

Effects of a resistance training program and subsequent detraining on muscle strength and muscle power in multiple sclerosis patients

Carlos Medina-Perez^{a,*}, Fernanda de Souza-Teixeira^b, Rodrigo Fernandez-Gonzalo^c
and Jose Antonio de Paz-Fernandez^a

^a*Institute of Biomedicine (IBIOMED), University of Leon, León, Spain*

^b*School of Physical Education, Department of Physical Education and Health, Federal University of Pelotas, Pelotas/rs, Brazil*

^c*Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden*

Abstract.

BACKGROUND: Although resistance training adaptations in multiple sclerosis (MS) patients have been described, the detraining response in this population is largely unknown.

OBJECTIVE: This study was designed to evaluate the effects of a 12-week detraining period on muscle strength (isometric and endurance) and muscle power of multiple sclerosis (MS) patients that had previously carried out a 12-week resistance training program (RTP).

METHODS: Forty-two MS patients were randomly assigned into two groups: an exercise group (EG) that performed a 12-week RTP for the knee extensors muscles; and a control group (CG), that did not perform any specific training. Knee extension maximal voluntary isometric contraction (MVIC), muscle power and muscle endurance were evaluated before and after the RTP, as well as 12 weeks after training completion. A strain gauge was used to measure the maximal voluntary isometric contraction and muscle power was assessed with a linear encoder. Muscle endurance was interpreted as the number of repetitions that a patient could perform in a single set of knee extension exercise.

RESULTS: The EG increased MVIC and muscle power after the training period, although the training did not affect muscle endurance. After 12 weeks of detraining, MVIC returned to pre-training values but muscle power was still greater than pre-training values in the EG. The CG did not present any change in the variables measured during the intervention.

CONCLUSIONS: A 12-week RTP improved MVIC and muscle power in MS patients. Additionally, 12 weeks of detraining blunted strength training adaptations in MS patients, although muscle power training adaptations were still evident after the detraining period.

Keywords: Multiple sclerosis, exercise rehabilitation, progressive resistance training, detraining, muscle strength, muscle power, lower extremity

1. Introduction

Multiple sclerosis (MS) is a chronic demyelinating central nervous system disease that represents the most common cause of neurological disability in young adults (Sadovnick, 1988). It is characterized by

*Address for correspondence: Carlos Medina-Perez, Institute of Biomedicine (IBIOMED), University of Leon. Campus de Vegazana, PC 24071, Leon, Spain. Tel./Fax: +34 987 293016; E-mail: carlosmedinaper85@gmail.com.

impaired strength and muscle function (Ng, 2004), with a greater impairment of the lower extremities (Lambert, 2001), which decreases the ambulatory capacity of MS patients. This decreased ambulatory capacity ultimately results in a loss of quality of life due to, at least in part, a reduction in physical activity (Cavanaugh, 2011).

Resistance training has been successfully used to counteract functional capacity losses in healthy elderly population, as well as in patients with different musculoskeletal disorders (Fatouros, 2005; Hunter, 2004; Kristensen, 2012). Consequently, several attempts have applied this training paradigm to combat muscle function impairments in MS patients with promising results, indicating that resistance exercise can be used as an effective therapeutic tool to increase muscle performance in this population (Broekmans, 2011; Dodd, 2011; Filipi, 2011; Dalgas, 2009; De Souza-Teixeira, 2009; Robineau, 2005; Debolt, 2004). Thus, 8 to 12 weeks of resistance training increased muscle performance (e.g. maximal strength, endurance, power) and functional capacity in the lower limbs of MS patients (Dodd, 2011; Dalgas, 2009; De Souza-Teixeira, 2009; Debolt, 2004). In addition, resistance exercise decreased fatigue perception (White, 2004) and improved quality of life and mood (Dalgas, 2010a) in MS patients.

However, low maintenance of activity at follow up has been reported in the population with multiple sclerosis (Kayes, 2011). Therefore, is important to know how detraining period affects to MS patients after a training program because it could reduce the training-induced adaptations (Mujika, 2001).

One of the few studies that have analyzed the detraining response in MS patients showed a complete loss of strength gains after 3 months of detraining (Robineau, 2005). Otherwise, after whole body vibration training improvements in functional mobility were still evident 2 weeks after completing 8 weeks of intervention, suggesting but not checking a residual effect of neural adaptations after training in this population (Mason, 2012).

