting four couples trained jointly three times per week for 7 consecutive weeks. Measurements of activity limitations, HRQOL, fatigue, functional abilities (ambulatory function and upper extremity function), and those of peak oxygen consumption took place 3 days before the beginning and 3 days after the conclusion of the training program. The functional measures' assessors were all members of the neurorehabilitation centre staff not involved in the study.

Table 1 Characteristic of participants

Variables	Mean	SD
Age (years)	46.5	8.4
Height (cm)	170	7.1
Weight (kg)	73.4	9.9
BMI (kg/m^2)	25.2	2.2
Years post-diagnosis	8.2	5.2
Expanded Disability Status Scale	3.3	0.8

Combined exercise program

The intervention consisted of 20 sessions of a combined aerobic and strength exercise training, which was performed by two participants simultaneously, to create a more communicative and socially comfortable context. The training was planned on the basis of the last recommendations for exercise prescription in MS [12] and all participants were advised to maintain both their usual activity levels and therapeutic program during the intervention period. Each training session took place in a standard rehabilitation room, with mat tables used for strength and flexibility exercises and a cyclergometer used for aerobic. After a warm up set at the beginning of each session, one participant performed aerobic exercise, while the other carried out resistance training, interchanging their position on the completion of the work. In the last part of the session, subjects performed flexibility exercises in pairs.

Each session consisted of a 20-min aerobic exercise, six resistance exercises for upper extremities and trunk, and flexibility training with seven stretching positions. Aerobic training was performed using MOTOmed® (Movement Therapy System, Reck, Germany), it began and finished with a 3-min passive cycling movement (with motor power), with two sets of 10-min active cycling movement at an individualized intensity of 65–75 % heart rate max in the middle. Baseline results from the peak oxygen consumption testing were used to estimate appropriate intensity for aerobic exercise. Furthermore, during exercise participants were asked to maintain a rating of perceived exertion of 11–14 at Borg scale, avoiding exhaustion. Between the two 10-min sets, there was a subjective rest pause to recover, which was progressively reduced by participants. Heart rate was continuously monitored by Polar® system.

Participants exercised in strength training with elastic resistance bands and 1-kg dumb-bells. They performed two sets of ten repetitions of six different exercises: lying pelvic retroversion, bench press, lying prone pull-ups, seated row, crunches, and lying butt bridge with legs on Bobath ball. Exercises involved only upper extremities and trunk core muscles, because lower limbs were trained by aerobic exercise. A particular focus on respiration, coordination, and control of movements was placed to maximize the results of the strength training.

The final part of the session consisted in seven standard stretching exercises performed by the two participants at the same time, lying on couches.

Measures

Activity limitations

The degree of independence in performing various self-care actions and mobility tasks (bowels, bladder, toilet use, feeding, transfer, dressing, stairs, bathing, mobility, and grooming) was evaluated with the Functional Independence Measure (FIM) [22]. The FIM consists of 18 items, based on a seven-point scoring system referring to the type and the amount of assistance required for the described tasks. The total score ranges from 18 to 126, with higher scores indicating higher levels of independence.

Health-related quality-of-life

The HRQOL was evaluated using the SF-36 (Short Form-36 Health Survey) [23], that is one of the most widely used self-reported health status measures, recommended for use in multiple sclerosis [24]. SF-36 investigates eight dimensions: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Score ranges from 0 to 100, higher scores correspond to a better HRQOL.

Fatigue

The sensation of fatigue was evaluated using two scales. The Fatigue Severity Scale (FSS) measures the excess of fatigue on daily functions; it was designed for individuals with MS and with chronic fatigue syndrome [25]. Subjects have to rate on a seven-point scale nine statements related to fatigue; the lower the score, the better the situation. The Fatigue Descriptive Scale (FDS) evaluates fatigue as a symptom and reveals the clinical phenomenon of fatigue as asthenia, fatigability, and worsening of symptoms without definite feeling of fatigue [26]. The scale ranges between 0 and 17, the higher score corresponds to the worst situation of fatigue perception.

Functional measures

The 6-Minute Walking Test (6-MWT) [27] and the Timed 25-Foot Walk (T25-FW) were used to assess ambulatory function, and these tests can be used safely and easily to provide information on MS patients' walking endurance and speed. The 9-Hole Peg Test (9-HPT) is a quantitative measure of upper extremity function by means of an arm and hand dexterity task. The tests were administered using a standardized protocol [28], T25-FW with trials 1 and 2, 9-HPT with trials 1, and 2 for dominant hand and trials 1 and 2 for non-dominant. Peak oxygen consumption (VO_{2max}) was measured with an incremental test on a cyclergometer [29], respiratory gas measurement was conducted breath-by-breath by means of a portable telemetric gas analyser (Cosmed K4 b^2). After 4 min and 40 s of warm up set at 25 W, participants cycled with an increased workload of 5 W every 20 s. The test was concluded on exhaustion or when any of the following criteria was met: symptom exacerbation, symptoms indicating risk for the safety or health of the participants, and plateau in oxygen uptake with increasing workload.

