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Effects of strength training in people with multiple sclerosis: literary review

Cadilla-Acevedo Tecla María[1] | González-González Yoana[1] | Alonso-Calvete Alejandra[1,2] | Da Cuña-Carrera Iria[1]

1. College of Physiotherapy, University of Vigo. Campus A Xunqueira s/n 36005, Pontevedra, Spain.
2. Research Team in Performance and Motor Functions of Rescue and Lifesaving. College of Education and Sports Sciences. University of Vigo. Campus A Xunqueira s/n 36005, Pontevedra, Spain.

Correspondence

Alejandra Alonso Calvete.
College of Physiotherapy. University of Vigo. Campus A Xunqueira s/n 36005, Pontevedra, Spain.

alejalonso@uvigo.es

Abstract

Introduction: Multiple sclerosis (MS) is the most common cause of non-traumatic neurological disability in young people. Its rehabilitation treatment focuses on improving symptoms and restoring functionality. Muscle strength training has been studied recently as a rehabilitation method, simultaneously with balance exercises, and improvement of gait and coordination. The objective of this review is to analyze the application of these training programs in subjects with MS.
Methods: In February 2020, the CINAHL and Medline databases were consulted using the MeSH descriptors "multiple sclerosis" and "resistance training". The search retrieved 89 results; 17 of which fitted the review objective and were analyzed.
Results: The effects of isolated strength training programs were analyzed using high-intensity continuous or interval aerobic protocols, with increases in workload or progressive resistance, as well as suspension training (TRX), resistance training with body weight, hatha yoga, and its combination with cardiovascular exercise, self-guided physical activity, neuromuscular electrostimulation, functional training or functional gait training. The variables of strength and neuromuscular function (spasticity, proprioception), functionality (mobility, motor capacity, balance, fatigue and fatigability), metabolic parameters (glucose tolerance, brain-derived neurotrophic factor (BDNF), sphingosine-1-phosphate (S1P), body composition, cortisol and DHEA, inflammatory mediators, immunomodulatory markers, aerobic capacity, and parameters such as quality of life, satisfaction, adherence and participation.
Conclusions: Strength training protocols, used alone or combined with other methods, improve muscle strength and gait functionality in subjects with MS, as well as their metabolic parameters. However, its involvement in the regulation of neuroprotective factors has not been demonstrated.

Keywords: *Multiple Sclerosis. Strength Training. Physiotherapy. Rehabilitation. Neurological disease.*

Introduction

Multiple sclerosis (MS) is classified as a demyelinating, chronic, autoimmune and inflammatory pathology,[1–12] with an unregulated evolution that complicates rehabilitation treatment.[4] Its affectation directly involves the axons of the central nervous system (CNS),[12,13] which leads to the loss of the myelin that sheath it and affecting neuronal continuity,[5] covering the affected area with scar tissue that produces sclerotic plaques.[1–5] Some patients register a single outbreak, however, this can be multiple and cumulative, which generates a progressive physical disability[1–5,7,14–19] that affects them functionally both at the motor and sensory levels, which has repercussions on fatigue and pain levels that influence their autonomy.[20]

MS is identified as the most frequent cause of non-traumatic neurological disability in the young population,[1–5,7,9,21-23] being predominant in women, with a proportion that varies between 2:1 and 3:1.[1 ,2,5,7,19,21,22]

The etiology of MS is not clear,[9,21] despite there is scientific consensus that relates it to genetic and environmental factors, in addition to risk factors such as smoking and vitamin D deficiency,[1,7,19,24-26] as well as viral causes,[5,7,24] such as the Epstein-Barr virus.[1,5,19] Regarding environmental factors, these cause the growth of autoreactive T cells that, after a few decades of latency , are activated by a systemic or local factor.[1,2,5,26]

As it is a disease with no cure, treatment focuses on reducing the frequency, severity and duration of relapses, improving symptoms and restoring functionality.[1,8–13,21,23,27–35] Physiotherapy, a multidisciplinary perspective, focuses on working on spasticity and muscle weakness[9,17,33,36] through muscle training that improves both[17] through balance, gait, strength and body skill exercises,[8–13,15,16,21,23,27–35,37,38] either isolated or combined.[8,32–34,38] Following this context, the objective of this literature review is to analyze the application of strength training programs in subjects with MS.