However, data describing the effects of detraining in MS patients after a traditional combined concentric-eccentric resistance training program are very limited. Dalgas (2009) showed that 12 weeks of intense progressive resistance training of the lower extremities lead to improvements of muscle strength and functional capacity in patients with multiple sclerosis and the effects persisting after 12 weeks of “follow up period” (non supervised training). Lately, the cited author reported a similar outcome that previously cited on knee extensor

muscle strength and the research added that maximal neural drive of knee extensors and knee flexors during maximal isometric contractions in MS patients is increased after 12 weeks of resistance training program and neural plasticity is preserved in those patients after a “follow up period” (Dalgas, 2013). This may seem surprising since this information could potentially help to design better training protocols to increase or maintain, muscle function in MS patients.

In healthy subjects detraining usually induces a loss of training adaptations and muscle performance (Mujika, 2001), although the specific responses depend on the detraining period and the frequency, intensity and duration of the training protocol. Additionally, it has been suggested that both age (Toraman, 2005) and subjects’ physical fitness play an important role on detraining responses (Andersen, 2005; Häkkinen, 2000; Henwood, 2008; Izquierdo, 2007; Kalapotharakos, 2010; Tokmakidis, 2009; Bosquet, 2013). For example, resistance-trained men did not lose any strength gains after 6 weeks of detraining (Kraemer, 2002). However, detraining induced a complete loss of strength adaptations in sedentary subjects (Andersen, 2005).

Therefore, this study aimed to evaluate the effects of 12 weeks of detraining following 12 weeks of knee extension resistance training in MS patients. It was hypothesized that functional variables (e.g. maximal strength, muscle power and muscle endurance) would increase after the training intervention. Furthermore, and given that Robineau (2005) showed that strength gains induced by an eccentric training program were completely lost after 3 months of detraining in MS patients, it was also hypothesized that functional variables would decrease to pre-training levels after 12 weeks of detraining.

2. Methods

2.1. Participants

Forty-two relapsing-remitting MS patients (23 women and 19 men) volunteered to participate in the study. All participants were recruited among six MS rehabilitation centers within the region of Castilla y León (Spain). After a group meeting where the details of the investigation were described to the patients, including possible risks and discomfort associated to the intervention, a formal invitation to take part in the study was offered. The patient inclusion criteria included a confirmed disease diagnosis by a neurologist, accord-

Table 1
Demographic data at baseline

	Exercise group (n = 30)	Control group (n = 12)	P-values
Age (yr)	49.6 ± 11.0	46.2 ± 7.5	0.395
Weight (Kg)	68.1 ± 11.4	63.3 ± 12.0	0.177
Height (cm)	165.0 ± 8.3	162.8 ± 6.0	0.485
BMI (Kg/m ²)	25.0 ± 4.1	24.0 ± 4.9	0.200
EDSS	4.5 ± 2.1	4.1 ± 0.5	0.380
Time since diagnosis (yr)	11.3 ± 6.1	12.2 ± 4.5	0.570

Data are given as mean ± SD. P-values: EG vs. CG at baseline. EDSS: Expanded Disability Status Scale.

ing to Mc-Donald criteria (McDonald, 2001); ability to walk (with or without aid) at least 20 m without rest; absence of other diseases that might have affected muscle function. After a medical evaluation that confirmed patients' aptitude and absence of contraindications to carry out the procedures involved in the study, subjects signed a written informed consent form to participate.

Participants were randomly assigned to two different groups, the exercise group (EG) or the control group (CG). The EG, which included 16 women and 14 men (49.6 ± 11.0 yr), performed 12 weeks of resistance training followed by a detraining period where resistance exercise or other structured physical activity was avoided. The CG, which did not follow any resistance training during the study period, included 7 women and 5 men (46.2 ± 7.5 yr). A neurological evaluation assessing the Expanded Disability Status Scale (EDSS; from 0, normal neurological exam, to 10, death caused by MS) ranged the patients between 1 and 6 (EG = 4.5 ± 2.1; CG = 4.1 ± 0.5) (Table 1). None of the patients had previous experience with resistance training.

A 12-week resistance training program similar to the one described in this study was offered to CG after completion of the intervention. The study was approved by the Research Ethics Committee of the University of Leon.