Statistical analysis

Pre- to post-intervention values were analysed using a series of paired t test. Cohen's d_z were calculated as measure of effect sizes for dependent samples according to Rosenthal [30]. A significance level of $p < 0.05$ was accepted.

Results

All participants completed the 20-session training program with 100 % compliance. No MS exacerbations were reported during the training period. Four participants reported mild soreness in leg muscles, with symptom remission within 48 h. Participants performed the aerobic exercise at an average intensity of 69.7 % VO_{2max} throughout the program.

No changes were observed in activity limitation measure, the FIM scored from 119.4 ± 5.2 to 120.4 ± 3.9 over the training period. Significant increases were observed in Role-physical (+120 %) and Vitality (+33.8 %) HRQOL indexes. Participants reported a significant decrease in fatigue at the end of the training period registered by means of both the FSS and the FDS (−12.9 %, $p = 0.034$ and −12.2 %, $p = 0.049$, respectively).

Some negligible adjustments were registered in the collected functional and fitness measures; no significant differences were reported in the post versus pre comparison for these variables. Descriptive statistics for all the variables are reported in Table 2.

Cohen's d_z revealed large effects for variables reporting significant changes in post versus pre measures (i.e., large effect was found for fatigue perception scales and the vitality and role-physical subscales of the HRQOL). Although without significance in the t test analysis, a medium-to-large effect size of the intervention was reported for Social functioning index of the HRQOL and the 6MWT ($d_z = 0.73$).

Discussion

Despite the well-established benefits of exercise, people with MS are relatively inactive and face unique barriers to exercise engagement which need to be overcome. The aim of this study was to pilot test a combined aerobic and strength exercise program, including social support in the form of a "partner in exercise". Possible beneficial effects on functional capacity, fatigue sensation, and HRQOL were investigated. We expected improvements in all the dependent measures, as a direct effect of training and as indirect consequences of the social support created by simultaneous practice of two participants. A previous study observed that bringing together persons with MS in a behavioural intervention program enabled patients to benefit significantly

Table 2 Psychological and functional measures before and after the 20-session combined exercise training

	Pre		Post		Cohen's d_z
	Mean	SD	Mean	SD	
SF-36					
Physical functioning	26.88	11.63	38.75	26.15	0.58
Role-physical	31.25	37.20	68.75*	37.20	0.93
Bodily pain	55.5	25.35	78.5	24.74	0.75
General health	36.75	32.28	42.00	29.18	0.47
Vitality	40.63	9.43	54.38*	9.8	1.11
Social functioning	53.13	23.86	71.88	27.35	0.73
Role-emotional	75.00	38.84	91.66	23.58	0.31
Mental health	68.50	14.09	72.5	14.09	0.31
Fatigue Severity Scale	5.90	0.67	5.18*	0.78	0.87
Fatigue Descriptive Scale	10.25	2.12	9.00*	2.14	0.79
6-Minute Walking test (m)	205	114	237	145	0.73
Timed 25-Foot Walking (s)	14	11	13	10	0.24
9-Hole Peg test (s)					
Dominant hand	28	5	28	7	0.03
Non-dominant hand	31	7	30	4	0.41
VO_{2max} (ml/min/kg)	22.6	4.9	24.3	5.5	0.32

* $p < 0.05$ at paired t test; Cohen's d_z calculated according to Rosenthal [30]

from the shared experience and socialization [31]. Significant changes after the combined exercise training were registered for role-physical and vitality subscales of the HRQOL and for the fatigue perception scales. These results confirm and boost previous findings reported for a group-based callisthenic exercise program [32].

Improvement in the vitality index here reported is in agreement with the previous data, where it increased by 46 % over a 4-week aerobic training [33] and seemed to sustain the positive effect of social support.

Fatigue is one of the most frequently experienced symptoms by MS patients. The findings from this study align with the results of the recent review from Heine et al. [10] reporting that mixed training may benefit fatigue by −7.1 points (95 % CI −11.9 to −2.2) on the FSS. The improved scores of both FSS and FDS in our study support the fact that a combined training can represent an effective approach to reduce fatigue symptoms in people with mild to moderate MS.

Participants' peak oxygen consumption values levelled to about 23 mL/min/kg both at pre-training and post-training. This can be compared with values reported in other studies [34], confirming that participants with MS are quite unfit. The absence of changes in aerobic capacity is in accord with the previous findings of short-term interventions [33], but in contrast with those showed over longer intervention period (VO_{2max} increased by 10 % over 15 weeks of aerobic training) [34]. Such differences might be due to the large variability in participants' degree of disability and in the exercise type and dose that is not univocally recommended yet.