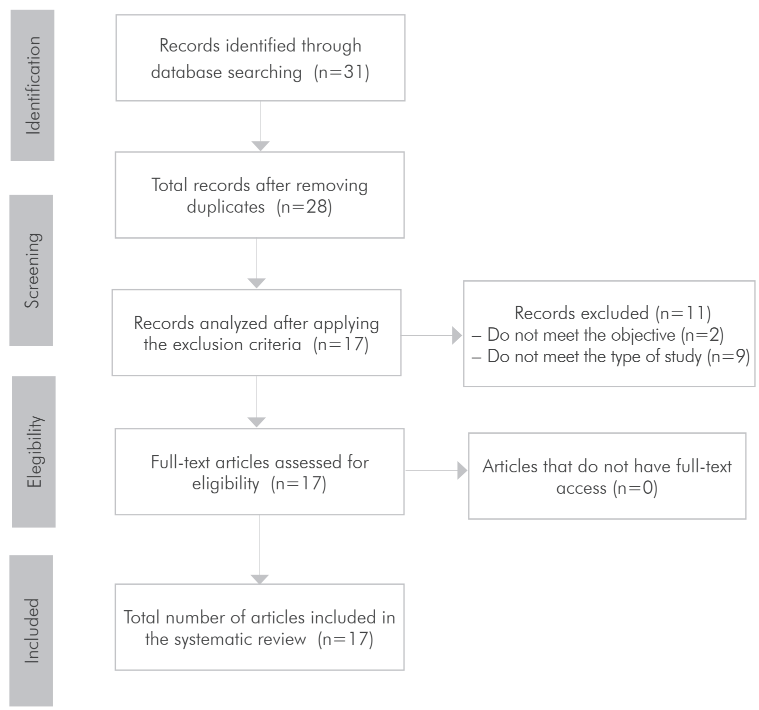
Material and methods

A literature search was conducted in February 2020 for recently published studies examining resistance training in people with MS.

The Medline and CINAHL databases were consulted, using the MeSH terms "multiple sclerosis" and "resistance training", as well as a variation of the term -- "muscle strengthening" -- in CINAHL.

As inclusion criteria, publications in English or Spanish from the last 5 years were selected, excluding those that did not fully analyze the effects of the application of strength training programs in subjects with MS. 89 results were obtained which, after applying the selection criteria and omitting three repeated results, constituted a sample with a total of 17 studies. See Figure 1.

Figure 1. Flow chart according to Prisma guidelines (2009)



Results

We analyzed the effects of isolated resistance training programs using high-intensity continuous or interval aerobic protocols, with increases in workload or progressive resistance, suspension training (TRX), body-weight resistance training, hatha yoga, and its combination with cardiovascular exercise, self-guided physical activity, neuromuscular electrostimulation, functional training or functional gait training. The variables of strength and neuromuscular function (spasticity, proprioception), functionality (mobility, motor capacity, balance, fatigue), metabolic parameters (glucose tolerance, brain-derived neurotrophic factor (BDNF), sphingosine-1-phosphate (S1P), body composition, cortisol and DHEA, inflammatory mediators, immunomodulatory markers, aerobic capacity, and other parameters such as quality of life, satisfaction, adherence and participation.

Tables 1 and 2 show the results of randomized controlled trials and quasi-experimental studies.

Discussion

All the studies analyzed examine the effects of resistance training programs in subjects with multiple sclerosis. Considering the methodological design, a distinction is made between randomized controlled trials (RCT) and quasi-experimental studies. Interventions are based on the application of a strength improvement program, either alone or in combination with other techniques.