2.2. Study design

The experimental period lasted 24 weeks. During the first 12 weeks, the EG performed a resistance training program for the knee extensors (2 sessions per week), followed by 12 weeks of detraining (e.g. no resistance exercise at all). The CG followed their habitual daily activities during the study period and they did not follow any kind of structured physical activity. Dependent variables included maximal voluntary isometric contraction (MVIC), maximal torque, aver-

Table 2
Progressive resistance training

Weeks	Set 1		Set 2		Set 3	
	Load	reps	Load	reps	Load	reps
1–2	35	10–12	50	8–10	35	10–12
3–4	40	10–12	55	8–10	40	10–12
5–6	45	10–12	60	8–10	45	10–12
7–8	50	10–12	65	8–10	50	10–12
9–10	55	10–12	70	8–10	55	10–12
11–12	55	10–12	70	8–10	55	10–12

Note: Load = percentage of MVIC; reps = repetitions.

age muscle power and muscle endurance. Testing was performed on three different occasions: before (week 0) and after (week 12) the training program, and after the detraining period (week 24). All testing procedures were selected according to previous studies (De Souza-Teixeira, 2009). Regardless disability status, all the subjects involved in the study were able to perform all the tests. Each participant completed the tests in a single session. Subjects were individually informed about the test procedures before initiating them. Firstly, MVIC test was performed and after a 10-minute recovery period average power and muscle endurance tests were carried out. The participants were not familiarized with the testing. Verbal standard encouragement was given throughout both tests in order to maximize motivation.

2.3. Resistance training

Subjects performed coupled concentric-eccentric bilateral seated knee extension training using a weight stack machine (BH[®] Fitness Nevada Pro-T, Spain) twice per week during 12 weeks, with at least 48 h of rest between sessions. After a standardized cycling warm-up, and one set of 5 repetitions (reps) with a light load, participants performed 3 sets of 8–12 reps with a load that was progressively increased from 35 to 70% of MVIC through the training period (Table 2). Recovery time between sets was 3 minutes. Subjects were requested to push with maximal effort during the concentric phase of the movement (90–180°) and to lower the load (eccentric action; 180–90°) in a controlled manner. All training sessions took place in MS rehabilitation centers and the patients were continuously supervised by physical therapists.

2.4. Measurements

Maximal voluntary isometric contraction: MVIC test was performed in the same knee extension device

described for the training program. It consisted of pushing against the fixed lever arm of the knee extension machine as hard as possible for 5 seconds with a knee flexion of 90° under strong verbal encouragement. Before the test, the lever arm of the knee extension machine was aligned with the center of rotation of the knee joint. A strain gauge (Globus Ergometer®, Italy; sample rate 1000 Hz) was placed in between the chains used to fix the lever arm of the machine, to measure the isometric strength of both legs. Data were recorded and analyzed with associated software (Globus Ergo Tester® v1.5, Italy). The tibial pad was individually adjusted proximal to the medial malleolus on the lower extremity for every subject. The distance between the axis of rotation of the knee joint and the tibial pad was measured for all participants, and torque (N·m) was then determined. Each participant performed two attempts interspersed with 3 minutes recovery, and the best attempt was considered for further data analysis.

2.5. Average power

Average power test was also carried out in the knee extension machine described for the training program. Participants were evaluated during a single set to volitional exhaustion with a load corresponding to the 40% of the pre-training MVIC (De Souza-Teixeira, 2009). Subjects were requested to perform the concentric phase of every repetition with a ROM of ~90–180 degrees, as fast as possible, and to lower the load (eccentric action; ~180–90°) in a control manner. The test was discontinued when the participant could not perform two consecutive repetitions over 75% of the target ROM. A linear encoder (Globus Real Power®, Italy; sample rate 300 Hz) adapted to the machine was used to measure the displacement of the load-plates across the knee’s range of movement (90° to 180°), and associated software (Globus Real Power® v3.11, Italy) was used to control for successful trials and to calculate average power for every repetition. Average power from

the first five repetitions was considered for further data analysis.

2.6. Muscle endurance

Muscle endurance data were obtained in the same set to volitional exhaustion described for the average power test. Thus, muscle endurance was interpreted as the maximal number of repetitions that a patient could perform in a single set of knee extension exercise with a load corresponding to the 40% of MVIC.

2.7. Statistical analysis

Data were analyzed using SPSS®17.0 (SPSS Inc., USA). Results are presented as mean ± standard deviation (SD). Shapiro-Wilk normality test was used to assess normal data distribution. To assess any training or detraining effect, as well as any difference between groups, MVIC, torque, average power and muscle endurance raw values were examined using two-way ANOVA with repeated measurements for group and time. Significant interactions and main effects were further analyzed using Bonferroni *post-hoc* comparisons. The level of significance was set at *P* < 0.05.