Walking deficits can significantly compromise family participation and social and leisure time activities among people with MS. In this study, ambulatory function did not increase over the 20-session training. The T25-FW negligibly changed by 2.10 % confirming results reported in other programs both in the short and in the long term. White et al. [35] found a variation of 2 % after 8 weeks, and Romberg et al. [36] showed a 12 % improvement in T25-FW after 6-month training; however, all are under the known cut-off point for true change in T25-FW (20 %).

Medium-to-large effect size has been reported for the 6MWT; however, the high standard deviation in the measure suggests that the positive result considering the average group level may have been influenced considerably by extreme values of few participants.

Intervention showed no effects on upper extremity function, in fact, the measures reported by 9-HPT are negligible. This suggests that a key factor in effective MS intervention is task-specific training: in our study, the person-tailored protocol was organized as a combined aerobic and strength exercise with no workstation task-oriented towards upper extremity dexterity. Measure of independence also did not change, FIM total score remained substantially the same at post-test, probably because it already presented a ceiling effect at baseline. This result is in line with a previous study with a longer training protocol [37].

Even if promising findings on HRQOL and fatigue perception were registered, when interpreting results of this study limitations should be kept in mind. The limited sample size, the lack of a control group, and lack of a direct measurement of social support let considerations regarding the pilot testing of a combined aerobic and strength training to mainly investigate its feasibility, with attention to peer support developed by exercising in two participants.

Conclusions

This pilot study shows that a short-term training of combined aerobic and strength exercise, may be beneficial for some aspects of psycho-social functioning of persons with MS. Participants' 100 % adherence and absence of worsening symptoms during treatment indicate this, underlining that continuous supervision and support may be crucial in modulating compliance and efficacy within a therapeutic program aimed at the treatment of MS.

The results of this pilot study add to the accumulating body of evidence that moderate intensity combined exercise training can have benefits for people with MS, particularly in reducing fatigue perception, and improve some aspects of HRQOL. Moreover, the findings suggest that partners in exercise could be a feasible and useful strategy to sustain exercise training participation. Further research is required to reinforce results of this pilot study. Evaluating the effects of the program with larger sample size and control condition, with follow-up measures, and among people with more severe disability due to MS, warrants attention in the future research. Moreover, the facility in which MS patients perform the training could affect subjective perceptions; thus, comparison between exercising in a clinical setting or in a gym may be interesting for further investigations that consider psycho-social aspects of exercise in MS.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest relating to the publication of this manuscript.

Ethical statement All procedures performed in studies involving human participants were in accordance with the ethical standards of the University of Padua research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from all individual participants included in the study.