RCTs with an isolated strength training intervention

The most used intervention was the application of a muscle strength training protocol with increases in workload or conventional progressive resistance work.[10,13,21,32]

Table 1. Results of randomized controlled studies

Author	Sample Age	Experimental group / Control group	Duration and Frequency	Variables and measurement instruments	Improvements (↑) Differences between groups (GE-GC)
Isolated strength training application					
Hosseini et al.[21]	26 subjects 15W/12M 32 y/o	Strength G: weight(25-30min) Yoga G: 60-70 min CG: usual activity	8 weeks 3 TW	-Extensor strength BLE (1RM) -Motor capacity (10MTW) -Balance (eyes open, closed, and monopodal support)	↑S en FG>YG>CG Motor capacity ↑ Monopodal support balance ↑
Aidar et al.[13]	23 subjects 15W/8M 43 y/o	EG: Progressive Strenght Training GC: Sedentary	12 weeks 3 TW	BLE function: TUG -BLE strength: T25FWT and Sit to stand test -Balance and fall risk: BBS	EG-CG in TUG, T25FWT, up and go test and BBS
Wens et al.[32]	41 subjects 22W/12M 46 y/o	EG: Progressive strength training CG: Sedentary HG: Healthy group	24 weeks 2-3 TW	-BDNF -S, exercise tolerance, body composition	BDNF: EG: ↑13,9%-8,8% / CG: ↓10,5%-4,1% S, exercise tolerance and body composition CG=EG
Jørgensen et al.[10]	30 subjects 22W/8M 44 y/o	EG: High intensity progressive resistance training CG: Usual activity	24 weeks 2 TW	-BDNF y S1P (análisis agudo y crónico) -Función y actividad neuromuscular Flex y Ext rodilla (MCV dinamómetro isocinético y EMG.	BDNF o S1P no cambios GE-GC: actividad neuromuscular y la fuerza muscular mejoró más en GE
Wens et al. [8]	34 subjects 15W/8M 45 y/o	HIIT G HIACT G CG: Sedentary	12 weeks 2-3 TW	-Glucose tolerance: oral test - Skeletal muscle: vastus lateralis biopsy	Glucose ↑ HIIT G and HIACT G Insulin and GLUT4 ↑ HIIT G
Brændvik et al.[31]	26 subjects 17W/9M 48 y/o	EG: Treadmill CG: Strength training	12 weeks 3TW	-Functional walk (GAITRite walkway) -Walking economy and balance (accelerometer)	Treadmill G > S training G Gait functionality, walking economy and balance
Moghadasi et al.[29]	34 subjects - 36 y/o	EG: Full body suspension training CG: Usual activity	8 weeks 3 TW 30 min	-Mobility (TUG, 2MTW, 10MWT and 5STS) -Propioception and knee S flex-Ext (isokinetic dynamometer)	↑:EG TUG, 2MTW, 10MWT and 5STS EG-CG: Non dominant LL propioception EG-CG: ↑ Knee Ext and reflexes on both lower extremities
Combined strength training application					
Deckx et al.[23]	45 subjects 26W/19M 48 y/o	EG: cardiovascular exercise + Progressive strength and resistance training CG: Sedentary subjects	12 weeks 2-3 TW	-Cortisol and DHEA -Inflammatory mediators -Inmunomodulatory markers: blood analysis	EG-CG in ↓inflammatory mediators and ↑ inmunomodulatory markers
Kjølhede et al.[11]	29 subjects - 43 y/o	EG: Progressive strength and resistance training + self guided physical activity CG: Usual activity	24 weeks 2-3 TW + 24 weeks follow-up	--Walking performance (T25FWT, 2MWT, 5STS, stair-climbing test y MSWS-12) -Neuromuscular knee function Ext and Flex (S isometric isokinetic dynamometer, EMG and thigh perimeter: MRI)	EG-CG: ↑Walking performance: T25FWT, 2MWT, 5STS, stair-climbing test, MSWS-12 an neuromuscular function
Coote et al.[30]	25 subjects 17W/8M 52 y/o	EG: Progressive resistance training + NMES CG: Progressive resistance training	12 weeks 2-3 TW	-Hip S Ext and knee S: dynamometer -Spasticity (nm VAS) -Function: BBS, TUG, MSWS-12MS, MSIS-29v2, MFIS -ENM device usability (questionnaire)	CG-EG: MFIS EG: ↑S quadriceps, balance, MSIS-29v2 and MFIS highly usable device