3. Results

All subjects taking part in the study (*n* = 42) completed all the scheduled testing protocols. Adherence to the training intervention (e.g. EG) averaged 22.9 ± 1.5 sessions from a total of 24 planned sessions. All participants from the EG completed more than 75% of the sessions included in the resistance training program. Missing sessions were caused by medical examination (*n* = 5), side effects of drugs (*n* = 3) and injuries not related to the training sessions (*n* = 2). No adverse effects or health problems attributable to the testing and training sessions from the present investigation were

Table 3
Muscular performance at baseline, week-12 and week-24

	Exercise group			Control group		
	Baseline	Week-12	Week-24	Baseline	Week-12	Week-24
MVIC (N)	754 ± 235	811 ± 283 ^{#¥}	755 ± 234 ^{§¥}	615 ± 109	606 ± 116	604 ± 126
Torque (N.m)	300 ± 106	323 ± 127 ^{#¥}	300 ± 107 ^{§¥}	238 ± 41	235 ± 45	234 ± 46
Power (W)	173 ± 72	200 ± 80 ^{#¥}	193 ± 78 [#]	149 ± 34	148 ± 29	155 ± 43
Endurance (reps)	21 ± 5	22 ± 7	20 ± 5	18 ± 4	19 ± 5	19 ± 5

Data are given as mean ± SD. #: Denotes difference to baseline within a group. §: Denotes week-12 to week-24 difference within a group. ¥: Denotes exercise group to control group difference.

noted. No differences in descriptive characteristics were found between groups.

The EG improved MVIC ($P=0.004$), torque ($P=0.004$) and average power ($P<0.001$) after the resistance training period (Table 3). Furthermore, the EG presented greater MVIC ($P=0.02$), torque ($P=0.025$) and average power ($P=0.035$) than CG after the training period. No significant changes in muscle endurance were found within or between groups. All variables remained unchanged in CG after the training period (Table 3).

The detraining period reduced MVIC ($P=0.014$) and torque ($P=0.014$) in the EG, although these values were still higher than those achieved by the CG ($P=0.042$ for MVIC, and $P=0.046$ for torque). However, average power did not decrease after detraining in the EG, remaining significantly higher than the values obtained before training ($P=0.001$). The CG did not show any significant change in any measurement after the detraining period.

4. Discussion

This study was designed to assess detraining functional responses in MS patients that had previously performed a 12-week resistance training program. The resistance training protocol improved maximal strength and muscle power, but not muscle endurance. However, the main finding of the present investigation was that muscle power training adaptations were maintained after 12 weeks of detraining in MS patients. Although the increase in strength and power after a resistance training program has been already shown in MS patients (Broekmans, 2011; Filipi, 2011; Dalgas, 2009; De Souza-Teixeira, 2009; Debolt, 2004), this is the first investigation describing the detraining response in this population after coupled concentric-eccentric resistance training.

The maximal strength gains found in the EG after training support data from previous studies with MS patients (Dalgas, 2013; Broekmans, 2011; Filipi, 2011; Dalgas, 2009; De Souza-Teixeira, 2009). Although this study was not designed to assess the factors behind the strength increments induced by the resistance training in MS patients, they are often attributed to neural adaptations, rather than to an increase in muscle mass (Dalgas, 2013; Broekmans, 2011; Dalgas, 2010 b; De Souza-Teixeira, 2009).

After detraining, maximal strength returned to pre-training values in the EG. Dalgas reported knee

extensors MVIC did not differ significantly from pre-training values after 12 weeks of self-guided physical activity (Dalgas, 2013). In contrast, same author found preserved MVIC in MS patients after 12 weeks of self-guided physical activity (Dalgas, 2009). In that research, they argued that the effect could be maintained partly due to a more active lifestyle in the exercise group during self-guided physical activity -follow up period- (Dalgas, 2009). However, is important to note that it did not involve a complete cessation of exercise by some patients, which may explain the different results. In healthy population, several studies showed that detraining after resistance training triggered a decrease in maximal dynamic strength (1RM) in both, middle age and older adults (Pereira, 2012; Kalapotharakos, 2010; Harris, 2007). A recent review showed that decrease in maximal force after detraining became significant from the third week of inactivity (Bosquet, 2013). According to data published by Hakkinen (Hakkinen, 2000; Hakkinen, 1983) it is hypothesize that central and peripheral adaptations involved in training process could decrease during detraining period (Bosquet, 2013). Also, differences in maintenance of training induced strength gains after a detraining period are likely to be related to training mode. Thus, it has been proposed that strength gains induced by high-intensity resistance training are better preserved than gains associated to middle-to-low intensity training (Tokmakidis, 2009; Hunter, 2004), which may be the case of the present investigation.