References

1. World Health Organization (2008) Atlas multiple sclerosis resources in the world. WHO Press, Geneva
2. Compston A, Coles A (2008) Multiple sclerosis. Lancet 372:1502–1517
3. Janardhan V, Bakshi R (2000) Quality of life and its relationship to brain lesions and atrophy on magnetic resonance images in 60 patients with multiple sclerosis. Arch Neurol 57:1485–1491
4. Stuv O, Oksenberg J (2006) Multiple sclerosis overview. GENE reviews, pp 1–10
5. Motl RW (2010) Physical activity and irreversible disability in multiple sclerosis. Exerc Sport Sci Rev 38:186–191
6. Motl RW, Arnett PA, Smith MM, Barwick FH, Ahlstrom B, Stover EJ (2008) Worsening of symptoms is associated with lower physical activity levels in individuals with multiple sclerosis. Mult Scler 14:140–142
7. Motl RW, Weikert M, Suh Y, Dlugonski D (2010) Symptom cluster and physical activity in relapsing-remitting multiple sclerosis. Res Nurs Health 33:398–412
8. Mayo NE, Bayley M, Duquette P, Lapierre Y, Anderson R, Bartlett S (2013) The role of exercise in modifying outcomes for people with multiple sclerosis: a randomized trial. BMC Neurol 13(1):1
9. Latimer-Cheung AE, Pilutti LA, Hicks AL, Ginis KAM, Fenuta AM, MacKibbon KA, Motl RW (2013) 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. Arch Phys Med Rehabil 94(9):1800–1828
10. Heine M, van de Port I, Rietberg MB, van Wegen EEH, Kwakkel G (2015) Exercise therapy for fatigue in multiple sclerosis. Cochrane Database Syst Rev 9:CD009956. doi:10.1002/14651858.CD009956.pub2
11. American College of Sports Medicine (2010) ACSM's resources for clinical exercise physiology: musculoskeltal, neuromuscular, neoplastic, immunologic, and hematologic conditions, 2nd edn. Lippincott Williams & Wilkins, Baltimore
12. Canadian Society for Exercise Physiology (2013) Canadian physical activity guidelines for adults with multiple sclerosis. http://www.csep.ca/CMFiles/Guidelines/specialpops/CSEP_MS_PAGuidelines_adults_en.pdf
13. Dalgas U, Ingemann-Hansen T, Stenager E (2009) Physical exercise and MS recommendations. Int MS J 16:5–11
14. Beckerman H, de Groot V, Scholten MA, Kempen JCE, Lankhorst GJ (2010) Physical activity behavior of people with multiple sclerosis: understanding how they can become more physically active. Phys Ther 90:1001–1013
15. Motl RW, McAuley E, Snook EM (2005) Physical activity and multiple sclerosis: a meta-analysis. Mult Scler 11:459–463
16. Learmonth YC, Motl RW (2016) Physical activity and exercise training in multiple sclerosis: a review and content analysis of qualitative research identifying perceived determinants and consequences. Disabil Rehabil 38:1227–1242
17. Christensen ME, Brincks J, Schnieber A, Soerensen D (2015) The intention to exercise and the execution of exercise among persons with multiple sclerosis—a qualitative metasynthesis. Disabil Rehabil 38:1023–1033
18. Kasser S (2009) Exercising with multiple sclerosis: insight into meaning and motivation. Adapt Phys Activ Q 26:274–289
19. Motl RW, McAuley E, Snook EM (2007) Physical activity and quality of life in multiple sclerosis: possible roles of social support, self efficacy, and functional limitations. Rehabil Psychol 52:143–151
20. Poser CM, Paty DW, Scheinberg L, McDonald WI, Davis FA, Ebers GC et al (1983) New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 13(3):227–231
21. Kurtzke JF (1983) Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 33:1444–1452
22. Granger CV, Cotter AC, Hamilton BB, Fiedler RC, Hens MM (1990) Functional assessment scales: a study of persons with multiple sclerosis. Arch Phys Med Rehabil 71(11):870–875
23. Ware JE Jr, Sherbourne CD (1992) The MOS 36-item Short-Form Health Survey (SF-36). I. Conceptual framework and item selection. Med Care 30(6):473–483
24. Nortvedt MW, Riise T, Myhr KM, Nyland HL (1999) Quality of life in multiple sclerosis. Measuring the disease effects more broadly. Neurology 53:1098–1103
25. Krupp LB, La Rocca NG, Muir-Nash J, Steinberg AD (1989) The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematodes. Arch Neurol 46(10):1121–1123
26. Iriarte J, de Castro P (1994) Proposal of a new scale for assessing fatigue in patients with multiple sclerosis. Neurologia 9:96–100
27. Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A et al (2003) The 6-min walk test: a quick measure of functional status in elderly adults. Chest 123(2):387–398
28. Fisher JS, Rudick RA, Cutter GR, Reingold SC, for the National MS Society Clinical Outcomes Assessment Task Force (1999) The multiple sclerosis functional composite measure (MSFC): an integrated approach to MS clinical outcomes assessment. Mult Scler 5:244–250
29. McArdle WD, Katch FI, Katch VL (2001) Exercise physiology: energy, nutrition and human performance, 5th edn. Lippincott Williams & Wilkins, Philadelphia
30. Rosenthal R (1991) Meta-analytic procedures for social research. SAGE Publications, Incorporated, Newbury Park
31. Visschedijk MAJ, Collette EH, Pfennings LEMA, van der Ploeg HM (2004) Development of a cognitive behavioral group intervention programme for patients with multiple sclerosis: an exploratory study. Psychol Rep 95:735–746
32. Pérez CLA, Fernández JADP, Sánchez VM, de Souza Teixeira F (2011) Individuals with multiple sclerosis who participate in a 6-week group exercise programme "show an improvement in their quality of life and fatigue". Sport Sci Health 6(2–3):85–88
33. Mostert S, Kasselring J (2002) Effects of a short-term exercise training program on aerobic fitness, fatigue, health perception and activity level of subjects with multiple sclerosis. Mult Scler 8:161–168
34. Petajan JH, Gappmaier E, White AT, Spencer MK, Mino L, Hicks RW (1996) Impact of aerobic training on fitness and quality of life in multiple sclerosis. Ann Neurol 39:432–441
35. White LJ, McCoy SC, Castellano V, Gutierrez G, Stevens JE, Walter GA et al (2004) Resistance training improves strength and functional capacity in persons with multiple sclerosis. Mult Scler 10:668–674
36. Romberg A, Virtanen A, Ruutiainen J, Aunola S, Karppi S-L, Vaara M et al (2004) Effects of a 6-month exercise program on patients with multiple sclerosis: a randomized study. Neurology 63(11):2034–2038
37. Romberg A, Virtanen A, Ruutiainen J (2005) Long-term exercise improves functional impairment but not quality of life in multiple sclerosis. J Neurol 252:839–845