HIIT: high intensity interval training, HIACT: high intensity aerobic continuous training, BBS: Berg balance scale, BDNF: brain-derived neurotrophic factor, T: training, ECW: energy cost of walking, EMG: electromyography, ESES: Exercise Self-Efficacy Scale, NMES: neuromuscular electrical stimulation, Ext: extension, S: Strength, FSMC: fatigue scale for motor and cognitive functions, Flex: flexion, CG: control group, EG: experimental group , GLUT4: glucose transporter type 4, M: man, W: woman, LE: lower extremity, BLE: bilateral lower extremities, MVC: maximal voluntary contraction, MFIS: modified fatigue impact scale, MSIS-29v2: 29-item multiple sclerosis impact scale version 2, MSWS-12MS: 12-item multiple sclerosis walking scale, MRI: magnetic resonance imaging, S1P: sphingosine-1-phosphate, T: test, TUG: timed up and go test, T25-FW: timed 25-foot walk test, TW: times per week, 1RM: 1 repetition maximum test, 2MWT: 2 minutes walk test, 5XSST: 5 times sit to stand test, 6MWT: 6 minutes walk test, 10MWT: 10 meter walk test.

Table 2. Results of quasi-experimental studies

Author	Sample Age	Intervention Training	Duration and Frecuency	Variables and measurement instruments	Improvements (↑) Differences between groups (EG-CG)
Patrocinio Oliveira et al.[9]	52 33W/19M 48 y/o	EG: eccentric S CG: resistance S ↑ load (according place of residence)	12 weeks 2 TW	-Knee Ext S: maximum isometric contraction and 1RM -TUG and CST	EG and CG ↑ S, 1RM, TUG Y CST EG-CG: no differences
Zaenker et al.[33]	26 19W/7M 44 y/o	High intensity training + resistance S with weight G1 and G2 (EDSS 0-3 y 3,5-5)	12 weeks 2 TW	-Aerobic capacity: VO2 Max, maximum tolerated and lactatos -Quadriceps and hamstrings isokinetic strength -Quality of life	G1 and G2: VO2 Max, maximum tolerated ↑ Quadriceps and hamstrings isokinetic strength ↑ Quality of life↑ Women> ↑ Men
Heine et al.[12]	10 6W/3M 49 y/o	CG: healthy subjects EG: subjects with MS: resistance training + walking	16 weeks 3 TW	-Ankle thrust (dynamometer) -Muscular, cardiopulmonary and self-report tests - Gait functionality (3D analysis and 10MWT) -Energy Consumption (ECW) -MFIS, FSMC, MSWS-12 and ESES	EG<CG: ankle thrust, and MSWS-12 in more affected lower extremity Post-program: ↑walking distance, ankle thrust, and speed in less affected lower extremity
Hameau et al.[34]	23 13W/10M 39/59 y/o	Intensive physiotherapy focused on gait and balance, strength and endurance	4 weeks 4 TW	-Fatigue and fatigability -Isokinetic dynamometer and MFIS -Flex and Ext knee S -Neuromuscular efficiency (EMG)	MFIS↓, fatigue ↑ immediately, but after rest = S↑ in isometric contraction as concentric EMG↑
Mañago et al.[28]	10 9W/1M 54 y/o	Isotonic and isometric strength training Ankle plantar flexors, hip abductors and trunk muscles strengthening	8 weeks Supervised and at home	-Satisfaction (Likert test) -Adherence (attendance at sessions) -Plantar flex, hip abductor, trunk musc. S Function T -Walking speed (T25FW) -Walking resistance (6MWT) -Participation (MSWS-12MS)	Satisfaction:100% Adherence: (Supervised training: 87%; at home: 75%) S ↑ in all muscles T25FWT ↑ 6MWT↑ MSWS-12MS↑
Keytsman et al.[35]	CuasiExp 16 7W/9M 52 y/o	HICT high-intensity interval cycle ergometer with strength training	12 weeks 5 TW	-Body composition -Blood pressure and resting heart rate -Oral glucose tolerance 2h. -Blood lipids -C-reactive protein	Better: resting heart rate (-6%), glucose concentration (-13%) and insulin sensitivity (24%)
Manca et al.[27]	CuasiExp 8 6W/2M 39 y/o	High intensity S training ankle dorsiflexors (less affected side) Subject, asymmetric affectation	6 weeks 3 TW	-S dorsiflexors (isokinetic dynamometer) -Gait functionality -6MWT, TUG, 10MTW, -Quality of life MS: MSQoL-54	Trained BLE (less affected) and untrained (more affected) improved similarly