The EG improved average power after the training protocol. These data support previous investigations from our group (De Souza-Teixeira, 2009), that showed increased peak power values in MS patients after a resistance training program. Since several studies have failed to show a clear relationship between the increments in muscle cross sectional area and power gains in MS patients (Dalgas, 2010b; De Souza-Teixeira, 2009), power adaptations after resistance training are often associated to neural mechanisms. However, the muscle power increments described in the present study are smaller than those described in healthy population (Henwood, 2008). Several factors including neural and muscular impairments caused by the MS disease (Kent-Braun, 2004), such as important strength deficits during dynamic muscle action (Chung, 2008), may account for these differences. Despite the magnitude of the adaptations, the power increments found in the EG may positively affect every-day tasks such as rising from a chair or climbing stairs (Pereira, 2012; Caserotti, 2008), improving the quality of life of MS patients.

The most surprising and novel finding of the present investigation was that MS patients were able to preserve, at least for 12 weeks, the power training adaptations. These results resemble data from previous studies where power gains following a training period were maintained by healthy elderly subjects (Pereira, 2012; Toraman, 2005) or recreationally-trained population (Kraemer, 2002). In contrast, detraining led to a significant loss of power in trained subjects (Izquierdo, 2007). Considering available data, daily living activities such as walking or standing may represent a stimulus strong enough to preserve power gains following resistance training in weak or untrained subject (Hennwood, 2008; Harris, 2007), including the MS patients from the present investigation, while it would not be enough to maintain such adaptations in trained individuals. Given the limitations of the present investigation, it is difficult to elucidate the mechanisms behind the power response after detraining. However, it is tempting to hypothesize that neuromuscular adaptations induced by the training protocol played a key role in this response (Häkkinen, 2000). Although studies regarding neuromuscular adaptations in MS patients are scarce (Kjølhede, 2012), it has been showed that resistance training increased the maximal neural drive in lower limb muscles (Dalgas, 2013; Fimland, 2010) and the effect persisted after 12 weeks of self-guided physical activity (Dalgas, 2013), so that, the neural plasticity in response to resistance training may be preserved in MS patients (Dalgas, 2013). Therefore this finding may help to explain the preserved training-induced power gains after detraining described in the present study.

Studies assessing healthy population (Lexell, 1995; Kannus, 1992) can also contribute to explain our data. Thus, a more efficient patten of motor unit recruitment, a more economical use of motor units, a reduction of the inhibitory inputs to the alpha motor neurons (Kannus, 1992) or the recruitment of fast twitch fibers of the trained muscles (Lexell, 1995) induced by the training program may have persisted after the detraining period (Pereira, 2012).

However, further research is warranted to specifically assess the physiological mechanisms that control detraining responses in MS patients. Despite the lack of a solid explanation for the findings herein described, it can be summarized that the resistance training paradigm used in the present investigation induced a preservation of power training adaptations but not other functional capacities (e.g. MVIC). Consequently, it is according to similar findings reported in healthy population (Pereira, 2012; Bosquet, 2013).

Since muscle power has been defined as an adequate predictor of functional independence in frail elderly people (Reid, 2008), the preservation of power performance during detraining may contribute to maintain functional capacity even after cessation of training. Therefore, this finding supports the effectiveness of resistance training as a therapeutic intervention for MS patients, since it may overcome, at least partly, the voluntary or enforced training disruptions in the training schedule.

Muscle endurance did not change in the EG throughout the intervention in the present study. In contrast, De Souza-Teixeira found that muscle endurance increased 84% after an 8-week resistance training period in thirteen MS patients (De Souza-Teixeira, 2009). Despite the lack of studies about this topic in MS population and a certain explanation of this phenomenon in previously research, we hypothesize that these discrepancies may be a result of the smaller and homogeneous simple size recruited by De Souza-Teixeira, the specific response at resistance training or/and the inter-subject variability commonly seen in MS patients (e.g. fatigue). Moreover, studies in healthy population can lead to physiological factors related to oxygen transport an energy production, which are involved in submaximal strength adaptation (Bosquet, 2013). Therefore, since similar training interventions may induce divergent adaptations in MS patients, it is crucial to adapt the resistance training protocol to the specific MS population to obtain the expected outcomes.

5. Limitations

There are several issues that might have limited our findings. First, the small sample size used. It would have been desirable to provide a larger control group, which would have had the same number of patients as the experimental group. Second, some patients did not complete all training sessions. Third, all participants were recruited among MS rehabilitation centers and they may not represent all MS patients, in particular those who are physically independent or who are severely impaired MS disease. Finally, the participants were not blinded to the intervention.

Future studies should address the precise physiological and neurological components responsible for response in muscular strength from detraining and discuss the effects based on duration of training cessation, age or training status in this population.

6. Conclusion

A resistance training protocol of 12 weeks increased maximal strength and power in a group of MS patients. However, it did not induce any change in muscle endurance. Additionally, this is the first study describing the detraining responses of MS patients after coupled concentric-eccentric resistance training. Data showed that 12 weeks of detraining were enough to reduce maximal strength to pre-training levels, although power gains were preserved. The present findings support the use of resistance exercise in MS patients.

Acknowledgments

The authors are grateful to all the patients for their participation in the study. This study was supported by a grant from the “Consejería de Sanidad y Consumo”. Government of Castilla y León (Spain).

Declaration of interest

The authors have no affiliation with any organization with a financial interest, direct or indirect in the subject matter or materials discussed in the manuscript. There is no conflict of interest between the authors of the publication.