HIIT: high intensity interval training, HIACT: high intensity aerobic continuous training, BBS: Berg balance scale, BDNF: brain-derived neurotrophic factor, CST: chair stand test, T: training, ECW: energy cost of walking, EDSS: Expanded Disability Status Scale, EMG: electromyography, ESES: Exercise Self-Efficacy Scale, Ext: extension, S: Strength, FSMC: fatigue scale for motor and cognitive functions, Flex: flexion, CG: control group, EG: experimental group, M: man, W: woman, LE: lower extremity, BLE: bilateral lower extremities, MVC: maximal voluntary contraction, MFIS: modified fatigue impact scale, MSIS-29v2: 29-item multiple sclerosis impact scale version 2, MSQOL-54: Multiple Sclerosis Quality of Life - 54, MSWS-12MS: 12-item multiple sclerosis walking scale, MRI: magnetic resonance imaging, S1P: sphingosine-1-phosphate, T: test, TUG: timed up and go test, T25-FW: timed 25-foot walk test, TW: times per week, 1RM: 1 repetition maximum test, 2MWT: 2 minutes walk test, 6MWT: 6 minutes walk test, 10MWT: 10 meter walk test.

In the study by Jørgensen et al.,[10] progressive resistance work was of high intensity; in turn, Wens et al.[8] compared the effects of a high-intensity continuous aerobic program versus an interval program. Other interventions were based on suspension training (TRX),[29] treadmill walking,[31] or hatha yoga.[21] All of the aforementioned conventional progressive resistance training programs contributed to a significant improvement in strength,[10,13,21] motor capacity,[21] neuromuscular activity,[10] lower limb function[13] and balance.[13,21] Through these studies it was shown that conventional strength improvement programs produce greater benefits than a yoga training program,[21] as well as participants continuing their usual activity[10,21,29] and not being sedentary.[8,13,32]

Studies on high-intensity programs analyzed their effects according to metabolic parameters (acute and chronic study of BDNF and S1P, glucose tolerance, insulin and GLUT4) and functional parameters (strength, function and neuromuscular activity of knee flexors and extensors, exercise tolerance and body composition). Wens et al.[32] observed an increase in BDNF in the intervention group in contrast to its decrease in the sedentary group, without changes in the functional parameters of strength, exercise tolerance and body composition. On the other hand, the high-intensity progressive resistance intervention by Jørgensen et al.[10] demonstrated functional improvements in neuromuscular activity and strength of knee flexors and extensors, without metabolic changes of BDNF or S1P.

Suspension training programs improved mobility, non-dominant lower limb proprioception, and knee extension strength and reflexes in both lower limbs, compared to participants who continued with their usual activity.[29]

Treadmill gait training[31] was found to be more beneficial for gait functionality, walking economy, and balance compared to a conventional strength training program.

RCTs with a combined strength training intervention

Protocols to increase strength combined with cardiovascular exercise[23] improve the concentration of inflammatory mediators and immunoregulatory markers, but do not modify cortisol and DHEA levels. Those combined with self-guided physical activity[11] improve walking performance and neuromuscular function. The combination of progressive resistance strength training with neuromuscular electrostimulation[30] provides greater benefits in the strength of hip extensors and knee flexors and in gait functionality, compared to resistance strength training without such stimulation.