References

- Andersen, L. L., Andersen, J. L., Magnusson, S. P., Suetta, C., Madsen, J. L., Christensen, L. R., & Aagaard, P. (2005). Changes in the human muscle force-velocity relationship in response to resistance training and subsequent detraining. *Journal of Applied Physiology*, *99*, 87–94.
- Bosquet, L., Berryman, N., Dupuy, O., Mekary, S., Arvisais, D., Bherer, L., & Mujika, I. (2013). Effect of training cessation on muscular performance: A meta-analysis. *Scandinavian Journal of Medicine & Science in Sports*, *23*, 140–149.
- Broekmans, T., Roelants, M., Feys, P., Alders, G., Gijbels, D., Hanssen, I., Stinissen, P., & Eijnde, B. O. (2011). Effects of long-term resistance training and simultaneous electro-stimulation on muscle strength and functional mobility in multiple sclerosis. *Multiple Sclerosis*, *17*, 468–477.
- Caserotti, P., Aagaard, P., Larsen, J. B., & Puggaard, L. (2008). Explosive heavy-resistance training in old and very old adults: Changes in rapid muscle force, strength and power. *Scandinavian Journal of Medicine & Science in Sports*, *18*, 773–782.
- Cavanaugh, J. T., Gappmaier, V. O., Dibble, L. E., & Gappmaier, E. (2011). Ambulatory activity in individuals with multiple sclerosis. *Journal of Neurologic Physical Therapy*, *35*, 26–33.
- Chung, L. H., Remelius, J. G., Van Emmerik, R. E., & Kent-Braun, J. A. (2008). Leg power asymmetry and postural control in women with multiple sclerosis. *Medicine & Science in Sports & Exercise*, *40*, 1717–1724.
- Dalgas, U., Stenager, E., Jakobsen, J., Petersen, T., Hansen, H. J., Knudsen, C., Overgaard, K., & Ingemann-Hansen, T. (2009). Resistance training improves muscle strength and functional capacity in multiple sclerosis. *Neurology*, *73*, 1478–1484.
- Dalgas, U., Stenager, E., Jakobsen, J., Petersen, T., Hansen, H. J., Knudsen, C., Overgaard, K., & Ingemann-Hansen, T. (2010a). Fatigue, mood and quality of life improve in MS patients after progressive resistance training. *Multiple Sclerosis*, *16*, 480–490.
- Dalgas, U., Stenager, E., Jakobsen, J., Petersen, T., Overgaard, K., & Ingemann-Hansen, T. (2010b). Muscle fiber size increases following resistance training in multiple sclerosis. *Multiple Sclerosis*, *16*, 1367–1376.
- Dalgas, U., Stenager, E., Lund, C., Rasmussen, C., Petersen, T., Sørensen, H., Ingemann-Hansen, T., & Overgaard, K. (2013). Neural drive increases following resistance training in patients with multiple sclerosis. *Journal of Neurology*, *260*, 1822–1832.
- De Souza-Teixeira, F., Costilla, S., Ayán, C., García-López, D., González-Gallego, J., & de Paz, J. A. (2009). Effects of resistance training in multiple sclerosis. *International Journal of Sports Medicine*, *30*, 245–250.
- Debolt, L. S., & Mccubbin, J. A. (2004). The effects of home-based resistance exercise on balance, power, and mobility in adults with multiple sclerosis. *Archives of Physical Medicine and Rehabilitation*, *85*, 290–297.
- Dodd, K. J., Taylor, N. F., Shields, N., Prasad, D., McDonald, E., & Gillon, A. (2011). Progressive resistance training did not improve walking but can improve muscle performance, quality of life and fatigue in adults with multiple sclerosis: A randomized controlled trial. *Multiple Sclerosis*, *17*, 1362–1374.
- Fatouros, I. G., Kambas, A., Katrabasas, I., Nikolaidis, K., Chatzinikolaou, A., Leontsini, D., & Taxildaris, K. (2005). Strength training and detraining effects on muscular strength, anaerobic power, and mobility of inactive older men are intensity dependent. *British Journal of Sports Medicine*, *39*, 776–780.
- Filipi, M. L., Kucera, D. L., Filipi, E. O., Ridpath, A. C., & Leuschen, M. P. (2011). Improvement in strength following resistance training in MS patients despite varied disability levels. *NeuroRehabilitation*, *28*, 373–382.
- Häkkinen, K., Alen, M., Kallinen, M., Newton, R. U., & Kraemer, W. J. (2000). Neuromuscular adaptation during prolonged strength training, detraining and re-strength-training in middle-aged and elderly people. *European Journal of Applied Physiology*, *83*, 51–62.
- Harris, C., DeBeliso, M., Adams, K. J., Irmischer, B. S., & Spitzer-Gibson, T. A. (2007). Detraining in the older adult: Effects of prior training intensity on strength retention. *The Journal of Strength & Conditioning Research*, *21*, 813–818.
- Henwood, T. R., Riek, S., & Taaffe, D. R. (2008). Strength versus muscle power-specific resistance training in community-dwelling older adults. *Journal of Gerontology, Serie A: Biological Sciences and Medical Sciences*, *63*, 83–91.
- Henwood, T. R., & Taaffe, D. R. (2008). Detraining and retraining in older adults following long-term muscle power or muscle strength specific training. *Journal of Gerontology, Serie A: Biological Sciences and Medical Sciences*, *63*, 751–758.