Quasi-experimental with two intervention groups

Quasi-experimental studies present two types of design, those that have two intervention groups and those that only include one. Those with two groups assigned participants according to their place of residence, the degree of impairment according to the Expanded Disability Status Scale (EDSS), or depending on whether they were healthy subjects or subjects with MS. The study by Patrocinio de Oliveira et al.,[9] which divided its participants according to place of residence, applied an eccentric strength training program to one group and a resistance strength training program with increases in workload to the other, obtaining the same results after the two interventions.

The study that divided its participants according to the level of affectation -- in the first group the most affected, G1: EDSS 0-3, and in the second, the least affected, G2: EDSS 3.5-5 -- applied a combined program of high-intensity strength training together with weight-resistance strength training, obtaining an improvement in MaxO2 consumption, max. tolerated, isokinetic strength of quadriceps and hamstrings, and quality of life, with no differences between groups. The study by Heine et al.[12] applied a strength training program combined with walking in a group of healthy subjects and another of subjects with MS. After the program, walking distance, ankle thrust, and speed increased in the less affected inferior limb.

Quasi-experimental with a single intervention group

The 4 studies that had a single intervention group applied intensive physiotherapy focused on gait and balance, as well as strength and resistance,[34] and obtained benefits in participation, fatigue, isometric and concentric strength, and neuromuscular function. Similarly, an isotonic and isometric strength training program was used to strengthen ankle plantar flexors, hip abductors and trunk muscles,[28] observing improvements in satisfaction, adherence, strength in all the muscles analyzed and in gait functionality. The other two studies applied high-intensity programs. The study by Keytsman et al.[35] applied HICT (high-intensity interval cycle ergometer with strength training) and observed better resting heart rate, decreased glucose concentration, and better insulin sensitivity. Manca et al.[27] performed a contralateral ankle dorsiflexor training on the less affected side, and obtained similar improvements, both in trained (less affected) and untrained (more affected) lower limbs.

In general, most of the studies analyzed use the combined method of strength training. Starting from the theoretical basis that an individual strength intervention produces physical-functional improvements,[15,16,37,38] combined methods are based on a multiperspective attention and multiple and simultaneous action of strength, gait, resistance, balance and proprioception, in order to achieve a comprehensive improvement.[38] Wens et al.[8,32] asserts that combined strength and resistance training improve physical parameters, since they not only increase people's tolerance to exercise, but also the physical strength and endurance of the muscles.

Regarding intervention times, they range between 6 and 24 weeks. The most common intervention time is 12 weeks,[8,9,13,23,30,33,35] followed by those that use a time of 8 weeks[21,28,29,31] and those of 24 weeks;[10,11,32] including Kjølhede et al.,[11] who used a follow-up period of 24 additional weeks, added to the 24 of the main intervention. Most of the studies are based on an intervention of medium-long duration, with the aim of increasing adherence to training and reducing reversibility effects. Likewise, Wens et al.[8,32] affirm that a longer intervention over time has greater effects at a physical-functional and physiological level, while Moghadasi et al.[29] point out the need to include the evolution in long-term studies and protocols, justifying it with the causes listed in previous lines. In contrast, Hosseini et al.[21] state that, despite the fact that long-term training is more beneficial, short-term training also produces positive results.

Concerning the muscles to be treated, most studies focus on the upper, lower limb and trunk,[8,10,11,13,21,23,28,29,32,34,35] while the rest of studies center on the lower limb.[9,12,27,30,31,33] This is justified since focusing all efforts on a single area produce greater improvement. Additionally, the gait limitation produced by MS is important and therefore the combined use of strength, balance and resistance training is recommended. As stated by Moghadasi et al.,[29] proprioception improves balance during walking. On the other hand, Mañago et al.[28] indicate that a lower limb treatment produces a significant improvement in gait, which represents the most compromised functional activity of subjects with MS.

In view of the obtained results, both general and by protocol, a stability of the variables is identified in all the control groups analyzed, while the opposite occurs in the intervention groups. The programs based on some type of training -- resistance, strength or combined -- present changes in the pre/post intervention score, in which improvement of the extensor and flexor musculature of both the upper and lower extremities is noticeable,[9,10,12,13,21,27-30,32-34] but more recurring in the later, as it is the area of the body most trained in the different interventions. This improvement is significant in almost all studies, although to a greater extent in programs based on a combination of resistance and strength training,[8,12,23,32-34] and it derives not only on the improvement in muscle tone, but also variables such as the reduction of fatigue in the MFIS scale,[34] decrease in heart rate,[12] and other cardiorespiratory parameters, including resistance to exercise,[32,34] decrease in mean response time[32] and mobility.[12] Metabolic improvements, namely an increase in the concentration of brain-derived neurotrophic factor (BDNF)[32] or an increase in VO2 peak and lactate[33] are also observed in combined training. Finally, in the study by Decks et al.,[23] increase of cortisol, decrease of inflammatory mediators secretion, and maintenance of DHEA concentrations was confirmed.

As one of the most compromised functions in MS, gait assessment was carried out using different functional mobility tests.[12,27-29] In all of them, an improvement was observed due to the increase in muscle function, although only Mañago et al.[28] identified this vinculation, which, in the case of Heine et al.,[12] is also associated with an increase in the maximum voluntary contraction of the plantar flexors.

In regard to the evaluation of physiological factors,[8,10,23,32,35] both Wens et al.[32] and Jørgensen et al.[10] carried out a pre/post comparison of BDNF concentration, one of the most important immune cells for pathologies such as MS; these studies recommend a line of action based on the coupling of strength exercise and combined exercise, in order to increase BDNF segregation. Wens et al.[32] associated an increase in BDNF concentration to strength and endurance improvements, proposing combined exercise as a useful tool not only to for the increasing of BDNF segregation, but also for the improvement of the main risk factors and symptoms of MS. On the contrary, Jørgensen et al.[10] did not observe a significant difference in BDNF concentrations, nor suggest any association between BDNF production and the rest of the physical improvements reported in their study.

Pertaining to adherence and satisfaction with the training programs, only two of the studies, Zaenker et al.[33] and Mañago et al.[28], conducted surveys, reporting a positive response in both variables.

Kjølhede et al.[11] and Manca et al.[27] carried out a one-year follow-up of the training programs results: the former observed an initial decrease in strength and resistance improvement, mainly on the non-dominant member. Manca et al.[27] identified reversibility in all variables related to strength, mobility and functional capacity, although they remained higher than the baseline level. This reversibility, reported in a higher dregree in the second study, could be associated with the intervention period. It should be noted that the Kjølhede et al.[11] program lasted 24 weeks and the one in Manca et al.[27] of 6 weeks; according to observed data, high training adherence and a longer intervention generate greater stability over time.

Finally, this review has limitations to be considered. In the first place, the heterogeneity of the studies and analyzed variables imply that the results should be interpreted with caution, taking into account the differences according to gender and between populations, both important in multiple sclerosis research. Future analysis of the same variables, including meta-analysis, could contribute to obtain more consistent findings.

Conclusion

Most of the analyzed studies carried out a combination of strength training with other methods, obtaining physical-functional improvements such as increased strength and endurance, improved balance and functional capacity, decreased fatigue, improvement of cardiocirculatory parameters and improvement of the quality of life of people with MS. Both types of training, whether simple or combined, produced an improvement of MS symptoms. However, it is postulated that the combination of several methods is more favorable for the improvement of all variables and their persistence over time, this due to the enhancement of several functional parameters.

The implication of strength training in the regulation of neuroprotective factors has not been demonstrated, and its influence on other metabolic parameters has produced contrasting results among studies, thus future research on both subjects could be of interest.

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Declaration of interests

The authors have no conflicts of interest to declare.

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