- Hunter, G. R., Maccarthy, J. P., & Bamman, M. M. (2004). Effects of resistance training on older adults. *Sports Medicine*, *34*, 329–348.
- Izquierdo, M., Ibañez, J., González-Badillo, J.J., Ratamess, N.A., Kraemer, W.J., Häkkinen, K., Bonnbau, H., Granados, C., French, D.N., & Gorostiaga, E.M. (2007). Detraining and tapering effects on hormonal responses and strength performance. *The Journal of Strength & Conditioning Research*, *21*, 768–775.
- Kalapotharakos, V. I., Diamantopoulos, K., & Tokmakidis, S. P. (2010). Effects of resistance training and detraining on muscle strength and functional performance of older adults aged 80 to 88 years. *Aging Clinical and Experimental Research*, *22*, 134–140.
- Kannus, P., Alosa, D., Cook, L., Johnson, R. J., Renström, P., Pope, M., Beynon, B., Yasuda, K., Nichols, C., & Kaplan, M. (1992). Effect of one-legged exercise on the strength, power and endurance of the contralateral leg. A randomized, controlled study using isometric and concentric isokinetic training. *European Journal of Applied Physiology and Occupational Physiology*, *64*, 117–126.
- Kayes, N. M., McPherson, K. M., Taylor, D., Schlüter, P. J., & Kolt, G. S. (2011). Facilitators and barriers to engagement in physical activity for people with multiple sclerosis: A qualitative investigation. *Disability and Rehabilitation*, *33*, 625–642.
- Kent-Braun, J. A., Ng, A. V., Castro, M., Weiner, M. W., Gelinias, D., Dudley, G. A., & Miller, R. G. (1997). Strength, skeletal muscle composition, and enzyme activity in multiple sclerosis. *Journal of Applied Physiology*, *83*, 1998–2004.
- Kjølhede, T., Vissing, K., & Dalgas, U. (2012) Multiple sclerosis and progressive resistance training – a systematic review. *Multiple Sclerosis*, *18*, 1215–1228.
- Kraemer, W. J., Koziris, L. P., Ratamess, N. A., Häkkinen, K., Fry, A. C., Gordon, S. E., Volek, J. S., French, D. N., Rubin, M. R., Gomez, A. L., Sharman, M. J., Michael, J., Izquierdo, M., Newton, R. U., & Fleck, S. J. (2002). Detraining produces minimal changes in physical performance and hormonal variables in recreationally strength-trained men. *The Journal of Strength & Conditioning Research*, *16*, 373–382.
- Kristensen, J., & Franklyn-Miller, A. (2012). Resistance training in musculoskeletal rehabilitation: A literature review. *British Journal of Sports Medicine*, *46*, 719–726.
- Lambert, C. P., Archer, R. L., & Evans, W. J. (2001). Muscle strength and fatigue during isokinetic exercise in individuals with multiple sclerosis. *Medicine & Science in Sports & Exercise*, *33*, 1613–1619.
- Lexell, J. (1995). Human aging, muscle mass, and fiber type composition. *Journal of Gerontology, Serie A: Biological Sciences and Medical Sciences*, *50* Spec No, 11–16.
- Mason, R. R., Cochrane, D. J., Denny, G. J., Firth, E. C., & Stannard, S. R. (2012). Is 8 weeks of side-alternating whole-body vibration a safe and acceptable modality to improve functional performance in multiple sclerosis? *Disability Rehabilitation*, *34*, 647–654.
- McDonald, W. I., Compston, A., & Edan, G. (2001). Recommended diagnostic criteria for multiple sclerosis: Guidelines from the International Panel on the Diagnosis of Multiple Sclerosis. *Annals of Neurology*, *50*, 121–127.
- Mujika, I., & Padilla, S. (2001). Muscular characteristics of detraining in humans. *Medicine & Science in Sports & Exercise*, *33*, 1297–1303.
- Ng, A. V., Miller, R. G., Gelinias, D., & Kent-Braun, J. A. (2004). Functional relationships of central and peripheral muscle alterations in multiple sclerosis. *Muscle & Nerve*, *29*, 843–852.
- Pereira, A., Izquierdo, M., Silva, A. J., Costa, A. M., González-Badillo, J. J., & Marques, M. C. (2012). Muscle performance and functional capacity retention in older women after high-speed power training cessation. *Experimental Gerontology*, *47*, 620–624.
- Reid, K. F., Callahan, D. M., Carabello, R. J., Phillips, E. M., Frontera, W. R., & Fielding, R. A. (2008). Lower extremity power training in elderly subjects with mobility limitations: A randomized controlled trial. *Aging Clinical and Experimental Research*, *20*, 337–343.
- Robineau, S., Nicolas, B., Gallien, P., Petrilli, S., Durufle, A., Edan, G., & Rochcongar, P. (2005). Renforcement musculaire isocinétique excentrique des ischiojambiers chez des patients de sclérose en plaque. *Annales de Réadaptation et de Médecine Physique*, *48*, 29–33.
- Sadovnick, A. D., Baird, P. A., & Ward, R. H. (1988). Multiple sclerosis: Updated risks for relatives. *American Journal of Medical Genetics*, *29*, 533–541.
- Tokmakidis, S. P., Kalapotharakos, V. I., Smilios, I., & Parlavantzas, A. (2009). Effects of detraining on muscle strength and mass after high or moderate intensity of resistance training in older adults. *Clinical Physiology and Functional Imaging*, *29*, 316–319.
- Toraman, N. F., & Ayceman, N. (2005). Effects of six weeks of detraining on retention of functional fitness of old people after nine weeks of multicomponent training. *British Journal of Sports Medicine*, *39*, 565–568.
- White, L. J., McCoy, S. C., Castellano, V., Gutierrez, G., Stevens, J. E., Walter, G. A., & Vandenberg, K. (2004). Resistance training improves strength and functional capacity in persons with multiple sclerosis. *Multiple Sclerosis*, *10*, 668–674.